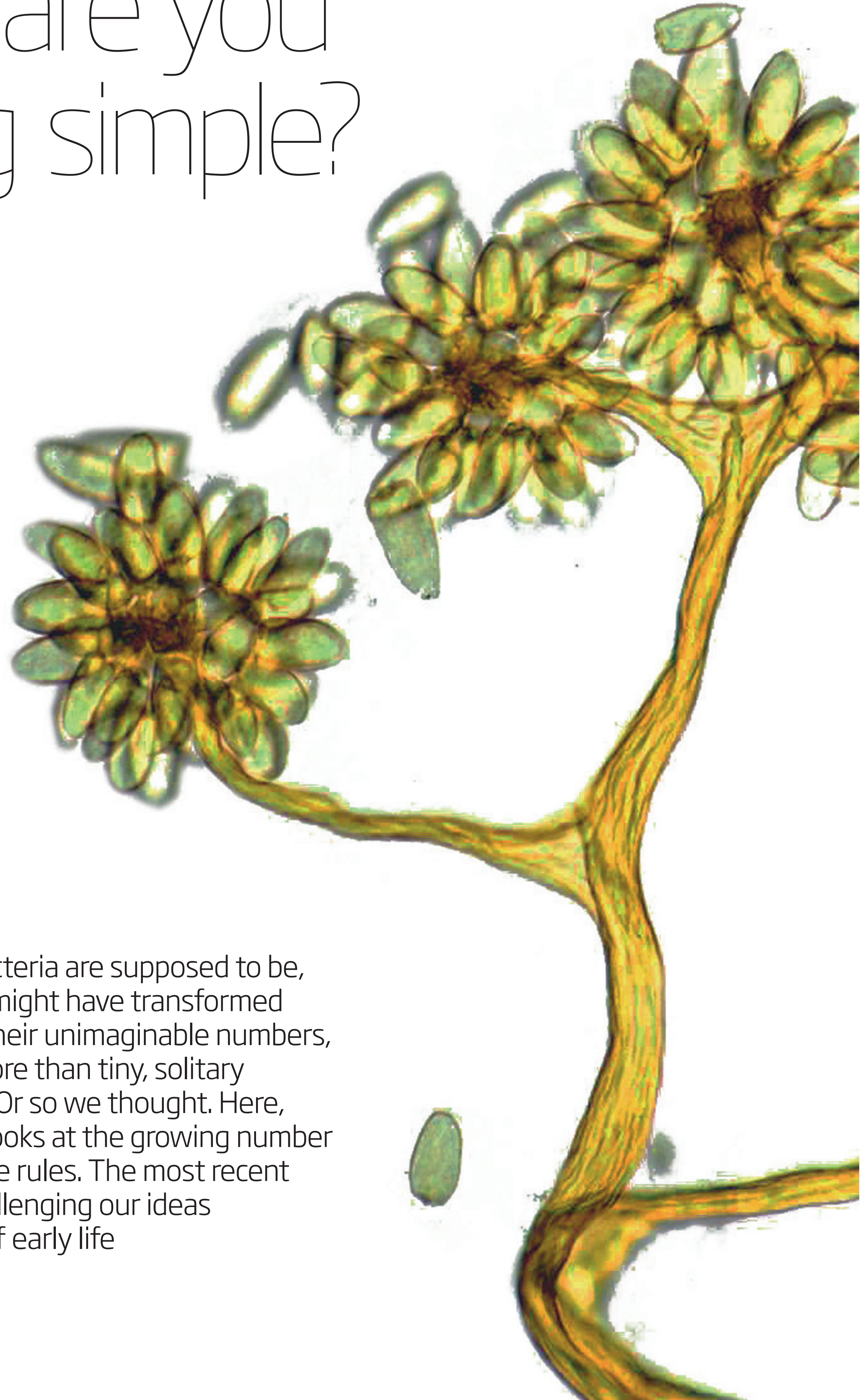
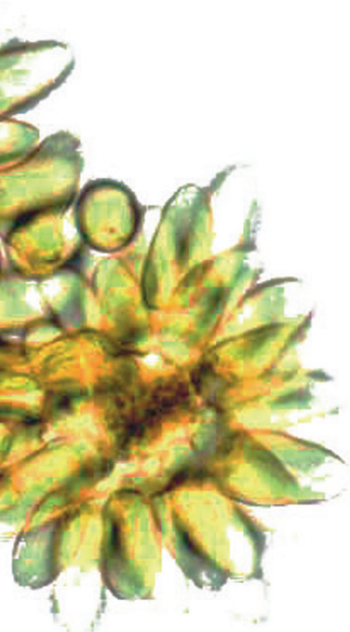
Who are you calling simple?



