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EDITORIAL

Life

There is nothing over which a free man ponders less than death; his wisdom is to mediate not on death but on life.
Spinoza

The preface to Erwin Schrödinger's book *What is Life? The Physical Aspect of the Living Cell* (Cambridge, 1944) contains the quotation from Spinoza, setting the stage for a famous analysis of biology, particularly heredity, by one of the founders of quantum mechanics. Schrödinger's book, based on a series of lectures at Trinity College, Dublin, delivered in the middle of the war years, 1943, was influential in persuading many physicists to look towards biology in the hope of discovering new laws of Nature. Schrödinger phrased his questions clearly: 'The large and important and very much discussed question is: How can the events *in space and time* which take place within the spatial boundary of a living organism be accounted for by physics and chemistry?'. He was emphatic in stating that 'the obvious inability of present-day physics and chemistry to account for such events is no reason at all for doubting that they can be accounted for by those sciences'.

To Schrödinger, the fidelity of the hereditary process displayed a remarkable degree of determinism, in contrast to the indeterminacy so favoured in quantum mechanics and the 'probability mechanisms' in physics. In his lectures, Schrödinger highlighted the 'Habsburger Lippe', a peculiar, inherited disfigurement of the lower lip of the members of Austria's Habsburg dynasty; a feature which he termed as 'a genuine Mendelian allele'. In analysing the transmission of genetically coded information to successive generations, Schrödinger noted: '. . . the gene has been kept at a temperature around 98°F during all the time. How are we to understand that it has remained unperturbed by the disordering tendency of the heat motion for centuries'. He went on to worry about the structure of chromosomes, influenced clearly by C. D. Darlington's book, *The Handling of Chromosomes* (Allen and Unwin, 1942). At a time when Oswald Avery's clear demonstration of DNA as the 'pneumococcal transforming principle' was still a few years into the future and a decade was to pass before the Watson–Crick structure of DNA, Schrödinger's musings focused attention on biology as science's new frontier. He was particularly struck by the irregularity and complexity of biological structures, leading to his famous characterization of the 'chromosome fibre' as an 'aperiodic crystal'. To him the inanimate, periodic crystals of physics and chemistry were profoundly different from the rich tapestry that he foresaw in the 'aperiodic crystals' of biology. Despite the uncertainties of the times, Schrödinger optimistically concluded: 'In the light of present knowledge the mechanism of heredity is closely related to, nay, founded on, the very basis of quantum theory'. He summarized the most important attributes of biology: 'The most striking features are – first, the curious distribution of the cogs (chromosomes) in a many celled organism . . . and secondly, the fact that the single cog is not of coarse human make, but is the finest masterpiece ever achieved, along the lines of the Lord's quantum mechanics'.

Over half a century has passed since Schrödinger's analysis. In the intervening years, molecular genetics has witnessed more than one revolution. Biology, once a collection of disparate disciplines, and the molecular sciences, physics and chemistry, have integrated in a manner that would have been impossible to foresee in the 1940s. The genome analysis projects of the 1990s are rapidly providing a wealth of molecular detail, as diverse organisms succumb to the power of modern DNA sequencing techniques. The relationships between organisms and the interplay between mutation and natural selection in evolution are clearly becoming understandable in molecular terms; a language that clearly derives its grammar from chemistry and physics. We are, in fact, wonderfully positioned to ask Schrödinger's question once again: 'What is life'.

