HISTORICAL NOTE

Linking life to the quantum—Schrödinger's views revisited

Exactly fiftysix years ago, during February 1943, the theoretical physicist Erwin Schrödinger gave a set of three lectures at Trinity College, Dublin, under the auspices of the Dublin Institute for Advanced Studies (DIAS) on the subject 'What is life?'. Coincidentally Schrödinger himself was fiftysix then, and the subject of quantum mechanics, whose wave-mechanical form he had discovered in 1926, was in its teens. These lectures were published in 1944 (*What is life? The physical aspect of the living cell*, Cambridge University Press), and have long since become a classic of popular science. They have been reprinted any number of times (most recently in 1992 as a Canto Cambridge Science Paperback), and have been reviewed, praised and criticised on scores of occasions. In 1993 a meeting was organized at Trinity College to celebrate the fiftieth anniversary of the original lectures. Quite a record for a tract of barely a hundred pages.

The background to these lectures in interesting. Schrödinger fled his native Austria in 1937 and, after a stay at Oxford, moved to neutral Ireland in 1939; he was to remain there as professor of theoretical physics at DIAS till 1956. In the early 1940s the theoretical physicist P. P. Ewald brought to Schrödinger's attention a 1935 paper by Timoféeff-Ressovsky, Zimmer and Delbrück titled 'The nature of genetic mutations and the structure of the gene'. There was also an obligation for DIAS to arrange an annual public lecture. Schrödinger was so fascinated by the 1935 paper and his own thinking and reading on the subject that he gave the three lectures 'to an audience of about four hundred which did not substantially dwindle'. He further explains that he was inspired by the need to preserve the universality of knowledge. In this age of great specialization, once in a while someone well versed in one area should attempt to build bridges to others, even at the risk of being accused of having inadequate background. In this spirit, he was addressing himself both to physicists and to biologists.

The book consists of seven short chapters, and an epilogue on Schrödinger's Vedantic philosophical views. Right at the start he poses his basic question—'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?'—and immediately gives his conclusion: '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.' In

developing this answer the discussion keeps hovering between physics and biology.

The aim of the first chapter is to show how a physicist, trained in the Boltzmann–Gibbs tradition of classical statistical mechanics, would approach this problem. (Schrödinger himself was a product of the Viennese School founded by Boltzmann.) Faced with the ubiquitous presence of heat noise or random atomic motions, reliable and stable patterns of behaviour appear in a statistical manner only in systems composed of very large numbers of atoms—the $\sqrt{n}$ law of fluctuations is illustrated via several examples (paramagnetism, diffusion, Brownian motion,...), and is also invoked to explain why we are so much bigger than individual atoms. One has to reach values of n of the order of the Avogadro number, about 6×10^{23}, before stability and orderliness appear. The accuracy of statistical laws grows with the number of atoms in the assembly. Chapter 2 then immediately shows that such classical arguments are invalid in the biological realm. The basic mechanisms of heredity—cells, their sizes and chromosomal content, the processes of mitotic and meiotic division with crossover—are briefly and lucidly explained, and the sizes of genes estimated. The upshot is that, far from a value for n of the order of 10^{23}, biology creates and uses molecular structures with no more than about a million atoms, already overcoming heat noise and displaying stable and orderly behaviours. This implies that we are concerned here with new forms of organization of matter not yet (in 1943) familiar to physics and chemistry. The following chapter 3, devoted to mutations, both natural and artificially induced, further reduces the size estimate of the gene to the range of about a thousand atoms. So the great puzzle is: how can an object consisting of just a thousand atoms, maybe even less, show such great permanence (of the order of a few centuries if not tens of thousands of years) and regularity of behaviours overcoming heat noise?

For this, Schrödinger turns in chapter 4 to the quantum theory, with its basic nonclassical features of discrete states, energy gaps and quantum jumps. By now he is able to declare, 'In the light of present knowledge, the mechanism of heredity is closely related to, nay, founded on, the very basis of quantum theory'—a striking statement which could have come only from one of the creators of quantum mechanics! The basic recognition is that the nature of the chemical bond is intrinsically and unambiguously a result of quantum mechanics, and that holds the key. This is a truly remarkable insight, comparable to the way in which Niels Bohr introduced his model of the atom to account for the stability of

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matter, somethings classically ununderstandable. In the case of life and heredity too, Schrödinger saw that a reasonable degree of permanence of structure at the level of the gene could only come from quantum-mechanical principles. The picture emerges of the gene, indeed any large biological molecule, as an 'aperiodic crystal', a concept and phrase brought in earlier. Schrödinger conveys this idea by comparing a machine-made wallpaper pattern repeated in unchanging fashion with a Raphael tapestry embodying thoughtful design. Delbrück's contribution to the 1935 three-man paper mentioned earlier was his model of the gene as a large molecule governed by quantum mechanics and possessing many isomeric states, with transitions between them—mutations!—determined by energy differences and temperature. This model is taken up in chapter 5 and an effort is made to show that its main features explain available data on mutation rates, both natural and induced, quite satisfactorily.

Having approached the problems of gene stability, mutations and orderliness in this way, the question that remains for chapter 6 is: how do biological processes 'evade' the second law of thermodynamics, and retain and reproduce existing order? Again Schrödinger points to a consequence of quantum mechanics, the Nernst heat theorem, which shows that the entropy of any system vanishes at the absolute zero of temperature. He contrasts two ways of creating order and stability: from disordered heat motion to order by the classical statistical-mechanical '$\sqrt{n}$ route'; and from order to order by retention as exemplified by life processes, thanks to quantum-mechanical principles. Indeed he concludes by referring to chromosomes as 'cogs of the organic machine', and as for the gene, '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'.

Schrödinger's account is many decades old, and enormous progress has taken place since then in the areas and questions he touched. He has often been criticised for major omissions: his knowledge of genetics was from a very narrow set of sources; he ignored the roles of enzymes, catalysts and complementary structures; and 'what was true in his book was not original, and most of what was original was known not to be true even when it was written' (Perutz). Much later, in his own Tarner Lectures on 'Origins of life', Freeman Dyson appreciatively points out that Schrödinger restricted himself mainly to the problem of replication, and avoided linking it up to metabolism, or even asking the question (wisely at that juncture) of how life arose in the first place.

But Schrödinger spoke (and wrote) to convey his fascination for the subject, and to express what seemed important to him at that time as a physicist. Two of his original ideas have become—after the discovery of the structure of DNA in 1953—parts of modern biology: that the gene is best viewed as an aperiodic polymer, and that its message for development and reproduction is expressed in some code. And while the degree of influence may vary from person to person, he seems to have inspired many (physicists included) to turn to problems of modern biology: Maurice Wilkins, James Watson, Joshua Lederberg, Seymour Benzer, Francis Crick, ... Compared to Niels Bohr's expectation that the Complementarity Principle of quantum mechanics would become indispensable for the understanding of life (which thought turned Max Delbrück from physics to biology), Schrödinger's general ideas seem to have come much closer to modern biology, and had a more tangible impact. He succeeded in showing that some of the basic questions of biology could be phrased—and phrased eloquently—in the language of physics, and this was invaluable.

Schrödinger has also been criticised for having treated his interest in this subject as a passing fancy—he got deeply involved in it for a while, expressed his views to a general audience, but did not seriously follow up what he had begun and instead turned to other interests. But then, such is the nature of a polymath functioning to preserve the universality of knowledge. Who today would wish to say that *What is life?* should not have been written?