# Microscopical Substantiation of Intelligence in Living Cells

*Brian J Ford*

**We pride ourselves, as humans, on our intelligence. It is often construed as a characteristic specifically exhibited by our species above all others, though there are examples of intelligent behaviour in other life-forms that can be cited. A recent book bears the bold title 'Animal Intelligence' (Reznikova, 2007). It considers intelligent behaviour, not only mammals and birds, but even in invertebrates. The examples described show remarkable abilities in many forms of animal life that allow them to adapt to difficult situations, to take extraordinarily complex decisions, and to adapt to changing circumstances.**

In this paper I propose that this problem-solving propensity, define it how you will, is evident even in single cells. Rather than being the lowly building-blocks of higher and more illustrious forms of life, I postulate that cells embody the fundamental properties of intelligence. The manifestation of mental ability in more highly evolved organisms is not a feature that emerges from their complexity; rather, it is inherent in each cell. The community harnesses and amplifies this ability, but only because it is a property of the single cells of which these life-forms are comprised.

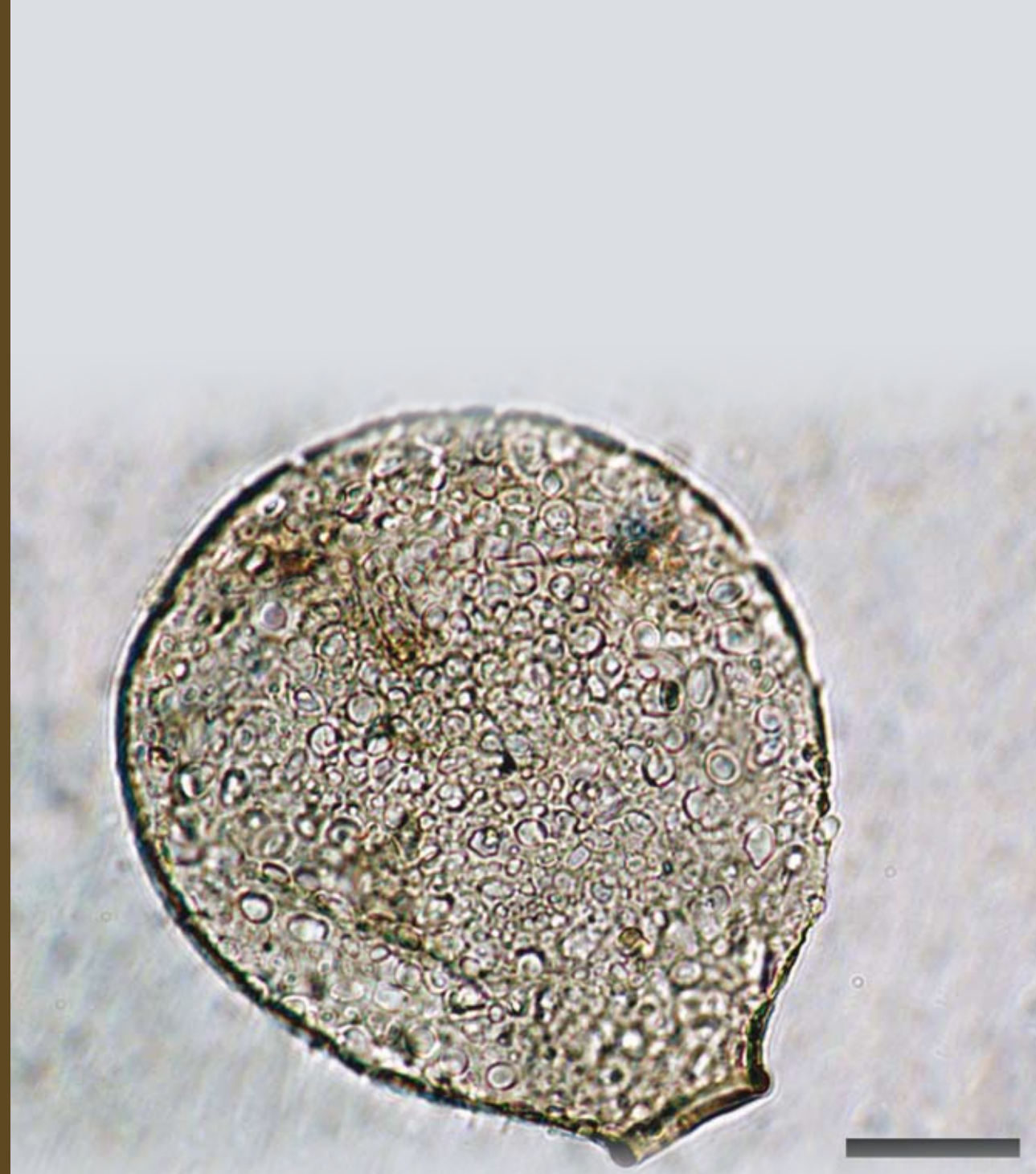

*Fig. 1. The testate amoeba Nebela produces a delicate, spheroidal shell that protects the cell. Scale bar 25 µm.*

