A sparkling reminiscence

What Mad Pursuit: A Personal View of Scientific Discovery. Francis Crick. Basic Books, New York. Price $ 16.95. 182 pp.

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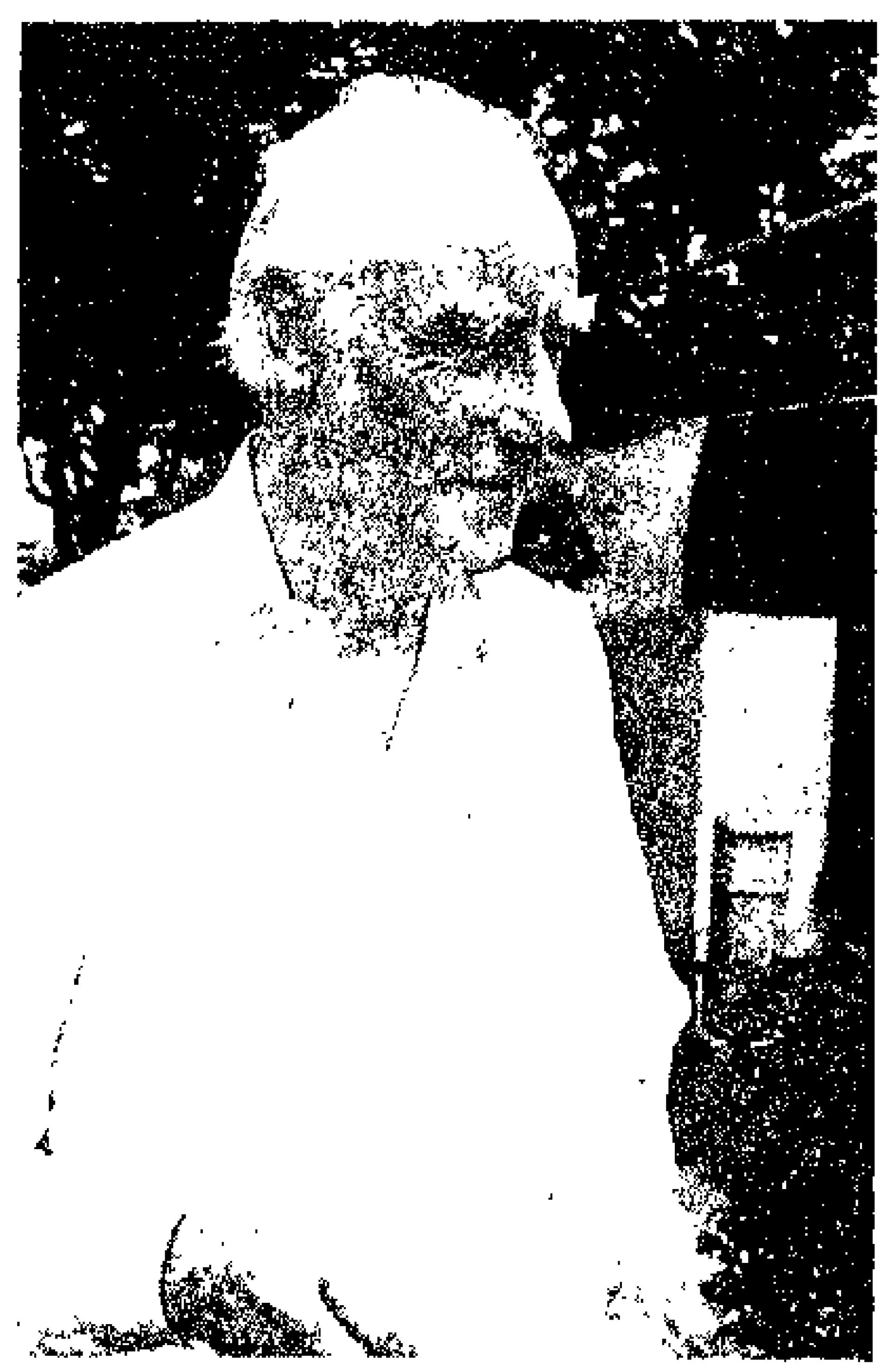
This is a very difficult book to review. Not because it is difficult to read, but for exactly the opposite reason: it is written in such an engaging and lucid style, with so much that is both new and interesting, that only reading the book in its entirety could give one a feeling for the richness of its contents. Having made this apology in advance, let me say that the book is Francis Crick's account of the early days of molecular biology and his central role in shaping the field. Told and retold as it has been a number of times, the history of how the structure of DNA was unmasked does not take up much space (though even here one comes across surprises, as for instance Crick's feeling that Watson 'stumbled on the correct base pairs' in DNA without Chargaff's rules being in the forefront of his mind). An autobiography occupies much of the prologue and bits and pieces of the main text. The chief intellectual thrust of the work, its flesh and blood so to speak, is made up of Crick's views on science (biology in particular) and, related to this, on the implications of evolution by natural selection being *the* predominant agency which has moulded the detailed properties of living forms. What I will proceed to do is to first give an indication of the contents in roughly serial order and follow it up with a description of what Crick has to say about the importance of understanding the role played by natural selection.

