WHY DNA?

Information is central to the evolution of biological complexity, a physical system relying on a continuous supply of energy. Biology provides superb examples of the consequent Darwinian selection of mechanisms for efficient energy utilisation. Genetic information, underpinned by the Watson–Crick base-pairing rules, is largely encoded by DNA, a molecule uniquely adapted to its roles in information storage and utilisation. This volume addresses two fundamental questions: First, what properties of the molecule have enabled it to become the predominant genetic material in the biological world today; and second, to what extent have the informational properties of the molecule contributed to the expansion of biological diversity and the stability of ecosystems. The author argues that bringing these two seemingly unrelated topics together enables Schrödinger's *What Is Life?*, published before the structure of DNA was known, to be revisited and his ideas examined in the context of our current biological understanding.

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FROM DNA SEQUENCE TO BIOLOGICAL COMPLEXITY

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Preface

This book was first conceived many years ago over a dinner on the banks of the River Weser with my long-term friend and colleague Georgi Muskhelishvili simply as an exploration of the unique properties of the DNA polymer that could explain its predominance as the currently preferred genetic material. But during the subsequent, very extended, gestation of the concepts, the implications of the capacity of DNA to store information in different ways became more and more apparent. The project morphed in the writing and became a personal intellectual journey to explore the role of DNA as an information carrier in the evolution of complex systems. DNA is precisely that – a carrier or vehicle for two modes of information, and it is that information per se that drives the burgeoning increase in biological complexity.

But first a disclaimer. A book on DNA could cover a vast range of highly topical aspects of modern medical practice, forensics and genetic engineering to name but a few. If you are looking for enlightenment on those and related topics this book is not for you. It is concerned, as the subtitle suggests, with the relationship between DNA, information and complexity and traces the evolution of that relationship from the origin of life.

It is a given that biological systems are subject to the laws of physics, but how do the principles that govern the generation of the immense panoply of biological diversity fit with our understanding of the physical world? More than 60 years ago, in the 1940s, three substantial cornerstones of this problem were put in place. In 1946 in *What Is Life?*, the Nobel prize–winner Erwin Schrödinger proposed that biological systems, essentially complex chemical systems, evolved by using energy to minimise entropy – or in his terminology to increase *negentropy*. At about the same time Claude Shannon developed his 'Mathematical Theory of Communication', derived from considerations of the efficiency of the transmission of information in undersea cables, while John von Neumann distinguished between different ways of encoding information. Meanwhile in the laboratory, Oswald Avery and his collaborators realised that a preparation highly enriched in DNA from the bacterium *Pneumococcus* could transform a rough-coated bacterium to a smooth-coated one, an early example of using DNA for genetic manipulation. In the biological context these strands coalesced with the discovery by Watson and Crick of the structure of DNA and their realisation that the sequence of bases in the molecule could constitute a heritable genetic blueprint. Since then the mechanisms by which the information encoded in DNA is utilised and manipulated have been largely elucidated. But even knowing that the DNA molecule is the fundamental carrier of genetic information in the biological world and how that information is used still leaves interesting questions. What is it about this molecule, and not other similar ones, that has driven its selection as the principal genetic material? At the most fundamental level is it that it is simply slightly different, and therefore distinguishable from the closely related RNA? An equally fundamental issue is why biological systems – molecular assemblies, organisms, ecosystems – tend to increase in diversity and complexity over evolutionary time. This phenomenon necessarily parallels an increase in the amount of information carried by the ensemble of associated DNA molecules. But is there a principle driving these expansions that is compatible with Schrödinger's original insights?

If the evolutionary increase in organisation is driven by energy, its primary source, usually light, is processed by a biological system acting as a whole. But an increase in organisation implies a concomitant increase in information, and ultimately this information is encoded in DNA. And so appreciation of the full implications of *What Is Life?* includes not only an understanding of DNA structure and genetics but also, at the other extreme, of how ecosystems and even complex cosmological systems work. In his preface Schrödinger included the apology:

> But the spread, both in width and depth, of the multifarious branches of knowledge during the last hundred odd years has confronted us with a queer dilemma. We feel clearly that we are only now beginning to acquire reliable material for welding together the sum-total of what is known into a whole; but, on the other hand, it has come next to impossible for a single mind fully to command more than a small specialised portion of it. I can see no other escape from this dilemma (lest our true aim is to be lost forever) than that some of us should venture to embark on a synthesis of facts and theories, albeit with second-hand and incomplete knowledge of some of them, and at the risk of making fools of themselves.

To me this caveat seems even more apposite now and the risks even greater. Biological science now encompasses an even greater number of specialisations, each requiring expert knowledge and accompanied by its own esoteric argot that can only be acquired over many years. I have tried to navigate through this minefield but with what success only the reader can judge. Invariably and necessarily so, in science some of the issues I've discussed may be contentious, but if so, I hope that the views argued here will provide a basis for discussion.

Ultimately this is yet another book about the ever fascinating topic of evolution. Perhaps writing this is symptomatic of a common affliction of biologists for, unlike the inhabitants of idyllic Grantchester,

> when they get to feeling old,
> They think of evolution, I'm told.

Acknowledgements

Just as the Cambridge Botanic Garden, where I now work as a guide (and so finally have become more familiar with the joys of botany), can be thought of as a cradle of evolutionary thought, the Laboratory of Molecular Biology (LMB) was a cradle for molecular biology and, of course, DNA. Importantly, during 44 years there, LMB was a melting pot of creativity. Discussions and collaborations with many fellow scientists – including students and postdocs – shaped my outlook – most notably including those with Horace Drew, whose DNA-centric perspective challenged my more biological approach. My scientific debt to LMB is tremendous. I believe that LMB by example taught me to think as a scientist. Over half a century ago, Francis Crick's crystal-clear exposition of the progress of the 'wobble' hypothesis in successive seminars was especially influential.

And also my gratitude to the wider scientific diaspora. The essence of science is – or should be – that when your ideas are challenged, you are forced to think more clearly and so I am extremely grateful to those who, during my scientific career, took issue with, to them, some of my perhaps more speculative notions. My experience is that the outcome of such apparent disagreement is often that both points of view are largely correct but incomplete. Often scientists think they've done the same experiment as someone else but have actually performed a completely different experiment. The consequent synergistic synthesis then adds substantially to an understanding of the problem. There are so many scientific friends who have sustained and inspired me over the years that I cannot acknowledge them all here, but special mentions must go to the chromatin group in the Department of Biochemistry at Cambridge and to those erstwhile colleagues from my time at Harvard who remain in touch.

In the wider world, included amongst those who have led me onto paths I might not otherwise have taken are Ernesto Di Mauro, who first introduced me to DNA topology and the problem of the origin of life; Henri Buc and Malcolm Buckle, who taught me that physics is crucial to the understanding of biology; and Georgi Muskhelishvili, who encouraged me to think holistically and who more than anyone else was responsible both for the genesis of this book and also for the development of many of the ideas discussed in it. And of course there was always the element of chance – being in the right place at the right time. Also latterly the DNA sculptures and cosmic thinking of the late Charles Jencks have been inspirational. To my great regret, I was never able to discuss the cosmos with him.

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