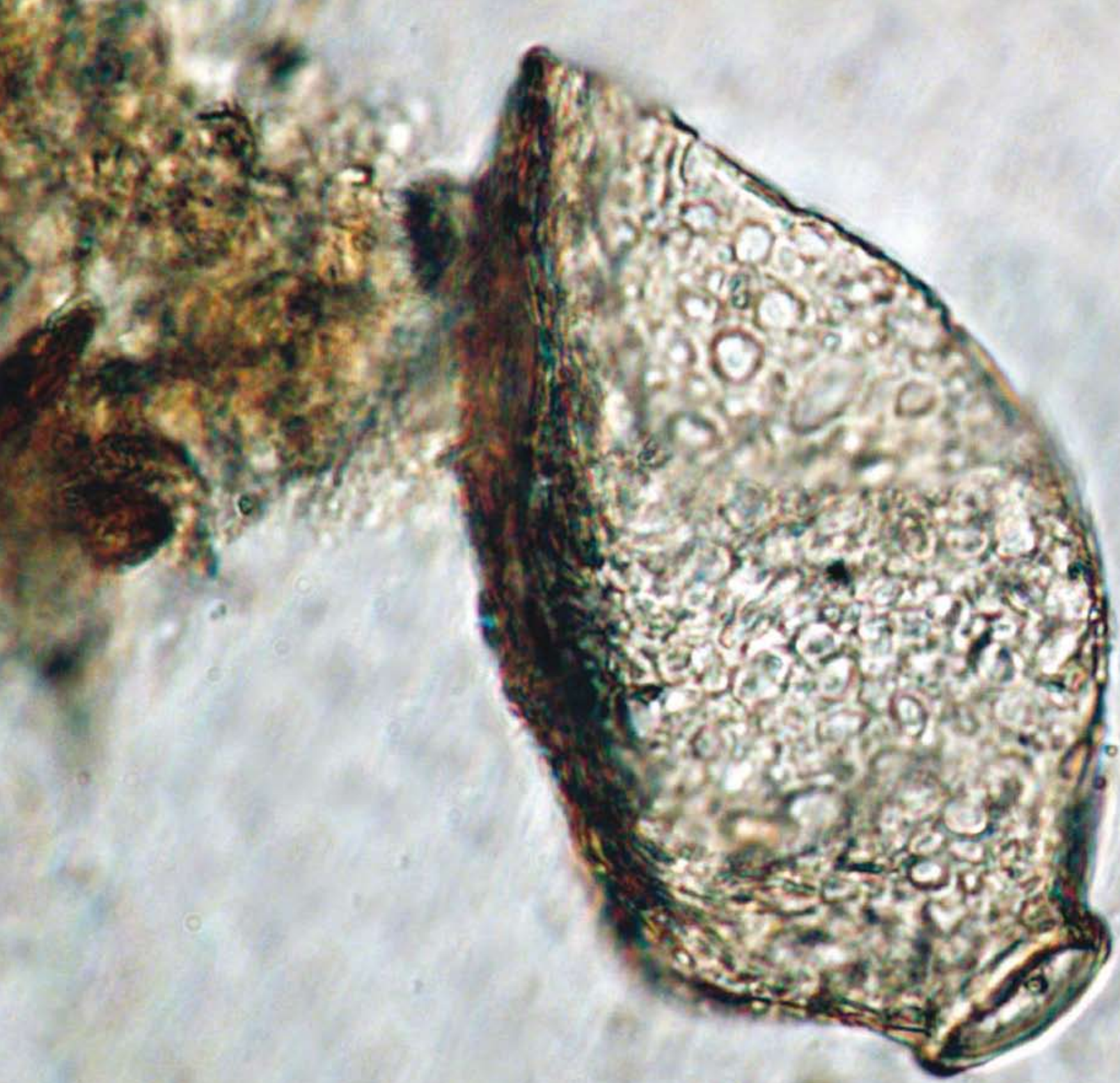

*Fig.2. In oblique view, the flattened contour of the test can be clearly seen. It is not symmetrical. Scale bar 50 µm.*

*My interests centre, not on the minutiae within a living cell, but how cells behave, how they respond and adapt – and what they look like.*

## Concepts of Single Cells

It is a paradox that, even though we live in an era where the biosciences are evident everywhere, the public wouldn't recognise a living cell if they saw one (Ford, 1975). Worse, many bioscientists wouldn't either. We are adept at reductionism: peering ever deeper within the mechanisms of cellular chemistry and trying to define genetics, until few biologists ever look at what living cells do. My interests centre, not on the minutiae within a living cell, but how cells behave, how they respond and adapt – and what they look like.

The eminent computer games developer Will Wright has produced a new game called 'Spore' (Geere, 2008). He recently said in a lecture on YouTube "I actually realise that cells don't have eyes, but, ah, it helps to make it cute." Cells don't have eyes? There has been no chorus of protestation, yet the number of cells that have eyes comprising concave retinas and refractile lenses is legion. They have been known for over a century.

Whether it is biological control in the greenhouse, new infectious agents threatening us with epidemics, home brewing, storing food, following modern medicine or making cheese, our interaction with microscopic living cells is multi-faceted and continual. There is no aspect of modern life with which we are more intimately concerned, so it's surprising that few people have the least idea what a living cell looks like through the microscope. That includes scientists. Search for "living cell" on Google images, and most of the examples are EM studies, models or computer graphics. Living they are not.

Unicellular organisms are seen as lowly, basic, fundamental structures. They are viewed almost as nanobots – indeed, those who are developing minute robotic devices in the field of nanotechnology confidently claim that their inventions can carry out manipulations that improve on what living cells can do. A report in *USA Today* (Cowen, 2005) reports a NASA scientist who said their nanobots had 'enough artificial intelligence to make smart decisions as well as know intuitively when and how to walk and swarm.' Single cells, of course, do this already; and do it better. They also reproduce themselves and are powered by the release of solar energy. They show remarkable powers of repair and regeneration, and these qualities remind us of the fatuity of claiming that digital, human-made devices can be thought of as showing 'artificial intelligence'.

There is a fascinating book entitled *Cell Intelligence, the Cause of Evolution* (Quevli, 1916). I found it while browsing through a dark, neglected corner of Cambridge University Library. Just as you did, I imagined that it had already made the same connection – but this isn't the case. The author's view is: 'The designers and builders of plants and animals were to us spiritual beings because we could not see them. In the same way the designers and builders of skyscrapers and battleships would be spiritual beings to us if we could not get near enough to the structures to see the builders.' Quevli sees these structures as built by smaller, clever beings. That's wrong. The smaller beings *comprise* the structures; they do not simply make them. It is not to a skyscraper we should look to discover the makers, if we want an analogy. Instead, we should look to the spectacular choreography of the Beijing Olympics. Here we have an example of an entire display acting almost as an 'organism'. The individuals play their separate parts, and give rise to the whole spectacle.

