A new era for whole cell biology

As the Society of Biology is born, there are crucial issues to address on the future of the biosciences. Many aspects of biology are now being neglected. Schools no longer expect students to know about the plant and animal species that surround them; Latin names are extirpated from science programmes on television; taxonomy is a dying art (at a time when it is of prime importance) while the focus of cell biology is now on the work of the molecular biologists.

We should now, I believe, move on.

Nobody can doubt the admirable achievements of geneticists and cell biologists, though few would have anticipated that these fashionable topics would divert our attention from the way entire cells behave. The study of the whole, living cell is widely misrepresented, for cells are currently seen as little more than binary switches or transistors with social pretensions – they are portrayed essentially as minute robots subject to the laws of Newtonian physics: little more than *nanobots*. In my view the cell is better construed as an essentially autonomous organism that embodies the essence of intelligence. These facts have been bypassed in the onward rush to reductionism.

Living cells

A search for 'living cell' on Google Images makes the point well. Page after page of the results show not living cells at all, but digital simulations of organelles and molecules. At the time of writing there is a light micrograph that does appear, captioned 'living cell from the leaf of a poplar tree'. It is underexposed, poorly resolved and conspicuously chromatic; and it stands as a rare example of a micrograph amidst the computer graphics.

Our detachment from what living cells are like is exemplified by the way they are used in television programmes. We sometimes see organisms used as generic icons of microscopic life. Thus, the harmless colonial chlorophyte alga *Volvox* is often portrayed as an example of a 'living cell'; it was a colony of *Volvox* that was chosen by the BBC to promote a *Panorama* programme on anthrax. When ITV came to examine the rising incidence of meticillin-resistant *Staphylococcus aureus* in hospital wards, they chose a culture of *E. coli* to illustrate the MRSA.

There is no other area of public knowledge in which this could be done. Were you to use a golf-club to promote the All Blacks playing at Twickenham, or a dollar-sign to illustrate the Japanese yen, there would be an outcry. When 'Del Boy' Trotter thinks that Evelyn Waugh is a woman, we laugh that anyone could show such a level of common ignorance; but when newsreaders speak of "a bacteria" or think that tuberculosis is a virus, the audience hardly notices.

Our current conception of the living cell as a small, essentially mechanical, device has had several consequences. One is that we perceive the immune response to be concerned with templates and keys, like components of a jigsaw. The notion of ingenious leucocytes seeking out pathogens and destroying them, like diminutive warriors, is not part of this picture.

In reality, cells will not only identify a potential pathogen but they give chase and ensure that the threat is eliminated (search on YouTube for 'bad ass leukocyte' for an example). These activities require ingenuity and a capacity for adaptation on the part of the individual cell. Contrary to the orthodox teachings, these cells are not centrally controlled, regulated by the brain, mediated by

What about the case of the kindergarten teacher?
It is thought that the teacher picked up TB while abroad, and could have been infected for up to six months. The virus can lie dormant for years – without the carrier developing any symptoms or being infectious.

Figure 1. A feature in the magazine of a national newspaper discusses tuberculosis. The tubercle bacterium is designated 'a virus' in this report. So detached are modern reporters from biology that the term 'virus' is widely used to mean 'germ'.

hormones or the central nervous system; the somatic cell is primarily an autonomous organism with a mission.

Most cells in the body are invisible to the brain, and are unaffected by its controls.

'Plasticine' biology

This tendency to simplify has recently extended to cell division. Instead of the astonishing complexity of mitosis, cells are often shown simply to fall into two parts. A recent BBC programme, *The Cell,* commissioned an expensive graphical simulation of dividing cells, in which the spectacular condensation and congregation of the chromosomes and the meticulously-coordinated actions of the spindle were abandoned; nuclei were seen, instead, to form a vague shape like an egg-timer, and fall apart like snowballs in the sun. Search for 'simulated cell division' on YouTube and the graphic images include a similarly simplified cartoon. This is plasticine biology; the choreographed intricacy and beauty are gone, replaced with mechanistic modelling that diminishes the majesty of life.