Simple cells like bacteria are supposed to be, well, simple. They might have transformed Earth because of their unimaginable numbers, but they're little more than tiny, solitary bags of chemicals. Or so we thought. Here, **Caroline Williams** looks at the growing number of exceptions to the rules. The most recent discoveries are challenging our ideas about the nature of early life



1 They're not just bags of chemicals

Complex cells like the ones that make our bodies can form all kinds of different shapes even though they are enclosed only by a soft membrane. The secret is their internal skeleton, or cytoskeleton, a scaffold that is continually adjusted by adding or taking away segments. It not only maintains a cell's shape, it even functions as a railway for transporting molecules around the cell and also ensures everything ends up in the right place when cells divide.

It was long assumed that bacteria, which are surrounded by a thick, rigid wall, have no need of such a sophisticated piece of kit. But in recent years it has emerged that many bacteria and archaea – the other branch of simple cells – have their own versions of the proteins that form the cytoskeleton.

In at least some bacteria these proteins form a cytoskeleton that does much the same job as in complex cells, such as maintaining the rod shape of cells like *E. coli*. The cytoskeleton also helps anchor structures such as the whip-like flagella that some bacteria use to swim. And in magnetotactic bacteria, cytoskeletal proteins keep the magnetic particles inside them aligned, allowing the entire cell to act as a living compass needle.

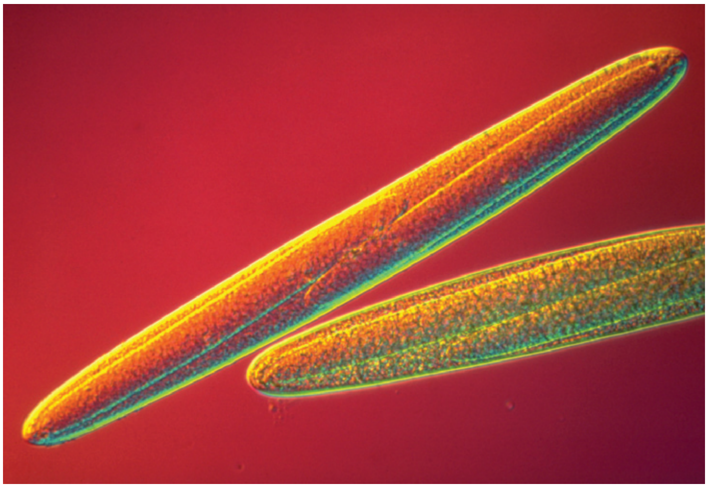
GEORGE BARRON

2 Many have internal compartments

According to the textbooks, only complex cells have internal compartments, or organelles, but numerous exceptions to this rule are being discovered. For instance, a quarter of the bacteria that have had their genomes sequenced have the genes for making "microcompartments" – tiny chemical factories that speed up reactions by concentrating the reactants and also help protect the rest of the cells from toxic by-products. The first to be discovered were the carboxysomes of cyanobacteria, which boost the efficiency of photosynthesis.

Other bacteria have internal stores rather than factories. Photosynthetic bacteria and archaea often have little internal bubbles, called gas vesicles, to make them buoyant.