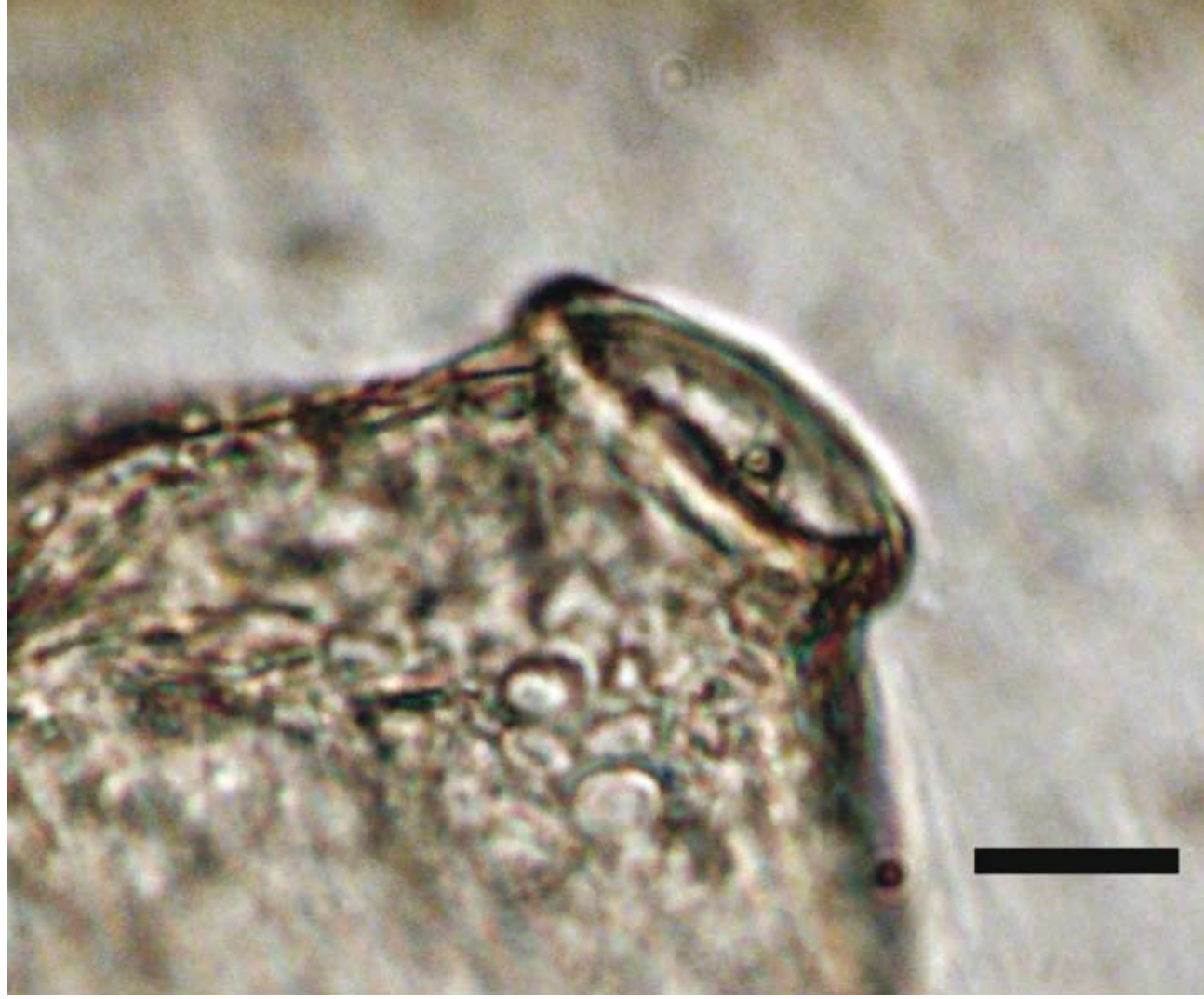

*Fig.3. Under high power we can observe the finely-formed neck of the flask-like test of Nebela collaris. Scale bar 20 µm.*

The question we now raise is – how ingenious are the components, when these components are single cells?

## Ingenuity in Animals

We do not have to look far to find examples of ingenuity shown by living cells (Ford, 2006). The testate amoebae (Ogden & Hedley, 1980) offer revealing examples. These protists construct mineral shells that protect the cell body. Descriptions describe them as 'constructing a shell' without stopping to consider what this means. Could it be that the cells secrete an adhesive to which granules adhere as the amoeba moves about? This is clearly not a viable explanation, since the testate amoebae tend to show selectivity over what they use as building blocks. Some use silica sand grains, others use centric diatom frustules – and they clearly are discriminating about what they use.

At school, we showed admiration for the larva of the caddis-fly as it painstakingly built for itself a cylindrical home out of detritus from the pond. It seems miraculous that a lowly insect larva can exhibit such a degree of coordination. No two larvae build identical homes; as they locate the building materials they want, they have to pull them closer, hold them in place and cement them together. Each larva is adapting its skills to meet the contingency of what it can find. It seems a task of immense complexity for such a lowly creature.

*Fig.4. Refractile sand grains are crudely cemented together by Difflugia laceolata, producing a spearhead-shaped test. Scale bar 25 µm.*

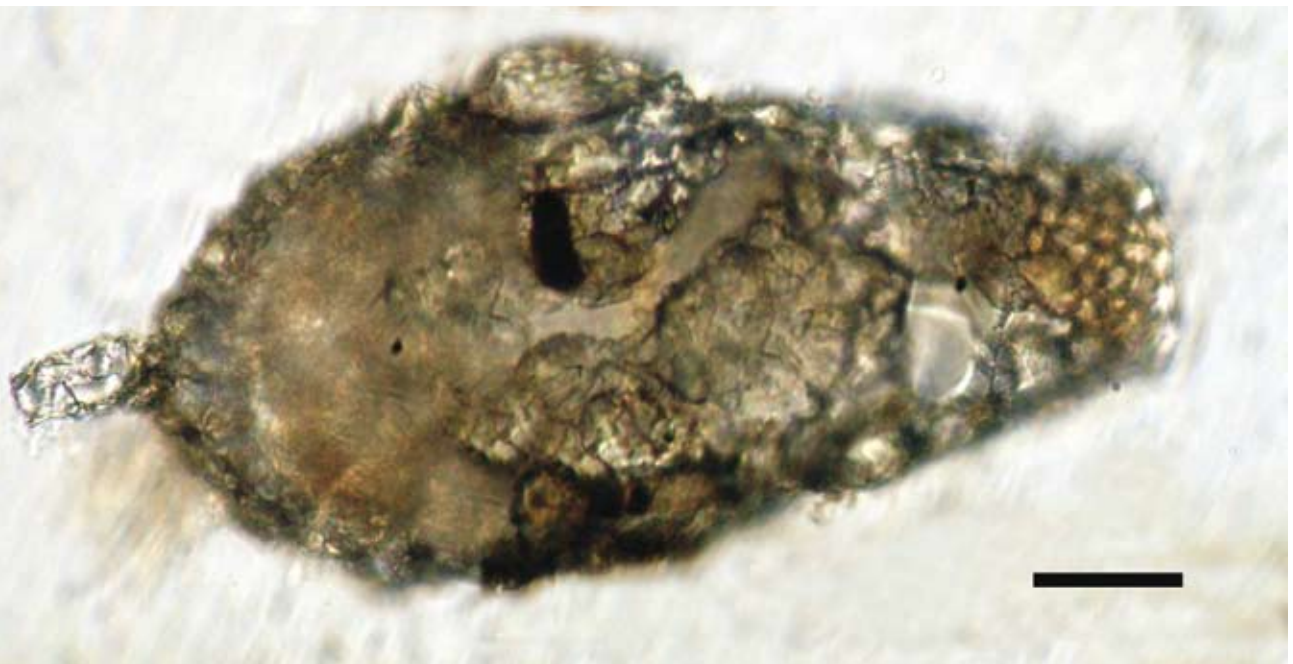

*Fig.5. In Difflugia acuminate we can observe gradation of the sand grains – largest near the middle, smaller towards the apices. Scale bar 50 µm.*

*Fig.6. High-power microscopy reveals the apical spine of D. acuminate to be carefully assembled from minute sand-grains. Scale bar 10 µm.*

Yet the larva has a brain, eyes, muscles; limbs and appendages, sensory systems of great complexity, cement glands, and jaws. Given these, the rough home that the larva constructs is relatively crude. Yet compare this with the testa that amoebae can construct. These are delicate and perfectly proportioned. If you made one like this in evening classes I'd be impressed. Yet an amoeba lacks the organs possessed by the caddis-fly grub. We know of no cement organelles, no systems for assembly, no grasping limbs or sensory mechanisms by which the amoeba could detect its raw materials – let alone position them so precisely. And where, do we suppose, is its template?

Silica is a common component of the shells. Sometimes we believe that they secrete the material themselves. Others collect siliceous material (such as the species which construct their homes from diatom frustules). In some genera, like *Euglypha*, the ovoid cells are between 50-100 µm across and become covered with transparent plates. *Nebela collaris* is larger (between 100-175 µm) and produces a rounded neck to the flask-like mineral shell. In many genera, the flask is lopsided, and not radially symmetrical. Less delicate and precise is the sand-grain shell constructed by *Difflugia* spp. Here the refractile grains are more roughly combined together – yet the notion that the template is crude or random cannot be sustained, for these organisms can construct a distinct spine at the apex of the shell. Many drawings of *Difflugia* show the grains to be roughly isodiametric throughout the shell. There is a fine illustration of this sort by Stuart Hedley (Patterson, 2003) that is meticulously well drawn – apart from one crucial detail. As I showed in an earlier though less well-drawn study (Ford, 1976) the size of the sand grains is not equivalent around the whole shell. Progressively smaller grains are used around the opening of the shell. Such discriminatory power is astonishing in a single-celled organism.