Even the cleverest of people now get cells wrong. Will Wright is a foremost designer of computer games. His latest is called *Spore*, which models the evolution of an entire ecosystem from simple beginnings. When

Figure 2. Testate amoebae construct homes, typically of mineral particles. Difflugia (above) selects sand-grains, cementing them together to produce meticulously constructed flask-like shells using senses and manipulative skills of which we know little.

announcing it, he showed the starting position: limpid pools of water in which his computer-graphic 'cells' start to swim. The first of them to appear looks like a wingless bee, with prominent eyes. Says Wright: "Yes, I know cells don't have eyes, but it makes them look kinda cute."

He can be forgiven for thinking that cells are sightless, for he is reflecting a general sense of ignorance about living cells. But in the real world that exists down the microscope, plenty of living cells have eyespots. They possess refracting lenses, concave retinas, light-sensitive pigments; everything you need for sight. And what an imponderable paradox this is. An eye, by definition, is made of large numbers of cells organised into a complex device, like a camera. Here we are faced with minute – but clearly recognisable – functioning eyes within a tiny part of a single cell.

Sentient

Cells are sentient. The ancients revered humanity for the classical senses of hearing, sight, touch, taste and smell. A single stomatal cell on the surface of a leaf responds to light and vibration, to chemical stimulation and atmospheric composition. Consider the implication of those facts – in their own way, these single cells manifest senses that are comparable to our own. Watching a predatory ciliate that rounds upon its prey, sensing it in the watery medium and darting forward to ingest it when the moment is right; all this is reminiscent of watching a cat hunt a mouse. Observe a ciliate nosing through detritus in search of food particles and we are inevitably led to compare it with an elephant using its trunk to sift through leaf litter, or your own fingers searching for keys in a briefcase.

Cells exhibit intelligence. The behavioural intricacy that we can observe connotes well with definitions of intelligent behaviour, yet few biologists now observe living cells. Molecular biologists rarely look at the cells whose components they study. Their mechanistic models cannot account for the complexity of what we can witness.

A major focus

My aim is now to see whole cell biology emerge as a major focus of teaching and research.

Let us consider an example. Cell repair mechanisms in algae are never taught in school, and have hardly ever been investigated at university, yet they reveal a remarkable degree of problem-solving. Cells of the rhodophyte *Antithamnion* can detect if a single cell in the colony is destroyed. The neighbouring