The "organelles" within bacteria are usually made of proteins and have regular geometrical shapes, like the shells of viruses. However, a few do have membrane-bound compartments like those of complex cells. Several sulphur-eating bacteria store nitrate in internal vacuoles, for instance, including *Thiomargarita namibiensis.* ›



ESTHER ANGERT/CORNELL UNIVERSITY

3 They are not always small

If you know nothing else about bacteria you'll know this: they are minuscule, far too small to be seen with the naked eye. There are good reasons for this. The complex cells of plants and animals have sophisticated internal transport systems for moving molecules around. By contrast, bacteria rely mainly on diffusion to move things around the cell. Since diffusion only works well over distances of up to a few millionths of a metre, bacteria cannot grow too big.

Yet a handful of species do grow very large. In fact, at least three are so large that they can be seen without a microscope. The first giant was discovered in 1985 but because of its size was not recognised as a bacterium until eight years later. This rod-shaped bacterium, *Epulopiscium fishelsoni* (pictured above), lives in the gut of surgeon fish in the Red Sea and is up to 0.7 millimetres long, hundreds of times longer than the *E. coli* in our guts, which is around 0.002 millimetres long.

E. fishelsoni busts the "maximum" size limit by having tens to hundreds of thousands of copies of its DNA. This means it can produce proteins in many different places in its cell, so the proteins need only diffuse a short distance to get to where they are needed. Recent calculations show the ratio of DNA to volume is actually the same as for a normal-sized bacterium.

E. fishelsoni held onto its title as the biggest bacterium until 1997, when *Thiomargarita namibiensis* came along (*Science*, vol 284, p 493). *T. namibiensis*, which means "sulphur pearl of Namibia" for the shimmering sulphur granules inside it, is up to 0.75 millimetres across. It relies on the same trick as *E. fishelsoni*, with thousands of copies of its DNA. While it has a volume up to 100 times greater than *E. fishelsoni*, most of this space is used for storage: up to 98 per cent of the cell is taken up by an enormous membrane-bound sac, or vacuole. This contains up to three months supply of nitrate, which it uses to oxidise the hydrogen sulphide it feeds on. The store is needed because the supply of nitrate to its sea-floor home is patchy, depending on dead animal material falling from above.

An almost identical sulphur bacterium which, at 0.5 millimetres across, is also visible to the naked eye, was discovered in Mexico in 2002. There are probably more gargantuan bacteria out there waiting to be found.