For an amoeba gathering granular building materials from the muddy surfaces, no two situations are ever identical, and these single-celled

*Fig.7. At the commencement of observations, this Derbesia tenuissima gametophyte has been punctured with a steel needle. Scale bar 1 mm.*

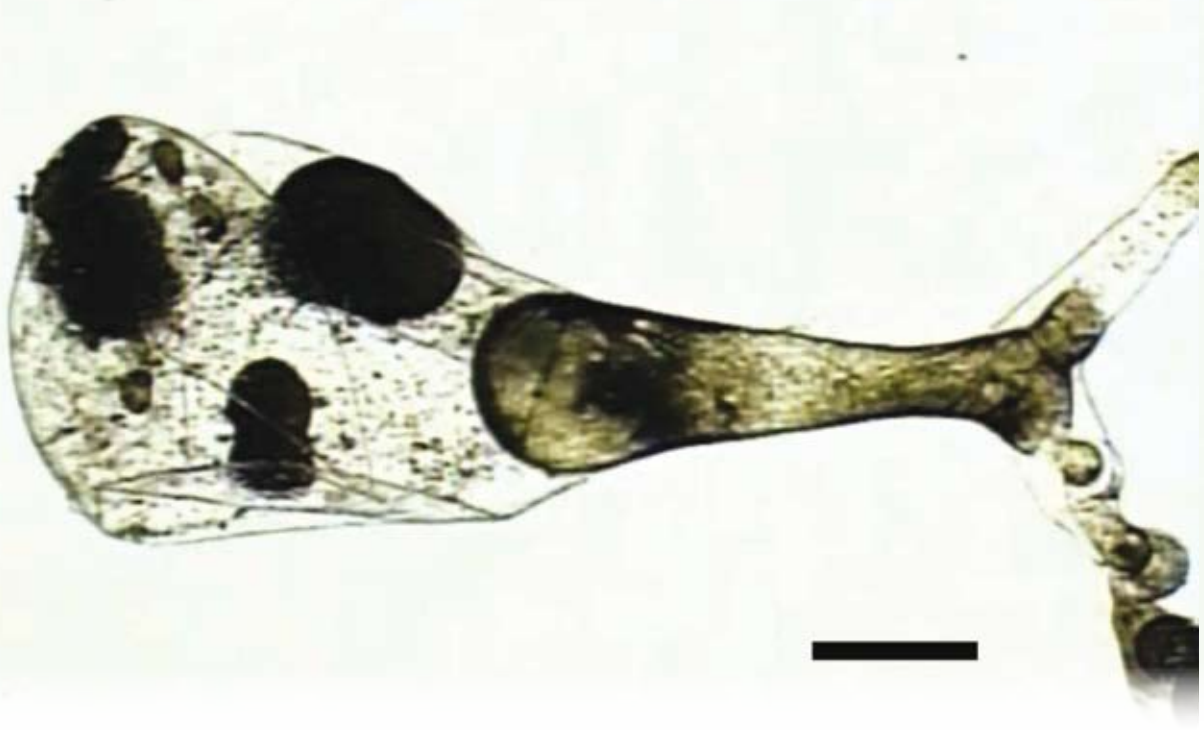

*Fig.8. The gametophyte of Derbesia was originally identified as a separate genus, Halicystis. Cytoplasm soon re-enters the cell. Scale bar 1 mm.*

*Fig.9. Over several hours, the cytoplasm continues to expand. Time-lapse suggests two-way communication with the parent plant. Scale bar 1 mm.*

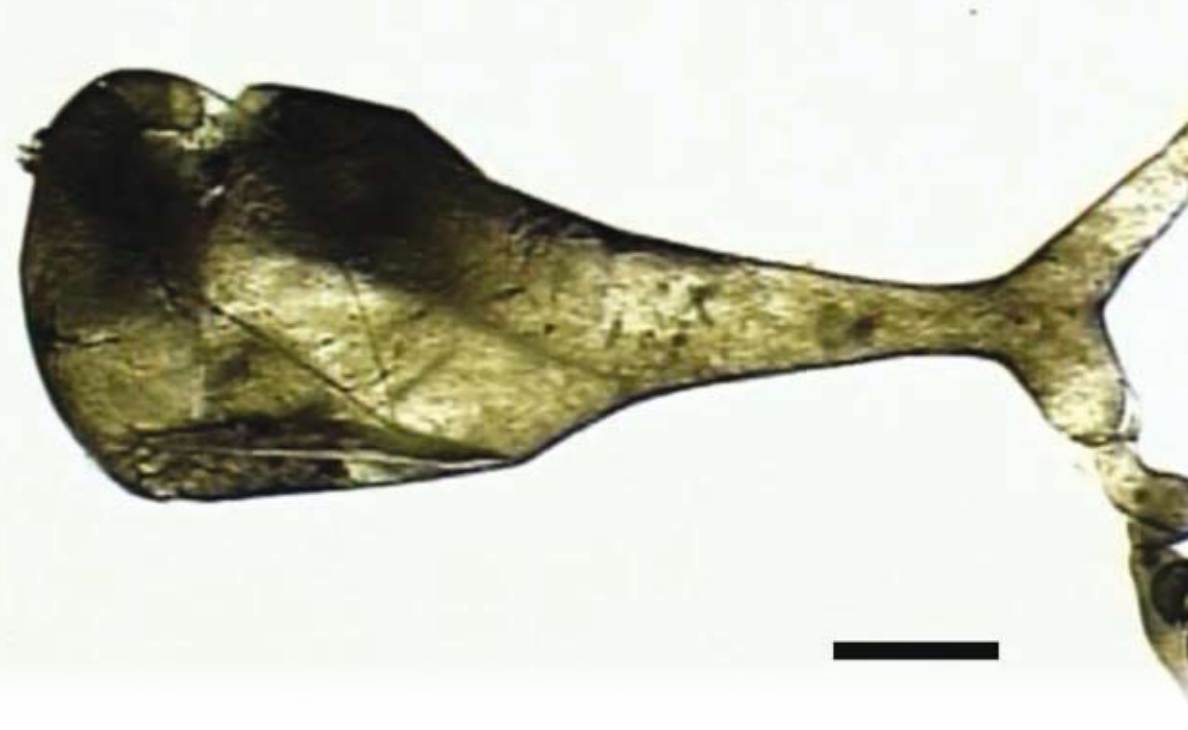

*Fig.10. By fifteen hours, the puncture is repaired and internal pressure has begun to re-inflate the cell wall to its original contour. Scale bar 1 mm.*

*Fig.11. Two-way flow of cytoplasm is shown by time-lapse, as the pressure is regulated to inflate (but not rupture) the cell wall. Scale bar 1 mm.*

