Revealing the ingenuity of the living cell

We believe everything depends on the brain. Although the brain is important for coordinating movement, most of the body functions independently of it. Cells can show their own ingenuity.

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I saw the viewpoint that 'everything depends on our brains' extolled recently on a television programme. Susan Greenfield insisted that all aspects of human experience will be explained in terms of physical processes in the brain – and this view typifies current thinking in biology. Brain is all. It is the ultimate resource and controls everything we do, and all we are. A current popular book on the topic puts it with graphic simplicity: "Everything, from the beating of the heart, the pulsing of the gut, the production of new blood cells, right down to the raising of individual hairs on our arm when we get a fright, all this is controlled by the nervous system, and so ultimately the brain."

My view is very far from this. In the real world, most of what we do has nothing whatever to do with the brain; the brain does not even know what is going on. Living cells have a responsive, almost a sentient property. They make their own decisions, undertake complex responses, demonstrating ingenuiousness and extraordinary manipulative skill.

Not long ago I met a young woman professor of zoology in West Virginia. She was pleasantly intrigued by my own work with microorganisms, and then let fly with a remark that I have never forgotten. Her comment typifies much of modern biology teaching. "You make the light microscope sound fascinating," she said. "But I've never used one. I have never looked down a microscope in my life." She had worked exclusively with scanning electron micrographs all her professional life. I am firmly of the view that nobody should get to the age of 10 without looking at pond life and experiencing the sense of wonder that Leeuwenhoek knew in the summer of 1674, when he first studied aquatic microorganisms and bequeathed to us the new science of microbiology.

My concept is founded on the realm of living biology that can be observed under the microscope, and not on today's reductionist imperatives. Studying cells by analysing what they produce is like trying to understand how people work by examining their urine. Working with fixed and stained permanent preparations – as most microscopists do – is like trying to understand sociology through corpses. Looking at scanning or transmission electron micrographs offers monochrome images of reality, compared to the intricate majesty of watching life in full colour under the lens.

We have been seduced by molecular genetics. Printing out the human genome (or, at any rate, the various drafts currently available) has been heralded as the answer to genetic disease. At last, trumpeted the papers, we can understand the nature of life. This is hype – spin, wild exaggeration. You could similarly print out the huge sequence of ones and zeros that represent the digital encoding in your computer; yet, if someone said that this meant you would now know how graphic designers create virtual dinosaurs for the movies, you would think they were ridiculous. While molecular biologists retreat into minute models of small corners of a cell, real organisms – living cells in the daily course of life – are carrying out extraordinarily complex tasks of unmatched ingenuity. Nobody knows how. Hardly anyone seems interested in finding out.

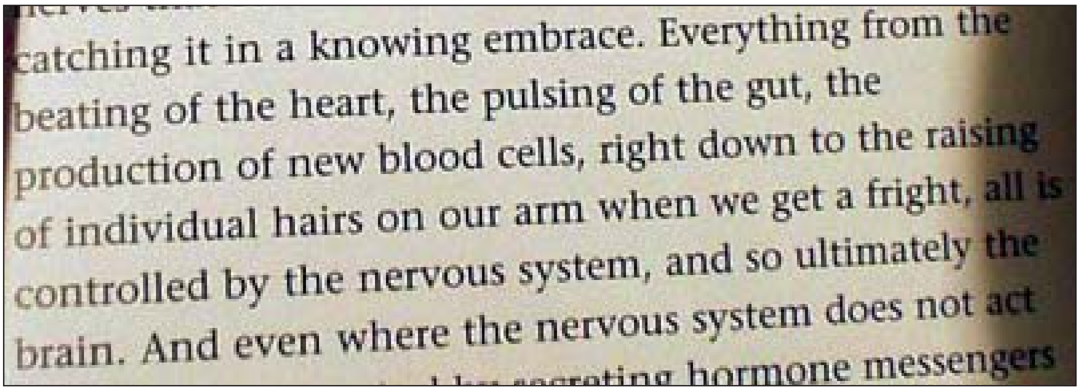

catching it in a knowing embrace. Everything from the
beating of the heart, the pulsing of the gut, the
production of new blood cells, right down to the raising
of individual hairs on our arm when we get a fright, all is
controlled by the nervous system, and so ultimately the
brain. And even where the nervous system does not act
... hormone messengers

Figure 1: Current views on the centrality of the brain in regulating the body, an extract from John McCrone's book, *How the Brain Works* (published in the Dorling Kindersley 'Essentials' series).