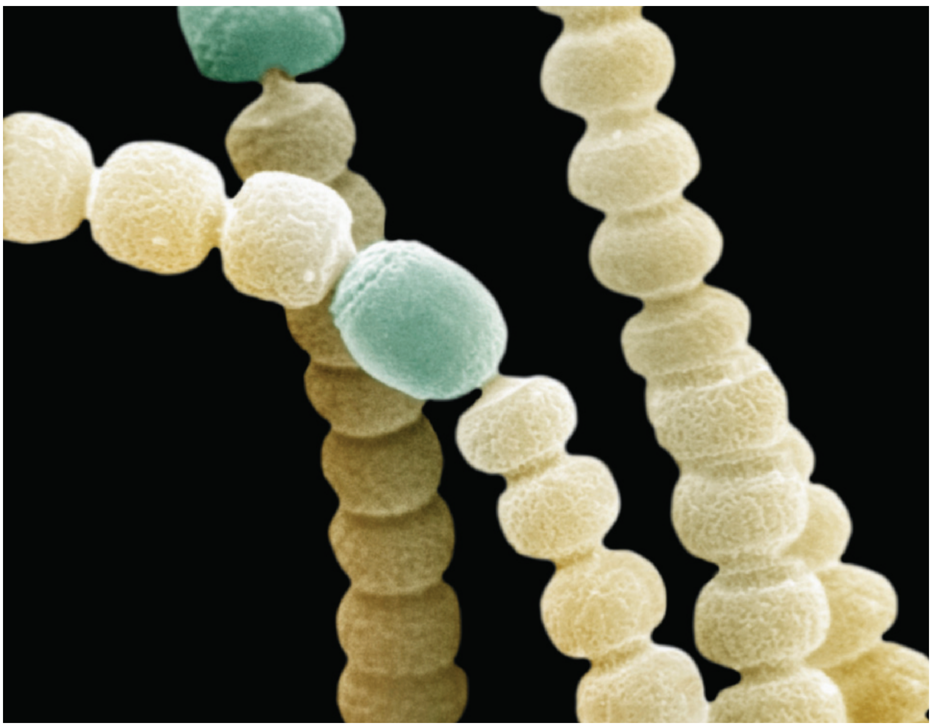
4 They work together

It has long been known that bacteria communicate with each other by releasing chemical signals. Among other things, these signals allow bacteria to sense how many of their kind are nearby and launch collective action once their numbers are great enough – a strategy called quorum sensing.

Bioluminescent marine bacteria sometimes use quorum sensing to ensure that they only produce luminescent chemicals when there are enough of them to ensure a worthwhile amount of light is produced, such as the *Photobacterium fischeri* that provide light for their fish or squid hosts.

Slime bacteria called *Myxococcus xanthus* hunt in packs like wolves, swimming together in huge swarms and rippling back and forth over their bacterial prey, releasing enzymes to break it down. Collectively, they can tackle much larger prey than they could alone – much the same reason that real wolves pool their hunting efforts.

It seems that even bacteria of different species are capable of extremely close cooperation. In a recent study, two species of *Geobacter* were grown in a medium containing ethanol and sodium fumarate. One of them, *G. metallireducens*, can break down ethanol, but in this medium it had no way of getting rid of the excess electrons this produces. *G. sulfurreducens*, on the other hand, can offload electrons onto sodium



RICHARD KESSEL & GENE SHIH/VISUALS UNLIMITED/SPL fumarate, but cannot break down ethanol. In theory both species should have perished, but instead they thrived. It turned out that they had grown a network of tiny "nanowires" connecting them into an electron-conducting grid that enabled them to pool their talents. Some biologists think such networks are common in soils and ocean sediments.

5 Some are multicellular

OK, so bacteria can be more socially complex than we thought. At least we can count on them being only single-celled. Or can we? When food is scarce, slime bacteria come together to form fruiting bodies that produce spores. Their height gives the spores a better chance of finding fresh pastures to exploit than if individual bacteria turned directly into spores.

Fruiting bodies can be simple mounds of cells, all of which then turn into spores. Others, like that of *Stigmatella aurantiaca* (pictured on page 38), are more complex branching structures in which some cells form the support structure and only some get to form spores. This kind of division of labour is one of the hallmarks of multicellularity.

Some biologists refer to this as multicellular behaviour rather than true multicellularity, because normal growth occurs when the cells are separate. However, cyanobacteria in the genera *Anabaena* (pictured left) and *Nostoc* tick all the boxes. When nitrogen is low, about 1 in 10 of these bacteria, which grow in long filaments of cells, specialise in fixing nitrogen. Once the cells have changed from a normal cell to a nitrogen-fixing one there is no going back and they become totally dependent on the other cells for energy. In turn, these cells depend on them for nitrogen.

Such examples were thought to be exceptional, but multicellular traits are turning out to be widespread. The biofilms formed by many bacteria, for instance, are not mere piles of cells but organised structures. There is even some evidence of cells taking on different roles within them.

