Q & A

Joe Howard

Joe Howard is a Group Leader and Director at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden. He has always been on the move. In his native Australia he did his PhD on the neurobiology of vision; in San Francisco he worked on hair cells and hearing; and in Seattle he developed single-molecule techniques to study microtubules and kinesins. He wrote a textbook on the Mechanics of Motor Proteins and the Cytoskeleton*. Currently he is becoming interested in problems in developmental biology.*

What turned you on to biology in the first place? I hated biology in school and never took any classes in it as an undergraduate. I studied mathematics. But I got increasingly worried about the foundations of mathematics and became convinced that our ability to reason was limited by our language and our brains: there is no hope of teaching a dog calculus. I did a PhD in neurobiology, though I never thought about higher brain functions. Back in those days, we would be beaten by our supervisors if we even mentioned the word consciousness, because it was considered to be experimentally intractable and only madmen worked on it. I had great fun working on vision in insects

Do you have a favourite paper? Horace Barlow's 1952 paper on compound eye design — *The size of ommatidia in apposition eyes*, J. Exp. Biol. *29*, 667-674 — had a big influence on me when I was a PhD student. He showed that, for an insect-type eye of a given diameter, there is an optimal size of the facets: if they are too big, then the image is too coarsely sampled, but if they are too small, then diffraction becomes a problem and the spatial resolution is reduced. Looking at a large range of eye sizes, he found that the observed facet sizes were within about a factor of two of his prediction. It stressed the importance of asking why.

What is the best advice you've been given? I think that science is driven by ideas. Even in experiments, you first have to have an idea and then you look to see if it is true. But you have to be looking, otherwise you probably won't see it. Also, ideas help you develop new techniques: necessity is indeed the motherhood of invention. And as Arthur Eddington advised, never believe an experiment until it's confirmed by theory.

What role does theory have in biology? Funnily enough, when I was a PhD student in neurobiology at the Australian National University, I had two supervisors — Simon Laughlin, a biologist, and Allan Snyder, a mathematician. In the immediate community that I grew up in, we developed theories to explain biological phenomena and we did experiments to test theories. I thought biology was like that. But it took 20 years before this approach diffused out of neurobiology and entered into the mainstream of biology — classical molecular and developmental biology, for example — and it may not even be there yet.

Do you have a scientific hero? Hermann Helmholtz. He made major contributions to many areas of science. Among other things, he derived the law of conservation of energy, introduced the concept of the potential, measured the speed of the action potential in frog nerve, invented the ophthalmoscope, worked out how a violin string is excited by the bow, and wrote two very influential books — *Physiological Optics* and *On the Sensations of Tone*. Helmholtz epitomized science in the 19th century, where one could do theory and experiment on one's own or with a small lab. 20th century physics went big, and it looks like 21st century biology is going the same way.

Why the interest in developmental biology? I think that developmental biology is the heart of biology. It is the most intractable to chemical and physical approaches. That makes it most interesting and challenging. Developmental biology means the creation of form. And obviously mechanical processes play central roles in everything from cell division to gastrulation. But it has been very difficult to incorporate mechanical thinking into development, and this is why Turing ignored mechanics in his seminal work on reaction-diffusion mechanisms: *The chemical basis of morphogenesis*, Proc. Roy. Soc. B. *237*, 37-72, 1952.

But things have changed. We now have a very good molecular understanding of motor proteins and the mechanics of the cytoskeleton, and we know what force means at the single-molecule level. I think this new understanding will be as important for cell and developmental biology as Hodgkin and Huxley's work on ion channels and the action potential was for neurobiology: it will put cell mechanics on a firm molecular footing.

The time is right for developmental biophysics. We can build molecule-based models for moving cells and tissues, solve them with the new techniques of non-linear analysis, and test them with measurements using advanced microscopy and imaging processing that allow us to see single molecules inside cells.

What do you think physics-based approaches might tell us about development? I think that mitosis is tractable. The key will be understanding how mechanical communication between the molecules regulates and coordinates the spindle. Then there is the cell cortex and its contribution to cell shape: this will be the key to understanding how cell shape changes drive tissue morphogenesis. I am intrigued by the possibility that there may be global mechanical signals that tell an organ about its overall shape.