Amoeba – not so simple

We were all raised with the notion that an amoeba is the lowest form of life. *Encyclopaedia Britannica* puts it thus: "The *simplest forms* of *life* do not have feet. In a one-celled animal, such as an *amoeba*, a bit of living substance is pushed out from the body . . .". Most people think of an amoeba as primitive. Yet think: it is comprised predominately of water-soluble constituents, and lives in a watery medium without dispersing into the void. Confine it in a cul-de-sac and the cytoplasmic granules mark how it turns round to come out again, suggesting that amoeba has a head and a tail. It finds its food, identifies it, isolates and engulfs it, throwing out the residue through vacuoles. Amoebae can do several neat tricks denied to humans: they can adapt their rate of reproduction to fit available food supplies, which would be a great idea for human societies to adopt, and many can construct a hermetically-sealed capsule inside which to survive when environmental conditions become inhospitable.

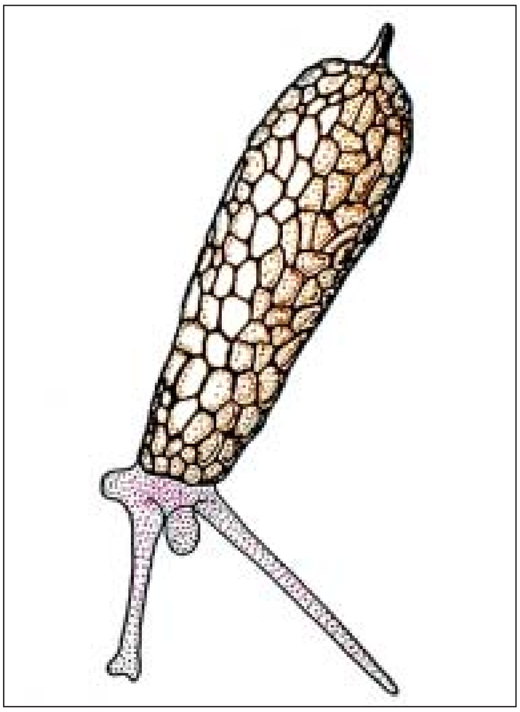


Figure 2: Youngsters always admired the caddis-fly larva making a home from detritus. Here's a far more remarkable feat – a testate amoeba *Difflugia* that constructs a home for itself out of sand-grains. x 21.

There is more. The testate amoebae construct homes for themselves. These phenomenal species collect granular material from the silt in which they live and glue the particles together to make a protective shell. Think about it. These are jelly-like, primitive living organisms – the simplest forms of animal life, people like to say. The testate amoebae use specific components to make their shells. Some utilise minute grains of silica sand; others select centric diatoms and glue them carefully together. They do not confuse their raw materials, for each species has a preference of its own.

What does this imply? These tiny organisms have such finely-tuned senses in their shapeless pseudopodia that they can identify one mineral from another. This in itself is a remarkable process of discrimination. The cell then picks up its chosen object, holds it in place; it then secretes some kind of adhesive and continues building its home. We have not the least idea how such finely-tuned senses might be manifest within the pseudopodium of an amoeboid cell. Nobody knows what the adhesive might be, where it comes from, or how it is applied. Most remarkable of all, each different amoeboid species produces its own distinctively-shaped shell. You can usually identify the species that made a shell from its unmistakeable morphology. I have to say that, if you made such an attractive, flask-like shape in a craft class I would be impressed.

