A microbe no one has even seen could explain our origins

The cells of animals and plants are far more complex than those of bacteria. One weird microorganism could help explain how they evolved

- By Deepa Padmanaban

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Between Greenland and Norway in the mid-Atlantic ocean, 7,546ft (2300m) below the surface, there is a black and smoky region where hot water spouts up from the sea bed. This strange place is called "Loki's castle" after the shape-shifting Norse God Loki: the one Tom Hiddleston played in *The Avengers*.

Close to Loki's castle, there lives a microbe like no other on Earth.

In 2015, a team of scientists led by microbiologist Thijs Ettema of Uppsala University in Sweden reported that they had discovered a new kind of micro-organism. They found genetic traces of this single-celled microbe in sea-floor sediments 9 miles (15km) from Loki's castle.

Writing in the journal *Nature*, the team called the new microbe "Lokiarchaeota". This quickly got shortened to "Loki".

This mysterious microbe turned out to be the closest living relative of the eukaryotes, the group that includes all complex living organisms; from plants and fungi to insects and humans. That means Loki could help us understand how the eukaryotes first came into being. In other words, Loki may help explain why people – and all other complex life – exist.

Obligatory shot of Tom Hiddleston as Loki (Credit: Collection Christophel/Alamy)

Loki the god has been described as "a staggeringly complex, confusing, and ambivalent figure". The same is true of eukaryotes. How eukaryotes first evolved is a puzzle that continues to flummox scientists the world over.

> If the eukaryotes had never formed, neither would we

Until a few decades ago, biologists thought that there were essentially two kinds of life on this planet: eukaryotes and prokaryotes. While the eukaryotes include both single-celled organisms and more complex ones like mushrooms and chimpanzees, the prokaryotes are all single-celled. The most famous prokaryotes are the bacteria.

The key difference between prokaryotes and eukaryotes is the complexity of the cells. Prokaryotes are simple cells, with only a few internal structures, whereas the cells of eukaryotes are much more intricate. Eukaryotic cells also tend to be bigger, often ten times as large as prokaryotic cells.

It is the complexity of eukaryotic cells, and the resulting extra abilities, that allow them to bolt together to form multicellular organisms like us. Prokaryotes cannot do this. So if the eukaryotes had never formed, neither would we.

This straightforward split between simple and complex held sway for decades, until one scientist showed that there was more to it.

A selection of eukaryotes, from cats to trees (Credit: Robert Harding/Alamy)

In the late 1960s, American microbiologist Carl Woese decided to look at organisms' DNA sequences to figure out how they were all related.

Woese identified a gene that all organisms carry, and compared all the different versions of it. Species that had more similar versions of the gene were probably closely related. In this way he built up a family tree of all the known living organisms.