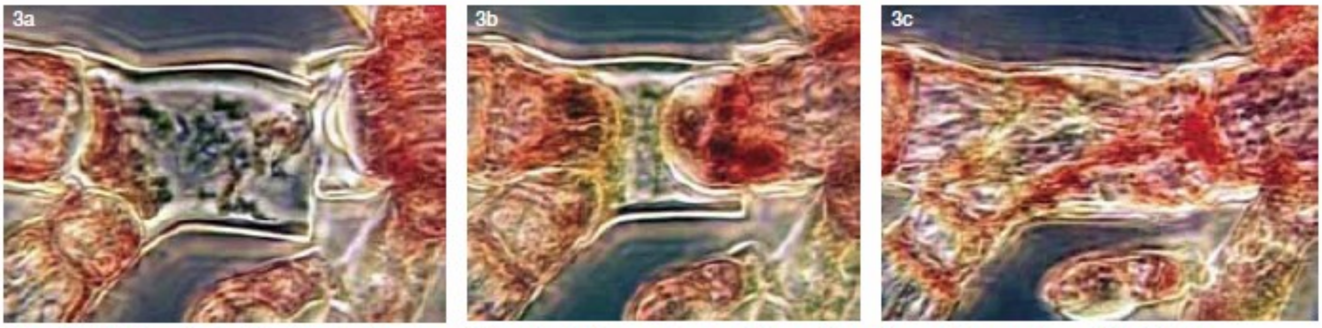


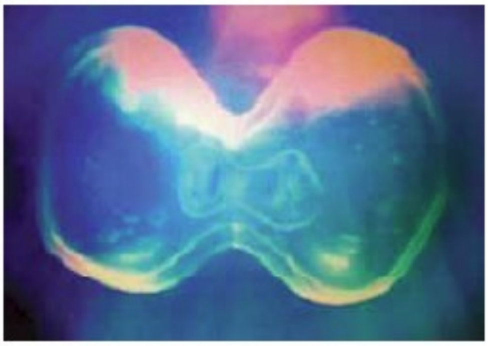
Figure 3a. *Antithamnion* is a Rhodophyte alga, shown in this optimised frame enlargement from a videomicrograph by my colleague Dr J Pickett-Heaps. The central cell has been disrupted by a micro needle and the cell wall severed. **Figure 3b**. Adjacent cells in the *Antithamnion* filament respond rapidly to the presence of their damaged neighbour. They detect the trauma and complex cell division and cytoplasmic migration results in the re-occupation of the empty cell wall. **Figure 3c**. Within 24 hours the empty cell wall in Figure 9 has been completely restored to full function. More remarkably, the displaced cell walls have been realigned and the site of the break has been invisibly restored to its original condition.

cells sense the damage and set out to repair the lesion. They divide in order to re-occupy the damaged cell wall and reinstate the original appearance. This is no simple, mechanical cell division; the damaged cell wall is meticulously brought back into alignment through mechanisms of which we have no knowledge. The result is an almost invisible mend which compares favourably with a healed wound or a bone mended after fracture.

In this example, the central cell has been destroyed, and the cell wall broken in two, by the experimenter's dissecting needle. It is difficult to envisage how something like this can happen in nature. However a filament is broken, whether through transverse shear or longitudinal stress, the severed ends will be remote from each other. The situation is unforeseeable, and the adjacent cells have to work out how to reinstate their missing neighbour.

This response to an unforeseeable predicament is a hallmark of intelligence. Binet, in his seminal paper on the new Binet-Simon scale of 1905, defined intelligence as "the ability to learn or understand or to deal with new or trying situations". David Weschler, in his 1939 book on adult intelligence, cites a quality that allows an individual "to deal effectively with his environment". In 1993, in his book, *Frames of Mind*, Howard Gardner refers to a property that enables the individual "to resolve genuine problems or difficulties that he or she encounters". The current Merriam Webster dictionary definition centres on "the ability to learn or understand or to deal with new or trying situations".

Figure 4. A poorly researched short series, entitled *The Cell* (scheduled to be repeated on BBC4 in the spring 2010), invested heavily in computer graphics. This simulation of a dividing cell was a gross oversimplification. Even the chromosomes were omitted.



The behaviour of these single cells is rich in the rudiments of intelligence.

Observe the beauty of a shell home constructed by a testate amoeba, and compare it with the home made by a caddis-fly larva or a stone wall constructed by a craftsman. All are marvellous to behold, yet only the latter two can we begin to explain. The source of human intelligence resides in our component cells. The cell community optimises and amplifies the propensity, but does not give rise to it.

Students – from the age of seven – need to be familiarised with the astonishing abilities of single cells. We must move on from the emphasis on 'biological molecules', opsonins, quorum sensing and the base-pairs of the DNA double helix. Understanding these remarkable insights matters, of course, but not as much as the way that single cells behave. Few people these days observe whole cells, and this attitude is due for revolution.

British biology now has its Society; I believe that it is now time we concentrated on the society – of cells – that makes us what we are.

Professor Brian J Ford is a biologist and an authority on the microscope. He served for many years on Council of the Institute of Biology, one of the 'parent' organisations of the Society of Biology. Email: mail@brianjford.com