Perversely, few people show any great interest in these miraculous propensities. And we do not have to look far to find ingenious amoebae. As you read these words, polymorph amoeboid cells teeming in your throat are identifying potential pathogens that are inhaled from the environment with each breath. The white cell population will recognise the invaders for what they are; send signals to their allies to join in battle to extirpate the foe, and will – almost always – destroy pathogenic bacteria before any damage is done.

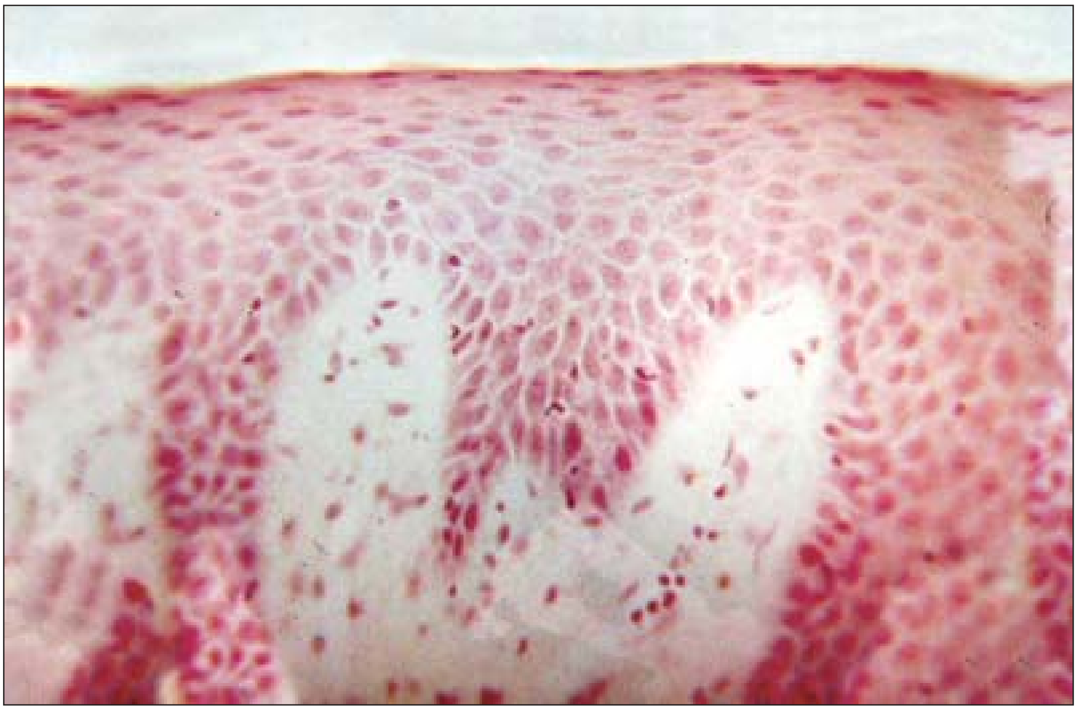


Figure 3: Complex changes in positioning and function underpin the repair mechanisms within the human buccal mucosa. The recovery of the tissues after a dental extraction is a complex process. x 750.

Once in a while, amoeboid white cells mistake the enemy and set about destroying cells within the body. The result is the tragic burden of an auto-immune disease. But – however the cells respond – they do so without any interference from the central nervous system. They are not exclusively controlled by the brain, regulated by nerves, influenced by our thoughts; these cells are a law unto themselves. They make their own judgements, take their own decisions, communicate (through a language that may be more complex than conventional cytokine theory) without external mediation.