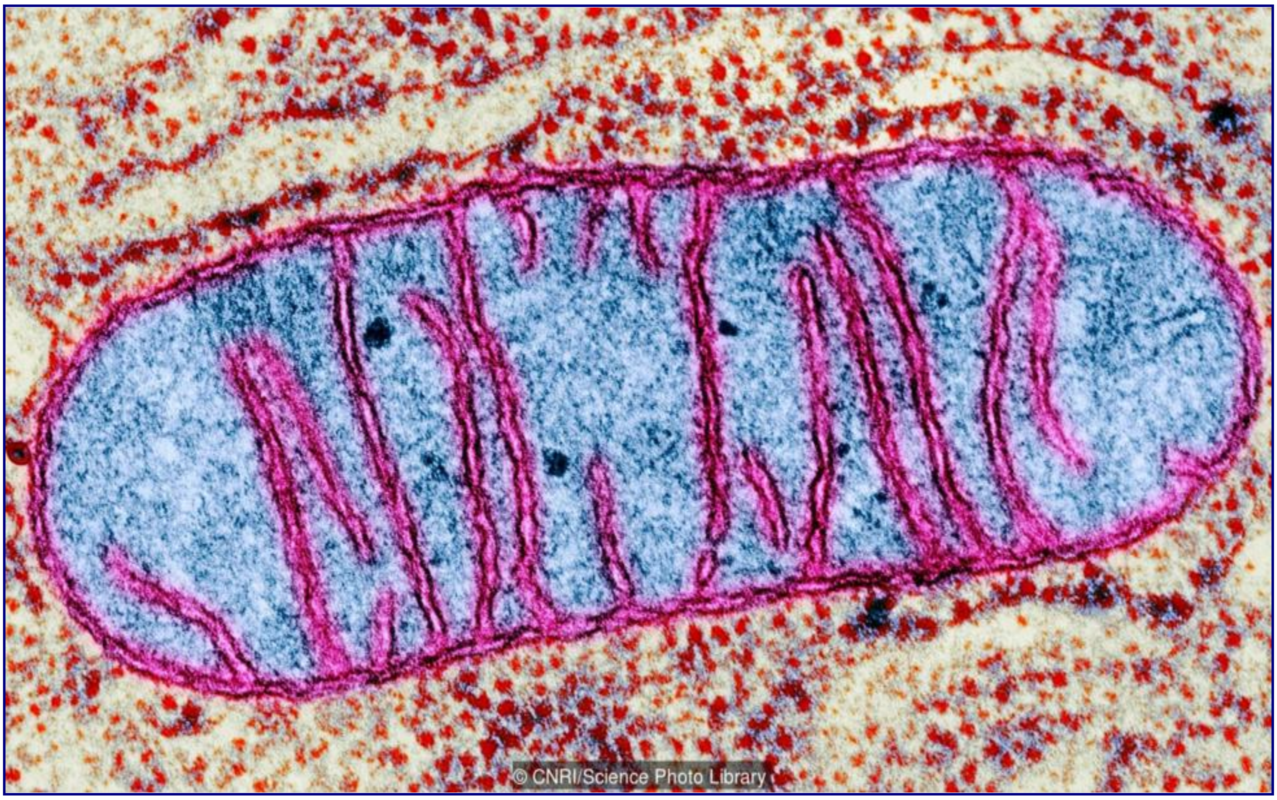
> Instead of two domains of life, there were three

Woese's analysis revealed that there were two kinds of prokaryote. As well as the bacteria, there was an entirely new group that he called "archaea".

Like the bacteria, the archaea were single-celled organisms with relatively simple cells. On the outside they looked similar to bacteria, but genetically they were clearly distinct. Archaea are found all over the world, and many of them can grow in extreme conditions such as near-boiling water.

Woese had redrawn the tree of life. Instead of two domains of life, there were three: bacteria, archaea and eukaryotes. In 1977, he published his findings in the journal *PNAS*. They were so revolutionary, Woese made the front page of the *New York Times*.

Woese's ideas would also set the stage for scientists to explain how the eukaryotes were born.



Mitochondria are the powerhouses of eukaryotic cells (Credit: CNRI/Science Photo Library)

The eukaryotes are the youngest of the three domains. While bacteria and archaea may date back over 3 billion years, the eukaryotes probably only came into existence around 2 billion years ago.

But how and why did this happen? Did the eukaryotes arise from the archaea, or from the bacteria? And why did eukaryotic cells become so big and complex, while the others stayed tiny?

> The first eukaryote must have formed when a host cell swallowed a bacterium

Perhaps the biggest clue comes from tiny structures inside eukaryotic cells called "mitochondria". These sausage-shaped objects are the cells' source of power, and without them eukaryotic cells could not grow as large as they do.

A decade before Woese published his tree of life, the biologist Lynn Margulis had begun arguing that mitochondria are descended from bacteria. Somehow these bacteria ended up inside another, larger cell, where they gradually became mitochondria. In 1978, the year after Woese's study, Margulis's idea was confirmed by experiment.

This means that the first eukaryote must have formed when a host cell swallowed a bacterium. Once that had happened, the two established a long-lasting and mutually-beneficial relationship, and the eukaryotes were on their way.

But that raises an obvious question. What was the host cell? Was it another bacterium, or an archaean?