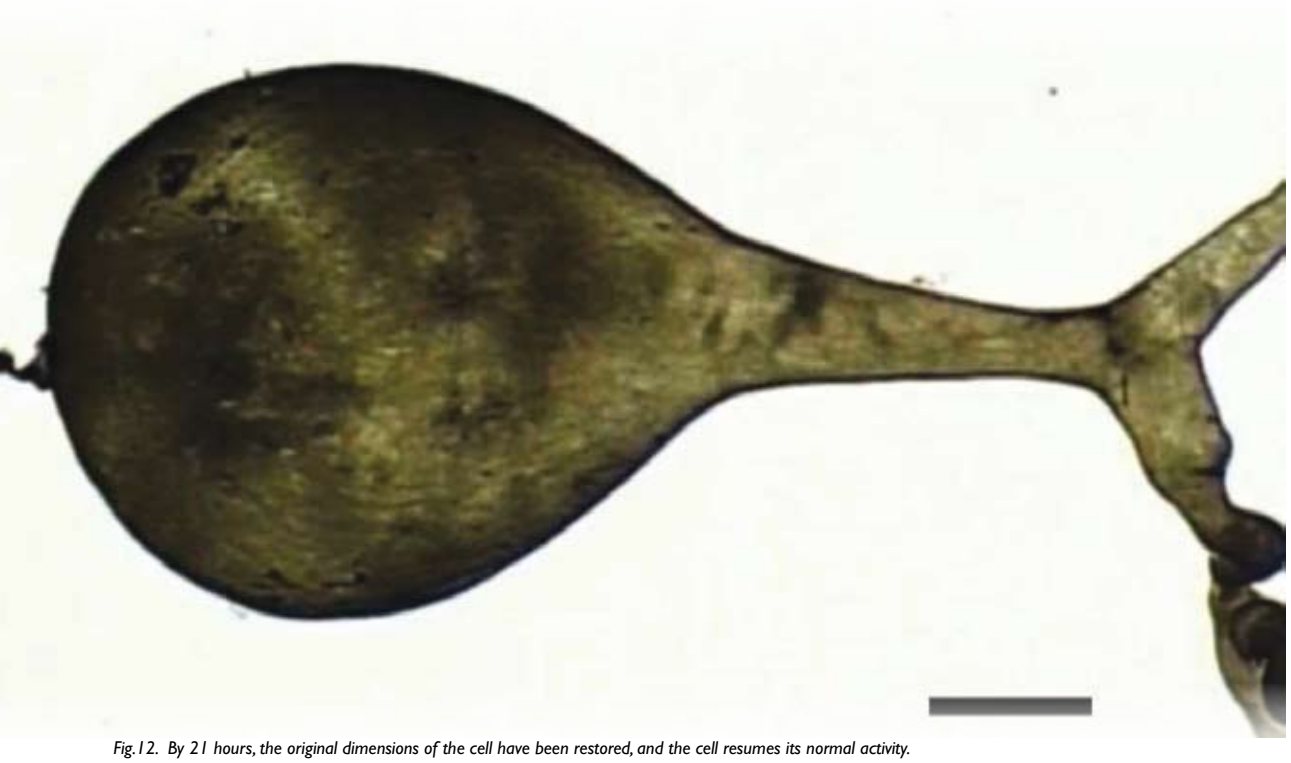

*Fig.12. By 21 hours, the original dimensions of the cell have been restored, and the cell resumes its normal activity. Scale bar 1 mm.*

organisms must exhibit considerable ingenuity in adapting their behaviour to suit widely varying circumstances. We know that testate amoebae can hunt their prey, and *Difflugia tuberspinifera* was recently observed to engage in complex hunting behaviour (Han *et al*, 2007). These amoeboid cells hunt, catch and consume rotifers. The amoebae manage to perforate the protective jelly coating that the rotifer secretes, and ingest the rotifer foot-first. Clearly, these cells demonstrate agility and adaptability. The notion of the amoeba as a lowly, simple particle of protoplasm cannot account for the ingenuity and persistence that these organisms show in their daily lives.

## Cell repair

Observing living cells under the microscope can give the impression of extreme vulnerability. Sometimes they rupture, and the cell spectacularly disintegrates in front of the observer's eyes. The cell wall can be punctured during manipulation, allowing the cell contents to flow out into the surrounding medium. Cells can be killed by high light levels, even by abrupt changes in temperature or pH.

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But this is not always the case. Some cells are famous for being able to repair themselves after being damaged. The syphonous *Derbesia* gametophyte has been studied intensively (Wheeler *et al*, 2008). This vesicular organism long been known to show remarkable abilities to recover from wounding. There are some informative time-lapse video clips on the Cryptographic web site (Erica *et al*, 2006) that show the high levels of activity observed within these algal cells. These remarkable sequences have been filmed by Jeremy Pickett-Heaps and they reveal the complex levels of coordination that the cells display during the process of self-repair. The cut edge of cytoplasm in a wounded cell can be seen to move away from the wall. Repeated expansion and contraction of the cytoplasmic vesicle occurs, and then waves of streaming fill the cell. A new cell wall is formed around the healed protoplast within 21 hours.

On this site there is an equally remarkable recovery from the crushing of the cell wall. In this case the cytoplasmic fragments can be seen to condense, and form new vacuoles before coalescing into a single protoplast. The damaged organism reinflates itself to full size within 12 hours. One revealing sequence shows the side view of a puncture wound as the cytoplasm responds to the trauma. The cell wall closes the wound within five minutes. Waves of cytoplasmic activity take place as the turgor pressure increases. It is as though the organism is sensing how far it should be reinflated in order to restore its spheroidal contour – but without running the risk of rupture. Within 21 hours, the cell wall is healed and the alga has repaired the damage.

These phenomena are extraordinarily complex, and they reveal these syphonous species as complex and sophisticated. They can repair damage using mechanisms that we do not understand, yet which restore a wounded organism to full function.

## Adaptability

Even though these mechanisms are complex, we could hardly construe them as intelligent. A sceptic could even argue against these algae manifesting ingenuity. It is clear that these large, rounded vesicles are peculiarly susceptible to puncture or crushing wounds. Repair mechanisms would be a necessary property of any such alga, if it is to succeed over an evolutionary timescale. The controlled sequence of events could be computer modelled, and – remarkable as it clearly is – there is insufficient evidence in these observations to give these algae unreasonable abilities.

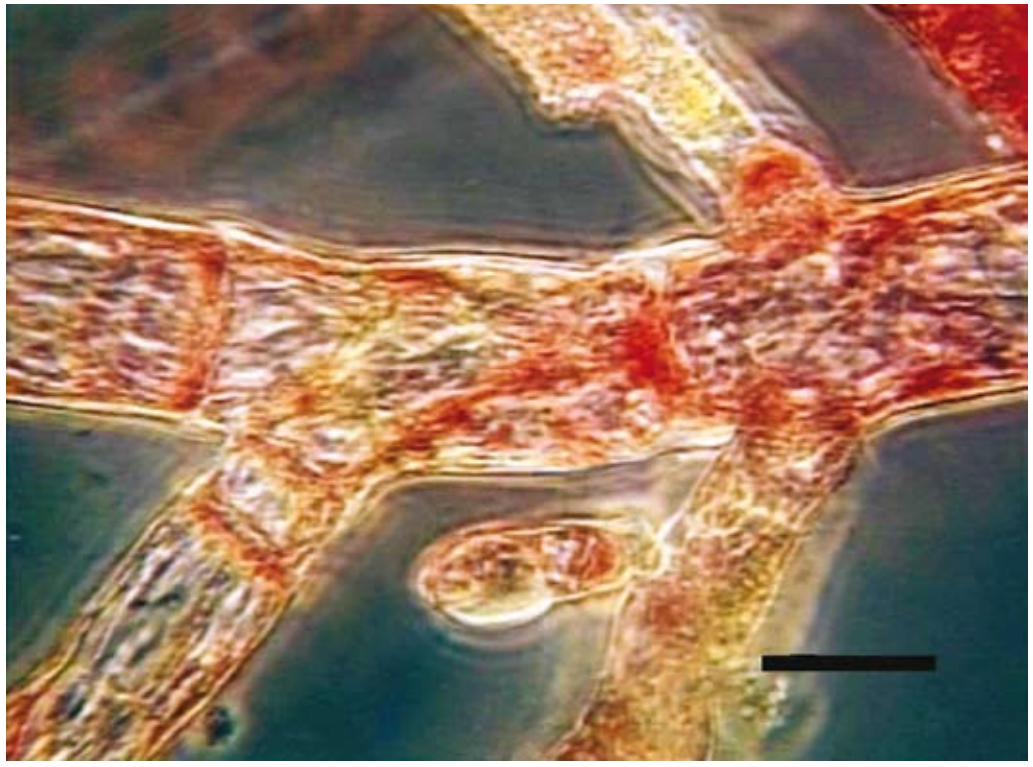

*Fig.13. A filament of Antithamnion sparsum, a marine Rhodophyte, in a video sequence kindly sent by Jeremy Pickett-Heaps (2005). Scale bar 50 µm.*