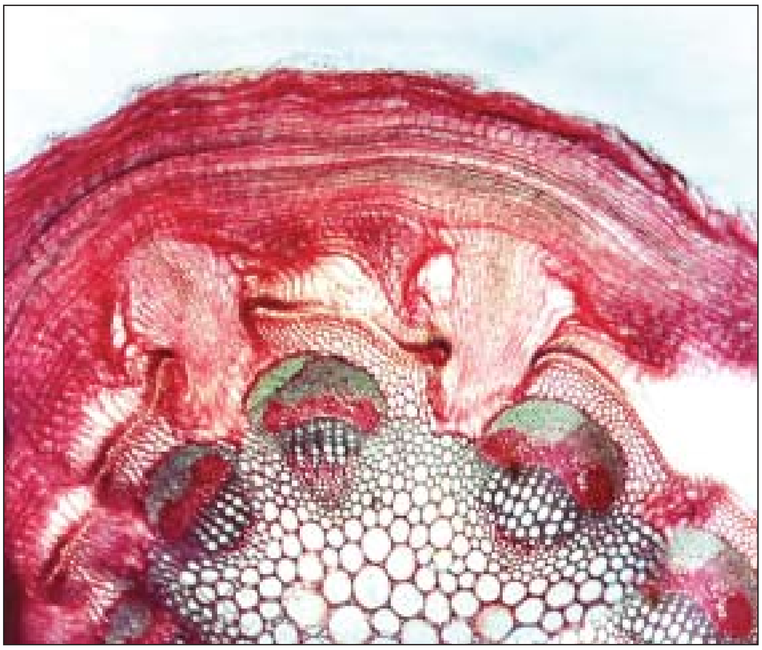
No brain/body dichotomy

Cells throughout the body are dividing, responding, reacting and controlling in ways that are independent of the human brain. To me, there is no brain/body dichotomy. The brain *is* the body. Neurons are cells that specialise in handling the cognitive, higher-order manifestations that make us look and behave like people. But the other cells in the body – no matter how diminutively – have minds of their own. There have been books and programmes claiming that human xenotransplant recipients sometimes manifest attitudes and traits they never had before, but which are identical to characteristics of the deceased organ donor. This is not much of a mystery to me; even if most of the personality resides in the brain, there must be some – perhaps a substantial amount – that derives from the choreographed community of autonomous cells that make us who we are.

I believe that there are lessons for our understanding of the neuron, too. It makes little sense to assume, if that lowly amoeba can build a home, that a neuron is simply a go or no-go gate – a simple, on-off switch that channels electrical impulses down dendrites like switching on a tap. The other cells within our bodies make daily decisions, and it must surely be that a cerebral neuron (so complex that even the phenomenon of reproduction is largely subsumed by a more complex order of function) is similarly making decisions of its own. It may be that the fundamental processes of thought are intra-, rather than exclusively inter-, neuronal.

Wherever we look, if we look closely, we see similar cellular complexity at work.

Figure 4: As the dodder *Cuscuta* invades its host plant, cells within the haustoria display coordinated developmental changes that allow the parasitic vascular system to tap efficiently into the host. x 45.