Archaea may be the ancestors of eukaryotes like us (Credit: Steve Gschmeissner/Science Photo Library)

The simplest way to approach this question is to take a leaf out of Woese's book, and look at eukaryotes' genes. Are they more similar to those of archaea, or those of bacteria? That would give a hint about which group they are descended from.

> It's the first prokaryote which has eukaryote building blocks

This question is trickier to answer than you might expect. The typical eukaryotic genome contains a mix of bacterial and archaeal genes, as well as genes specific to eukaryotes.

However, by 2010 it was pretty clear that the host cell was an archaean.

But there was still a problem. No known archaean seemed to be equipped to be a host cell. They all lacked the genetic and cellular machinery necessary to play host to another cell.

"The discovery of Loki changed that," says Ettema.

The cells of eukaryotes are intricate (Credit: Russell Kightley/Science Photo Library)

When Loki was found in 2015, it was immediately apparent that it was an archaean. But it was an archaean that had some surprising similarities to eukaryotes.

"It's the first prokaryote which has eukaryote building blocks," says Ettema. "We found a battery of 100 genes specifically related to eukaryotes."

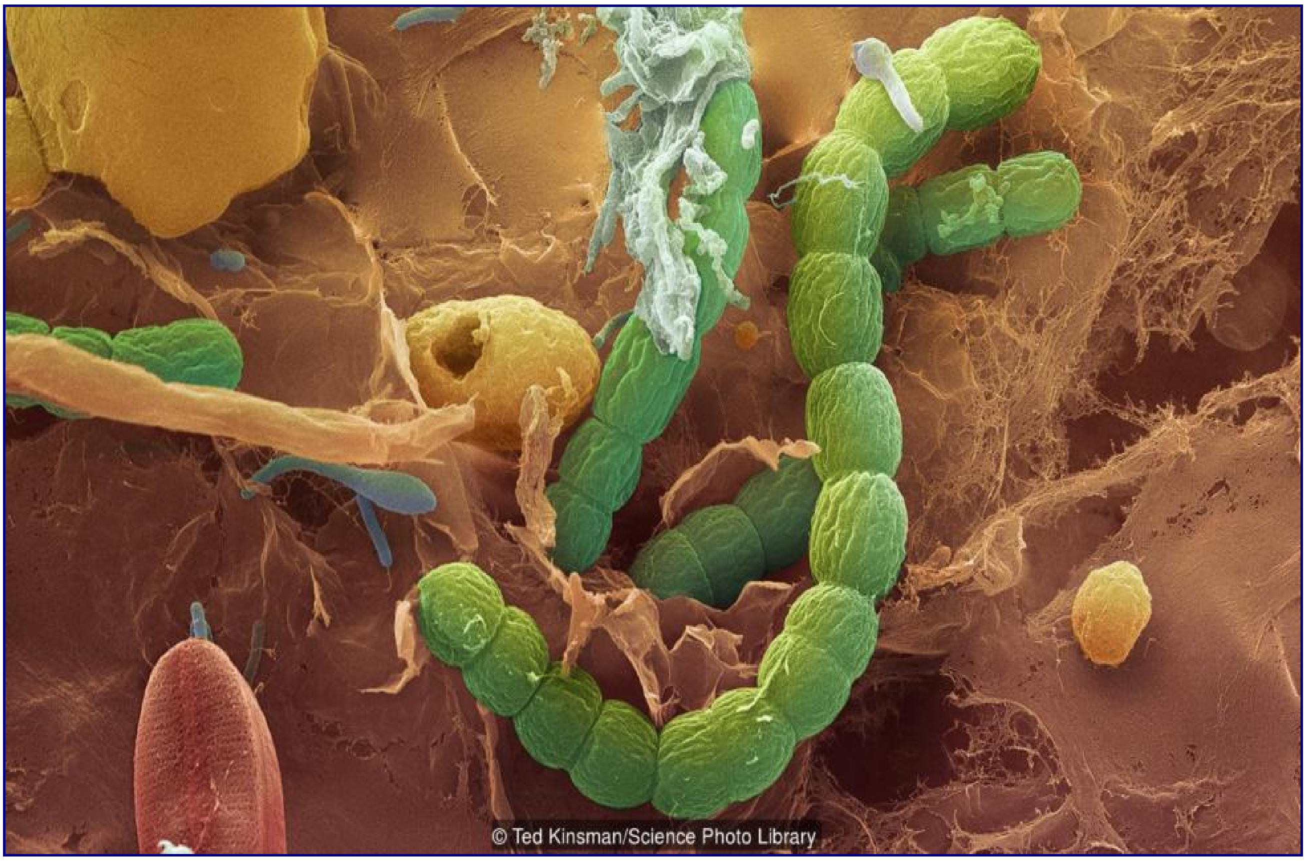
> All that Ettema's team found in the sea bed were fragments of Loki's genes. They have never actually seen Loki itself