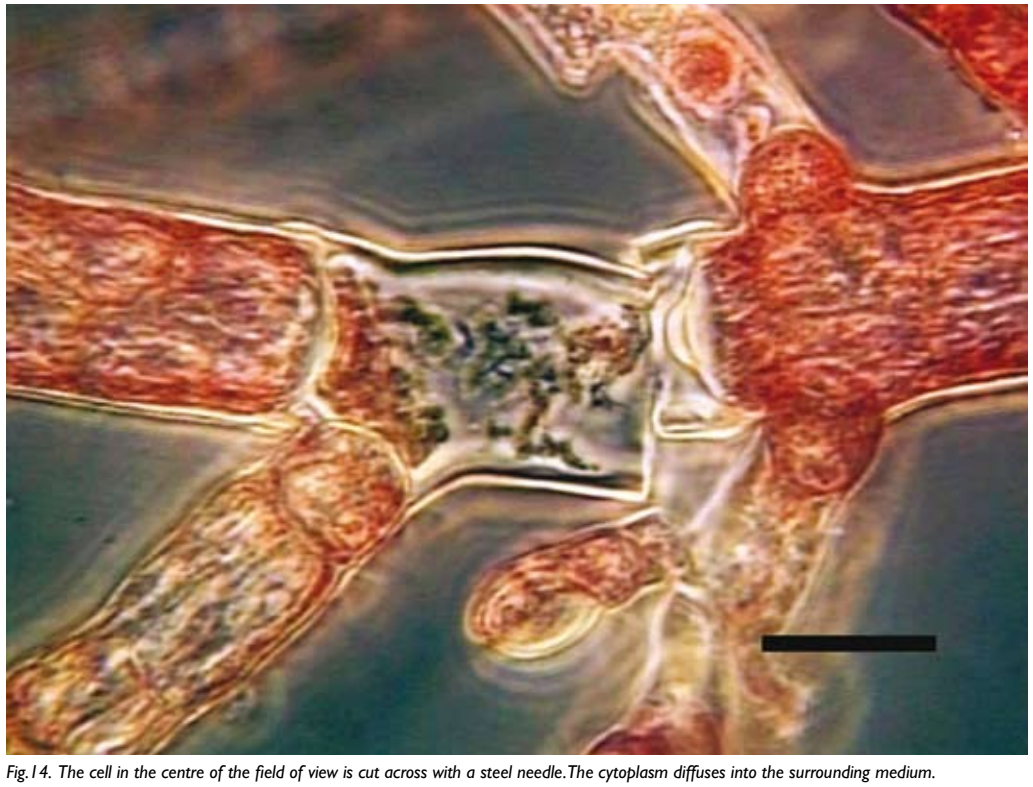

*Fig.14. The cell in the centre of the field of view is cut across with a steel needle. The cytoplasm diffuses into the surrounding medium. Scale bar 50 µm.*

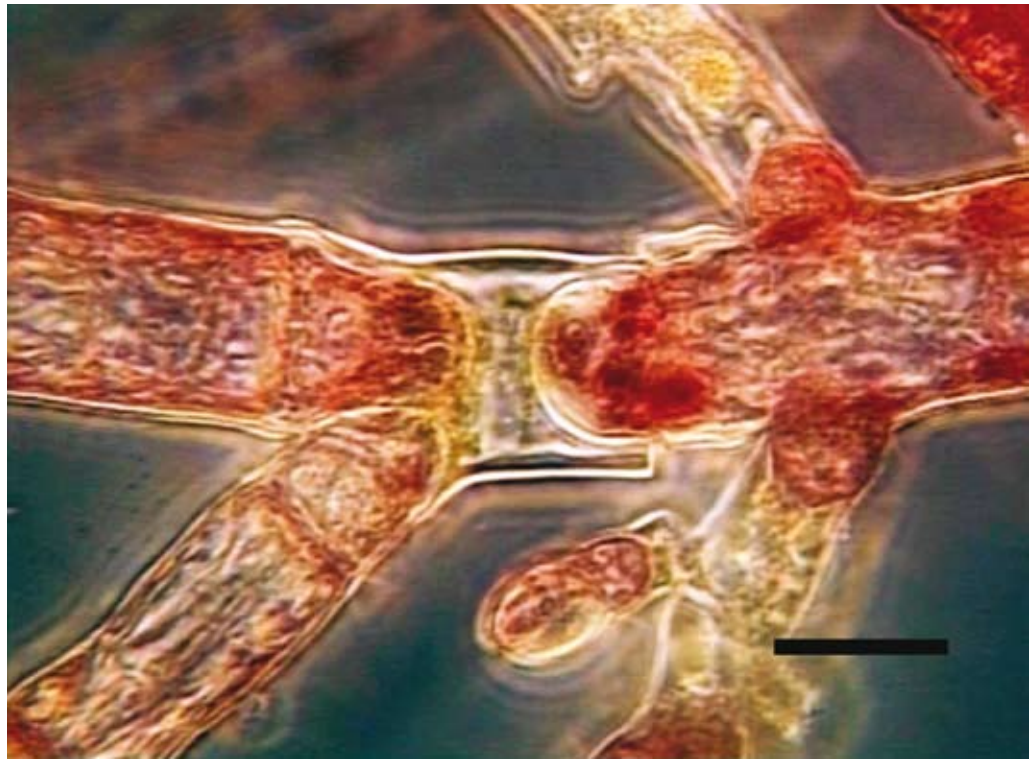

*Fig.15. Within six hours, neighbouring cells in the Antithamnion filament are moving in to fill the void. The broken cell walls are realigning. Scale bar 50 µm.*