The year 1999 provided scientific journals with a unique opportunity to bring out special issues, devoted to retrospective analysis and sometimes, a little bit of uncharacteristic speculation about the future. In a marvellous 'Millennium issue', *the Philosophical Transactions of the Royal Society (Biological Sciences)*, a journal with hoary traditions dating back to 1665, examines, in a collection of essays, the state of biology on a very broad front. Of particular interest to our present theme is a thoughtful essay entitled, 'Life: past, present and future', by Kenneth Nealson and Pamela Conrad, which traces 'the connection between life and planetary geochemistry, the interaction between these two forces and the pattern of evolution seen in both' (*Philos. Trans. R. Soc. London*, 1999, **B354**, 1923–1939). These authors highlight a view of the planet that is particularly 'prokaryote-centric', a tribute to the myriad, invisible, micro-organisms that constitute an overwhelming majority of living creatures on earth. The prokaryotes, single-celled organisms, lacking a membrane-limited cellular nucleus, are distinguished from their apparently more sophisticated 'eukaryotic counterparts by their toughness, tenacity and metabolic diversity'. Views of life on earth, which centre most often on *homo sapiens* and the few plants and animals that humans fear or cherish, ignore the teeming multitudes of adaptable organisms, that are capable of surviving almost any conceivable man-made or natural disaster. Some organisms, like the radiation insensitive bacterium, *Deinococcus radiodurans* R1, have already drawn the attention of the genome hunters (O. White *et al.*, *Science*, 1999, **286**, 1571–1577). Nealson and Conrad offer a definition of life and highlight its major attributes: (i) Life has some structure, with hardware for energy conversion. (ii) Life has unique chemistry. (iii) Life strives to replicate with fidelity. (iv) Life evolves; mistakes during replication permit inbuilt variability. (v) Life consumes energy from the environment. (vi) Life must develop some means for escaping from its own metabolic end products.

While the tendency of classifiers of life has been to view organisms in terms of structure, Nealson and Conrad prefer to think in terms of 'energy flow and metabolic capacity'. Their classification into functional groups is provocative, as they divide the living world into 'physicists, chemists and biologists'. The physicists are 'those organisms that use physical sources of energy such as light or heat (e.g. photosynthetic organisms); the chemists 'use chemical energy, either organic or inorganic', while the biologists are 'organisms that feed on other organisms, using behavioural adaptation to gain organic carbon, which they use as chemists'.

The growing body of 'extremophiles', prokaryotic micro-organisms, that have adapted to survive under conditions generally thought to be incompatible with life, may provide important clues to the 'evolutionary past' of our planet and may allow us to think of life elsewhere in the Universe. According to Nealson and Conrad: 'In essence prokaryotes spurn life as biologists while optimizing their skill as chemists'. It is this ability of rugged and adaptable micro-organisms to survive the harshest, most inhospitable and bizarre chemical environments, that makes them the best candidates for existence in extraterrestrial environments, which may be probed by man in the not-too-distant future. The Mars Surveyor programs slated for 2003 and 2008 may indeed be a beginning.

Interestingly, discussions of extraterrestrial life have now been consigned to the fringes of science and do not seem to attract much attention amongst the lay public. In the early and middle years of the 20th century, science fiction revolved around the possibility of life on other planets and the eventual colonization of outer space. It is hard to imagine now that Orson Welles' radio rendition of H. G. Wells' 'War of the Worlds' could have caused a public panic in the 1930s. Generations of Americans grew up on the popular TV serial *Star Trek*. Isaac Asimov and Arthur Clarke were read with enthusiasm and no one who watched the late Carl Sagan could have doubted that life would very soon be found away from the earth. But times have changed. The spirit appears to have gone from the searches for extraterrestrial life; the thrust for space exploration sinking into the quicksands of technical difficulties and diminishing financial inputs, even in America; clearly a sign that public opinion is turning inward. But to read Nealson and Conrad is to return to the halcyon days of the 1960s and 1970s, when the flush of success of the Apollo moon missions, raised hopes that the search for life on other planets, solar systems and even galaxies appeared to be worth dreaming about. Their conclusions are inspiring: 'The study of past and present life on our planet tells us that life has dramatically impacted the geochemical evolution of the planet, and suggests that if we really understood the intimate relationships of these two processes, then it might be possible to locate life by measuring these effects at scales presently not even conceived. This is the challenge, and this is our future'.

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