In particular, Loki's genome carries the genes for proteins called small GTPases. These are important for the shape and movement of cells. For example, eukaryotic cells have "skeletons" that maintain their shape, and the small GTPases control the skeleton. They also regulate sets of proteins that allow membranes to bend.

The fact that Loki has these genes suggests that, like a eukaryote, it has an internal skeleton – and that it could bend its outer membrane to engulf a bacterium. That makes it a suitable host cell, or at least the closest thing we know to one.

It may be that Loki belongs to a group of archaea that almost managed to become eukaryotes, but never quite made it. Ettema jokingly calls it "a failed eukaryote".

It looks like a convincing story. But there is one big problem.



Bacteria are found almost everywhere on Earth (Credit: Ted Kinsman/Science Photo Library)

All that Ettema's team found in the sea bed were fragments of Loki's genes. They have never actually seen Loki itself, let alone cultured it in their lab.

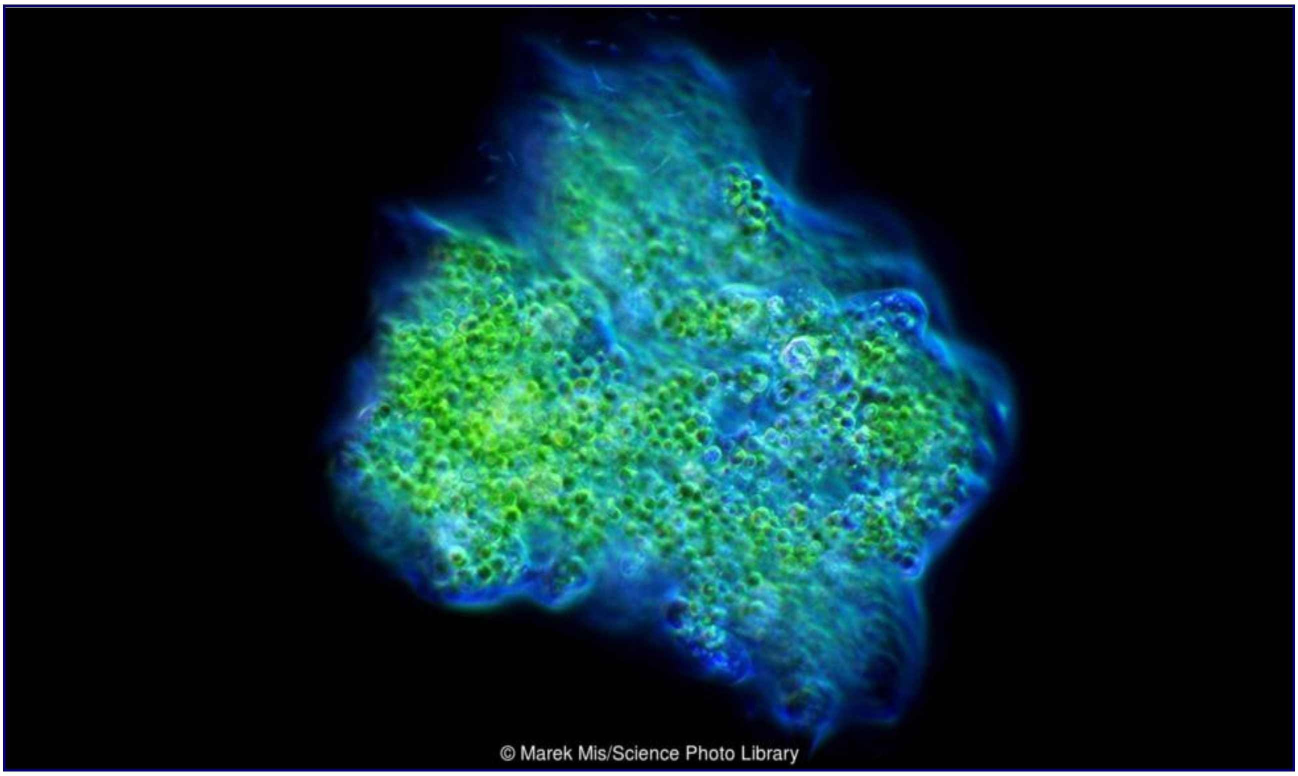
> Ettema jokingly calls it "a failed eukaryote"