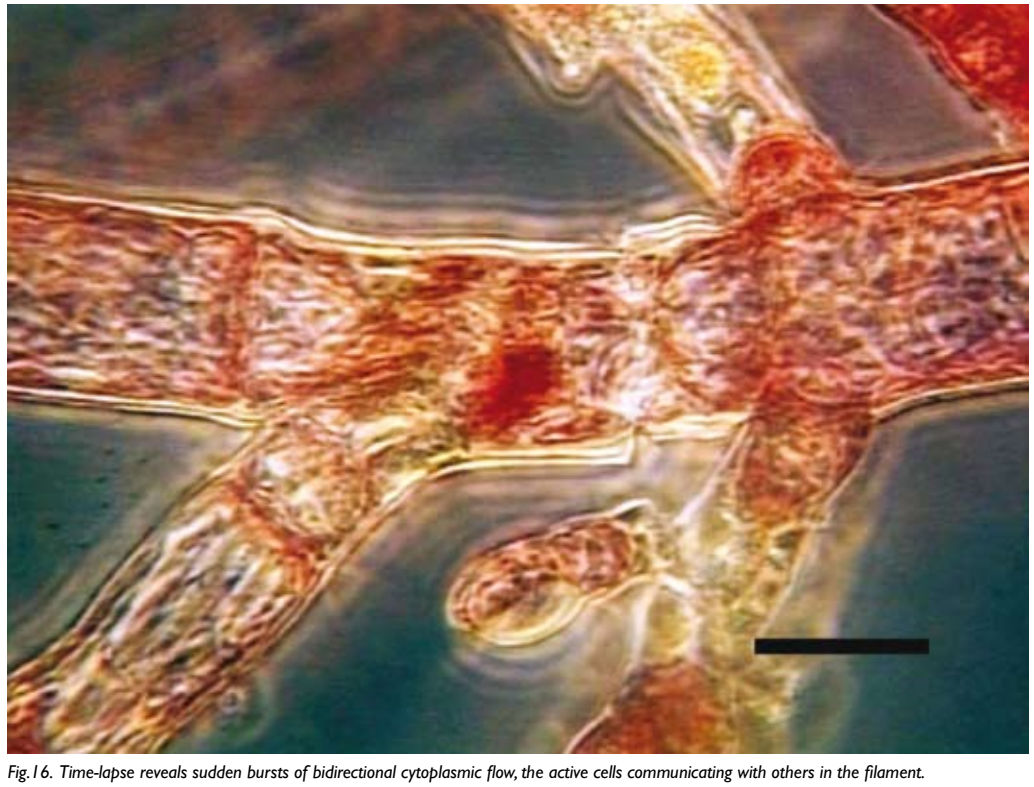

*Fig.16. Time-lapse reveals sudden bursts of bidirectional cytoplasmic flow, the active cells communicating with others in the filament. Scale bar 50 µm.*

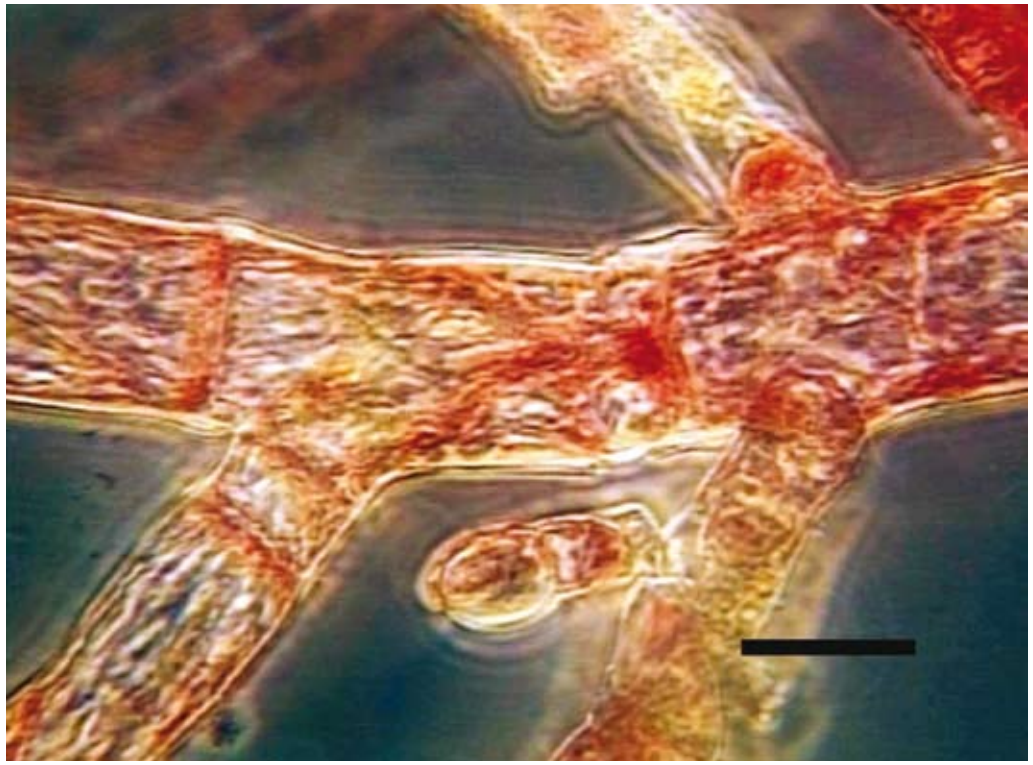

*Fig.17. After 15 hours, the cell contents have been restored and new cell wall material can be seen bridging the gap. Scale bar 50 µm.*

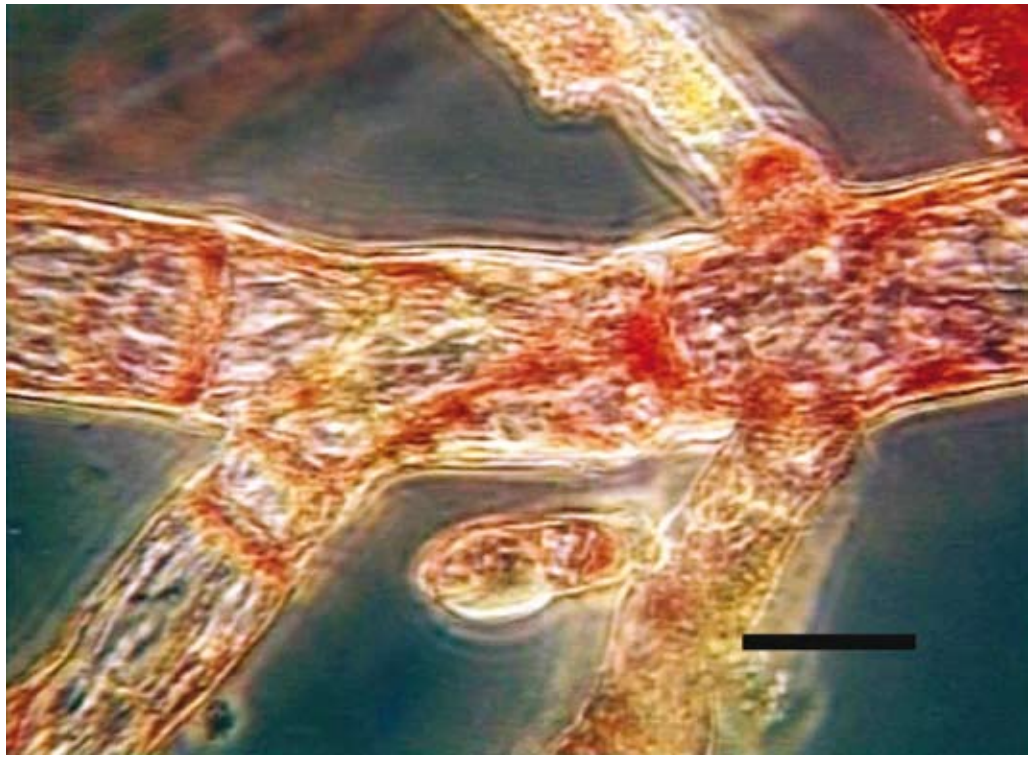

*Fig.18. Around 20 hours later, the cell walls have been perfectly realigned and cell wall repair has been completed. Scale bar 50 µm.*

The case of *Antithamnion sparsum* takes us into an extraordinary world, for the mechanisms we can observe cannot so easily be explained. In my view, it is clear that this species is adapting to unforeseeable situations in a broad-based fashion that clearly connotes ingenuity. This is an intriguing organism, and the ability of its gametes to home in on target has been extensively investigated (Kim *et al*., 1996). The role of lectins and carbohydrates as a double-docking recognition system has been carefully elucidated. And it is through investigations at the level of cell chemistry that many of the mechanisms characteristic of the genus, have been painstakingly revealed. Not everything is amenable to this form of examination, however, and a sequence filmed by Jeremy Pickett-Heaps seems to me of crucial importance.