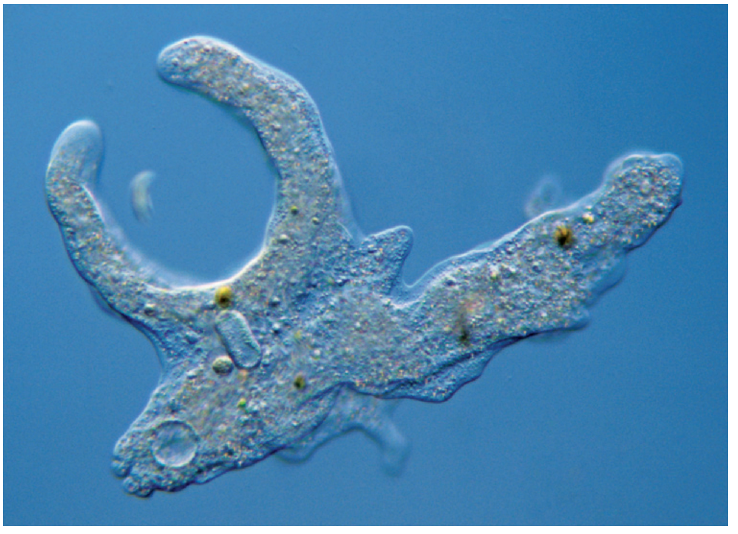
Perhaps the biggest surprise is the discovery that many bacterial cells commit suicide. In plants and animals, programmed cell death is vital – it is what separates our fetal fingers as we grow, for instance, and cells infected by viruses try to kill themselves stop the virus replicating. Programmed cell death appears to play similar roles in bacteria, too. It helps form the structure of some fruiting bodies and biofilms, and is also used to stop viruses spreading. In other words, many bacteria sacrifice themselves for the greater good.

6 A few have a nucleus

The defining characteristic of simple cells, or prokaryotes, is supposed to be the fact that their DNA floats freely in the cell rather than being enclosed in a nucleus. Indeed, the term "prokaryote" means "before nucleus".

Then, in 1991, John Fuerst and Richard Webb of the University of Queensland in Brisbane, Australia, noticed something strange about *Gemmata obscuriglobus*, a bacterium first described in 1984. It seemed to have "packaged" DNA. Images taken with an electron microscope confirmed that not only was its DNA separate from the rest of the cell, it was enclosed by a double membrane – just like the membrane envelope surrounding the nucleus of complex cells.

So is *G. obscuriglobus*, along with other members of the Planctomycete group to which it belongs, really a prokaryote? Its nucleus, such as it is, is not nearly as sophisticated as that of complex cells, and genetically it is very much like other bacteria. So many biologists were inclined to treat its "nucleus" as a curiosity unrelated to that of complex cells – until this bacterium was found to have another extraordinary trait...



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7 They can swallow

Complex cells like amoebae (pictured above) and white blood cells can "swallow" large particles by engulfing them and pinching off the "bubble" containing the particle, a process called endocytosis. Bacteria were only thought to be able to take in particles via channels in their cell membrane, through which only small particles can fit. But last year, a team led by Fuerst showed that the bacterium with a "nucleus", *G. obscuriglobus*, swallows large particles in a manner akin to endocytosis (*Proceedings of the National Academy of Sciences*, vol 107, p 12883).

To have one trait possessed by complex cells – membrane-bound DNA – could be a coincidence. To have two seems unlikely. What's more, most members of the larger group that *G. obscuriglobus* belongs to, the Planctomycetes-Verrucomicrobia-Chlamydiae or PVC group, have proteins that are very similar to those that control endocytosis in eukaryotes. The big question is whether this is a case of parallel evolution, or whether complex cells and bacteria shared a common ancestor capable of endocytosis.

If there was a common ancestor, the implications are huge. It means the shared ancestor – known as the last universal common ancestor, or LUCA – and its contemporaries must have been much more complex than they have always been assumed to be. Since the ability of PVC bacteria to form membranes around their nucleus involves many of the same proteins as endocytosis, it is even possible that LUCA had a membrane-bound nucleus too. This would turn our picture of how life evolved on its head. Rather than being "primitive" cells, modern bacteria may be streamlined, simplified versions of a more complex ancestor – perhaps not so much prokaryotes as "post-karyotes". ■

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