So we do not know if Loki's small GTPases perform the same functions as they do in eukaryotes. The only way to find out is to study living Loki cells.

That will be difficult, even if someone manages to find some Loki cells. These microbes live in the deep sea, where nutrients are scarce and microbes grow only slowly.

Still, Ettema and his colleagues have not given up looking for Loki. As well as the deep sea, it also seems to live in shallow sediments, estuaries and hot springs.

Meanwhile, other scientists are drawing on the evidence from Loki to refine our ideas about the origin of eukaryotes.



An amoeba with algae living inside it (Credit: Marek Mis/Science Photo Library)

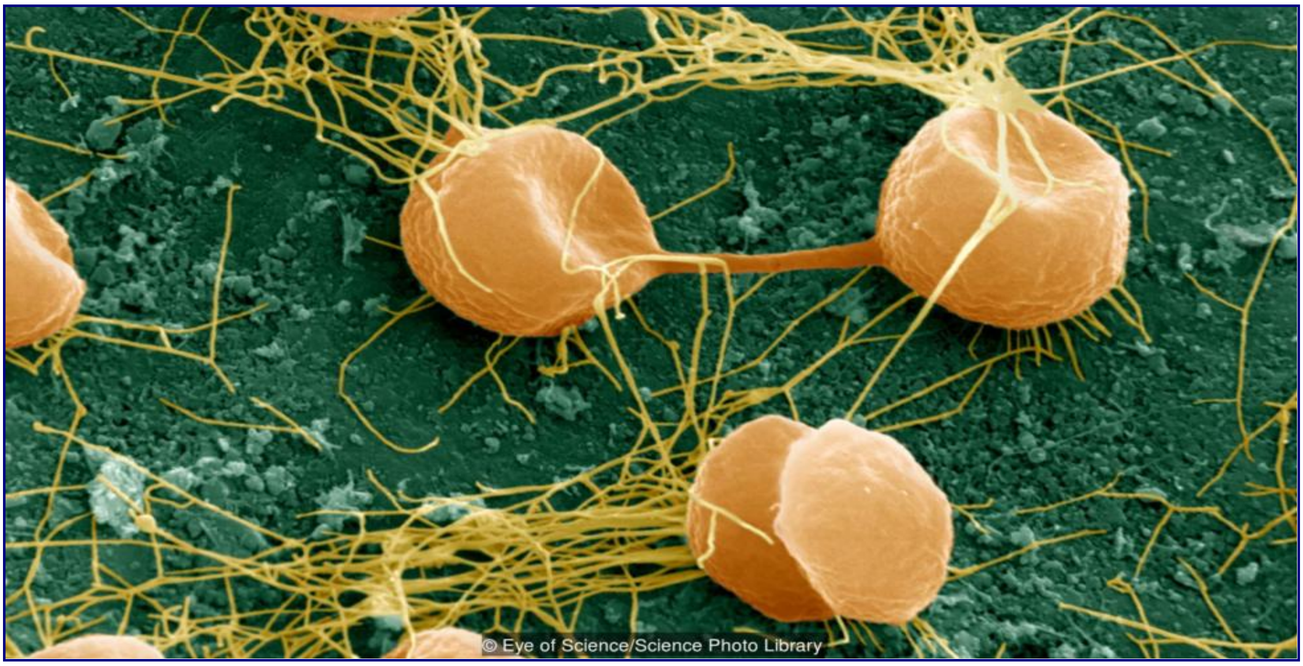
After the discovery of Loki, cell biologist Buzz Baum of University College London in the UK and his team made some suggestions about how the first eukaryotes could have evolved from simpler archaea. In a paper published in June 2016 in *Trends in Cell Biology*, they studied the eukaryote-like genes found in the Loki genome, especially the small GTPases.