A filament of this alga was imaged using phase-contrast and an analogue video camera was used to film the response of the alga to injury (Pickett-Heaps, 2005). Using a fine steel needle, the cell-wall in the centre of the field of view was ruptured. The entire cell was broken in two. The cell walls were cut across, and the cytoplasmic contents lysed and diffused into the surrounding aquatic medium. This is not an unfamiliar sight to any microscopist accustomed to observing aquatic organisms. When cells rupture, it is normal for the contents to disappear into the surrounding medium. These Rhodophytes are an exception, for they can heal themselves after severe trauma.

The sequence alongside is of stills from the resulting video. The void of the damaged cell does not remain empty for long. The two adjacent cells begin to respond, and 25x time-lapse shows rapid bursts of bi-directional cytoplasmic streaming as the neighbouring cells sense what has happened and initiate remedial action. In time, the void is completely filled with new cytoplasmic matter. The broken ends of the ruptured cell wall begin to be realigned, partly due to the hydrostatic pressure of the expanding cytoplasm, until the severed edges are roughly in apposition. At this stage, new cell wall material is secreted and the cell's mechanisms affect a neat, almost invisible repair.

It is important to recognise that none of these mechanisms has an explanation. We have no understanding of the range of sensory systems that could detect damage, let alone initiate a response. No organelles are known that can produce new cell wall material in this situation, particularly when the process involves the meticulous readjustment of the broken edges. So we start with behaviour that, even on the simplest level, we are unable to comprehend.

And there is more. It could be surmised that the healing response is an evolutionary mechanism, an innate reaction to trauma with predetermined outcomes. Yet this cannot be sustained. We can see why if we speculate on the mechanisms that, in nature, could cause this form of cell wall disruption. It could be due to tension applied to the Rhodophyte filament, which led to the rupture of the cell. We might imagine that a colony of *Antithamnion* was disrupted by a rock fall, or stepped on by browsing dinosaurs; there are many mechanical forces that could arguably result in a filament being snapped in two. Yet consider: whatever the mechanism, the broken ends of the filament would inevitably be separated by a considerable space.

Envisage the mechanism. If the filament is broken through tension, the snapped cell wall will be separated by hundreds of millimetres as elastic forces are released. Should it be some form of pressure rupture, the separation must be tens

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of millimetres at the very least. There is no mechanism in nature which could cut open the cell, while leaving the broken ends lying in apposition. This can only happen on the microscope slide, when a needle is used with precision to break open the cell, the empty remains lying adjacent to each other. It is difficult to envisage a mechanism that could cause this to happen in nature.

We thus have a filament of *Antithamnion* with a ruptured cell lying on the slide, the broken ends in close proximity, in a way that cannot happen in nature. The organism is faced with an unforeseeable situation. Its sensory systems and innate repair mechanisms cannot have prepared it for this. Responding to an imponderable situation by unique mechanisms is the hall mark of ingenuity, and a clear concomitant of intelligence. Definitions of intelligence vary, but most include the concept of general adaptability to new problems faced in life and adjustment to the environment in changing circumstances. In Reznikova's book, we encounter the idea of intelligence being manifested through the application of innate abilities to new situations. This is what we are witnessing here.

## Conclusions

Microscopical observation of living cells has taken a back seat in our mechanistic era of genetics. When we do observe them, we ordinarily look at dead cells. Studies are made of fixed and stained sections, or of electronmicrographs. And those who observe living cells are more interested in what they are like, not in what they can do. The use of fluorescence antibody techniques gives remarkable insights into where specific components lie within a living cell, but says nothing of how the cells go on to respond to events in their daily lives.

When we consider the significance of what we observe, an inevitable conclusion arises: single cells can build homes for themselves that are more delicate than those made by more highly evolved life-forms; they can take decisions, adapt to situations, and work out what to do when a problem arises. It is the single cell, and not the multicellular organism, that shows us the beginnings of our intelligence.

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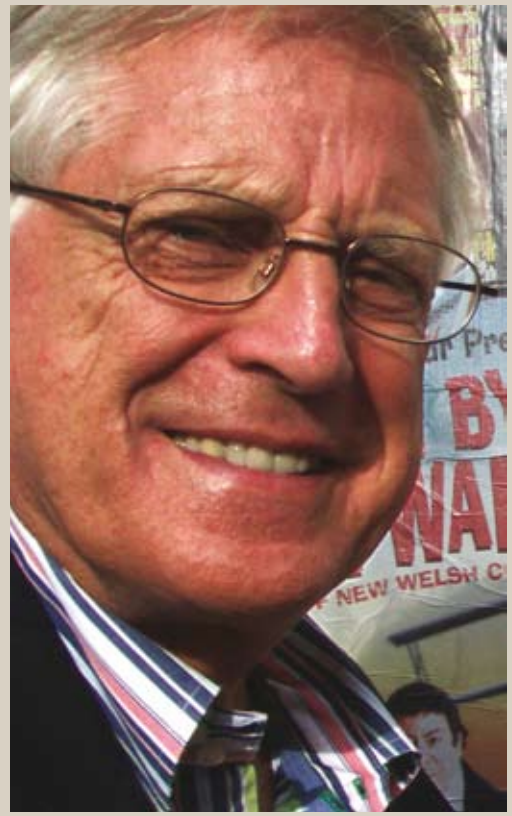
## Credits

Micrographs of *Difflugia* and *Nebela* taken by the author. Images of *Derbesia* and *Antithamnion* are stills from video images provided by Pickett-Heaps (2005), formatted and optimised with Adobe Photoshop CS2 by the author.

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Professor Ford, a Fellow since 1962, is well known for his many published papers in journals ranging from *Proceedings of the RMS* and the *British Medical Journal* to *Nature* and *Scientific American*. His books include *Microbiology and Food* (1970), *The Revealing Lens* (1973), *Microbe Power* (1976), *Single Lens – Story of the Simple Microscope* (1985), *Genes, the Fight for Life* (1985) and *Sensitive Souls – Senses and Communication in Plants, Animals and Microbes* (1999). The latest edition of the last title has been published in Chinese during 2008. He has lectured on 'cell intelligence' at the Universities of Surrey, Cambridge and Oxford, also widely in the United States, and elsewhere round the world. With Professor Pickett-Heaps, he has demonstrated aquatic microscopy at the McCrone Research Institute, Chicago.