But is quantification possible? I am very encouraged by the reproducibility of developmental events. For example, very early development of the worm involves surprisingly complex morphological movements, yet they are precisely repeated from one embryo to the next. This may be obvious to a developmental biologist: if you don't get everything right at the beginning, what hope do you have of building an entire worm? But it is a pleasant surprise for a biophysicist, because it makes good measurements possible.

Why have you chosen to work in Germany? It was a great opportunity to be part of something new — a mix of cell biologists, biophysicists and developmental biologists. In Dresden I have great colleagues and wonderful support from the Max Planck Society.

What is your greatest research ambition? I would like to understand the shapes of cells and tissues.

What do you think are the big questions to be answered next in your field? The biggest challenge is to simplify biology. There are too many proteins, genes, interactions.... and too little understanding.

Any strong views on journals and the peer review system? I think that the peer review system has broken down, as evidenced by the amount of rubbish that is published. In my view, publishing should primarily be done by the learned societies, though private companies can make valuable contributions such as that made to production quality by Rockefeller Press. The obsession with 'high-impact' journals is a disease — the important thing is to write good papers. And people should write more books.

Max Planck Institute of Molecular Cell Biology and Genetics,
Pfotenhauerstrasse 108, 01307 Dresden, Germany.
E-mail: howard@mpi-cbg.de

Quick guide

Mass extinctions

Simon Conway Morris

What are they? Ever been denied tenure, had a paper rejected by *Current Biology*, or even *N*******e*? This is much, much worse: death on a big scale, ecologies shot to pieces and a planet in turmoil. No accident that the 'Big Five' of mass extinctions (end-Ordovician (445 million years (Ma) ago, late Devonian (375 Ma), end-Permian (251 Ma), late Triassic (205 Ma) and most famously, the K/T (Cretaceous-Tertiary, 65 Ma)) are at or close to major stratigraphic boundaries. So biodiversity plunges, but the rates and durations of the extinctions are variable, and nearly always there is marked taxonomic selectivity. Some groups are hammered, but others don't seem to notice there is a mass extinction going on.

Dozing trilobites? It is customary to distinguish times of mass extinction as against the ongoing 'normal' times of background extinction. Along with the 'Big Five' there are, however, quite a number of minor extinction events. Nevertheless, with the latter there is a growing suspicion that confounding factors, such as volume of available sedimentary rock, influence or even distort diversity curves. Many species certainly went extinct when times got nasty, but perhaps the majority went to the wall quietly, but in the face of relentless competitive attrition. So those icons of palaeontology, the trilobites, were indeed a victim of the mother of mass extinctions, the end-Permian event, but they were already well on the way out.

When Gaia calls in sick. Planet Earth has its ups and downs: global warmings, stupendous ice-ages, mega-eruptions, but by and large the biosphere seems to cruise along. But not at the end of the Permian; here is a planet in deep trouble, with possibly 96% of all marine species becoming extinct. The cause for this has long remained elusive, but it is now looking as if two factors were responsible. First, the oceans ran out of oxygen, possibly with highly toxic H_2S spilling into the atmosphere. Second, there were truly massive episodes of flood volcanism, notably in Siberia. So, from that source add sulphate aerosols and maybe toxic organohalogens, and the scene is set for millions of years of misery.

Revenge of the microbes. The dust settles, the biosphere staggers to its feet (metaphorical or otherwise), and amidst the debris life restarts, or does it? Well, no. In many cases, the recovery rates are glacially slow. Following the end-Permian debacle, for example, marine communities remained in a state of shock for up to 8 Ma. Not only that, but with the metazoans away the microbes will play. Eerily, in post-extinction times the planet spins back into a Precambrian ecology, with widespread evidence for stromatolites and other signs of microbial resurgence. Actually these so-called anachronistic biota are a foretaste of what will happen in about a billion years (Ba) when the sun swells and the biosphere begins to shut down, forever.

Goodness me, was that an impact? Try speaking about the death of dinosaurs without also mentioning the litany of iridium, shocked quartz, fireball layers and tektites. The K/T event is the type example of what happens when a bolide doesn't miss. But here's a funny thing. No other mass extinction can be readily linked to an impact, be it asteroid or comet. Impacts are known, yet seemingly they have little effect. Well, the K/T asteroid was big and ground zero was rich in the mineral anhydrite ($CaSO_4$), so perhaps massive injection of sulphate aerosols into the atmosphere tipped the balance.

The bolide misses and the dinosaurs go home for tea...