> The more likely possibility is that archaea and bacteria first formed a stable partnership

In eukaryotes, GTPase proteins are involved in shuttling material across membranes inside the cell. To help with this, each GTPase carries "lipids": small fat molecules that help anchor it to the membranes. Without these lipid anchors, the GTPases would not be able to do their jobs.

The Loki genome does not have the necessary tools to add lipids to GTPase proteins. This implies that, if Loki really does show us what the ancestor of eukaryotes was like, the ancestor could not use its GTPases in this way. It would have needed to acquire the ability somehow.

Bacteria do carry plausible precursors of the lipid-adding machinery. This implies that an archaean somehow picked up the lipid modification enzymes from bacteria.



Pyrococcus furiosus, an archaean (Credit: Eye of Science/Science Photo Library)

Baum argues that this cannot have happened suddenly. If an archaean were to suddenly pick up so many new genes, its cellular processes would have been disrupted and it would probably have died.

> The linking of the two cells was anything but sudden

The more likely possibility is that archaea and bacteria first formed a stable partnership, and then gradually transferred genetic material and lipids a bit at a time. This sustained partnership could have led to the development of internal compartments and membrane trafficking.

In other words, the genesis of eukaryotes was a slow process. The dramatic "swallowing" of a bacterium, while it probably did happen, was only one step of many.

Baum also has a neat idea about how the swallowing happened.

An immune cell (green) that has "eaten" two bacteria (orange) (Credit: Dr Gopal Murti/Science Photo Library)

The classic image is an "outside-in" process, in which the archaeal host engulfed and "ate" the bacterium – but for some reason did not digest it. It is hard to see how this could have worked: if the archaean was eating a piece of food, why would it not digest it?

Ettema has found new relatives of Loki that are also closely related to eukaryotes

So in 2014, Baum and his colleague David Baum proposed an alternative that he calls the "inside-out" model. Again, this is built on the assumption that the linking of the two cells was anything but sudden.

Baum suggests that the archaeal host first extended protrusions towards the bacteria in its environment. These protrusions were not an attempt to eat the bacteria: instead, they allowed the transfer of materials between the two cells.

Eventually, the archaean formed more and more of these protrusions until they completely enveloped the bacterium. "These protrusions from a single cell then fused with each other to form a continuous outer layer," says Baum's post-doctoral fellow Gautam Dey.

For now we cannot tell if Baum's ideas are correct. But if Ettema can find more of Loki's relatives, we might get enough information to make a firm judgement.

An immune cell (purple) engulfing bacteria (pink) (Credit: Science Photo Library)

In the last few months, Ettema has found new relatives of Loki that are also closely related to eukaryotes. The work is still in the early stages, but he says these other archaea also possess some of the building blocks of eukaryotes.

> For now we cannot tell if Baum's ideas are correct

We do not yet know what these strange microorganisms will teach us about the origin of eukaryotes.

Ettema says the puzzle is still being put together piecemeal. When Loki or something similar is finally isolated, we should be able to find out how it makes a living and what it uses its eukaryote-like proteins for.

And that, in turn, will tell us about the microorganism that ultimately gave birth to all of us.