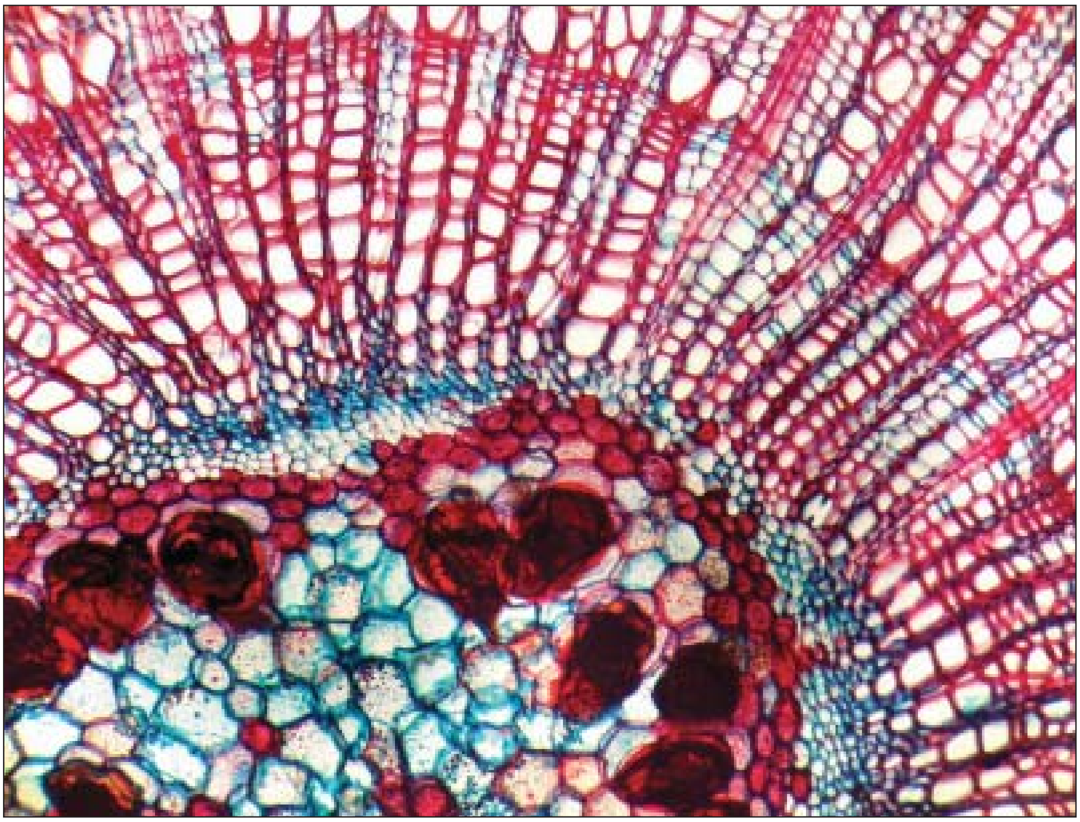


Figure 5: A transverse section of the grape, *Vitis vinifera*, reveals strongly differentiated cells in a well-ordered anatomical array that is conserved even when the plant is recovering from traumatic damage. x 65.

When *Cuscuta*, the dodder, invades a host plant, each replicating haustorial cell has to identify the xylem and phloem, and then create junctions that allow the parasitic plant to tap the nourishment it needs. The processes that are involved would do credit to a plumber with a blowlamp – yet they are done within the cells of the developing invader.

Look at the scar that the surgeon leaves on his patient. Within a couple of weeks the skin is smooth and unsullied. "My," we say admiringly, "What a superb surgeon!" It is simply not true. The ingeniousness is shown by the cells within the patient, which realign and redevelop to provide novel vascularity on demand, producing networks of fresh fibrocytes to give the tissues their structural cohesion, which differentiate into epidermal layers to finish the job so neatly. The French writer Voltaire (1694-1778) claimed that "the art of medicine consists in amusing the patient while nature cures the disease". Never was this truer than when you consider post-operative recovery.

My first introduction to this research came through John Bunyan (a descendant of his famous namesake) who funded my research into the cytology of wound healing. As I observed the way the cells reorganised, I was repeatedly reminded of the protists that I observed in samples of water. Each cell has a level of ingenuity that we have failed fully to recognise. This fundamental field of investigative research will do much to reveal the nature of humankind.

We imagined – with genetic maps emerging from laboratories around the world, that our voyage into biology was on the home stretch. I am certain that – once we begin to look at the extraordinary propensities of living cells – we will see that we have hardly begun. Once the novelty of DNA has settled into a more rational perspective, there is a whole internal universe that lies there, awaiting our attention.

Figure 6: Centric diatom frustules are visible in a testate amoeboid shell photographed in phase-contrast by my colleague Dr Hilda Canter-Lund. Manipulative complexity underpins the construction of these structures. x 65.

Professor Brian J Ford has written many books and research papers in the biosciences. He served for many years on IoB Council and chairs the History of Biology network. In 2004 he was awarded a NESTA Fellowship to support his research.
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