Francis Crick was born in 1916 into a middle class English family of modest background. His taking up a career in science seems to have been a matter of some financial risk, and it needed the support of relatives to see him through his starting days in research. An early loss of faith in Christian religion is claimed to have played a dominant part in shaping the course of his scientific life. A bachelor's degree in physics led to research on 'the dullest problem imaginable', measuring the viscosity of water under pressure at different temperatures. War and a few slices of luck intervening, Crick found himself in the Cavendish Laboratory in Cambridge working with Max Perutz on a newly funded project in the essentially unexplored area of X-ray diffraction as a tool to study protein structure. It was not *all* luck by any means. In a chapter titled *The gossip test* Crick describes how, by deciding that if you talked about something a lot it must mean that you were really interested in it, he knew he had to get into biology. Here, the toss-up was between (in modern terms) molecular biology and neurobiology. Both subjects were faintly mysterious; by virtue of being at the fringes of science as then known, appeals to faith would seem to be natural to anyone confronted with



the puzzles of life and mind. These, therefore, were important areas for science to examine. His opposition to religious dogma having helped in narrowing down the field thus, molecular biology won the contest (though in later years Crick was to turn increasingly to problems of the brain). An apprenticeship in the school of Bragg, Perutz and Kendrew—one gets hints of the exasperation, at times, to which his voluble clarity in analysing problems seems to have driven Lawrence Bragg—led to a thorough grounding in X-ray crystallography. Close familiarity with the reasons for the failure of the Cavendish group in its competition with Pauling for predicting the α-helical structure of proteins gave Crick invaluable lessons. Chemistry was important (and, one might add, Linus Pauling was important), careful model building was important, but it was even more important to know how to distinguish the essential from the non-essential *before* building a model. The famous meeting with Watson, recognition on the part of both that an understanding of the structure of DNA was crucial if genetics was ever to unite with biochemistry, and an obstinately persistent attack on the problem culminated in the stunning triumph of the double helix. DNA became, and continues to be, the paradigm for structure as the key to biological function [it is astonishing in retrospect that so much successful and interesting genetics was (and is) done without any role needing to be assigned to the chemical nature of the gene]. Much hard work was to follow, first in attempting to unravel the genetic code and then in the *tour de force* which showed that the code was a triplet. Perhaps here it is pertinent to allude to the remark (made towards the end of the book in relation to science in California) that one should not work so hard as to leave no time for serious thinking. DNA soon became part of popular folklore, probably not without a measure of appreciation of its importance, as attested to by a lapel-button vendor in New York: 'Dat's the gene'. Pitfalls are catalogued; the misleading hint from comma-less codes which succeeded in producing the magical number of 20 amino acids, the false assumption that since most of the RNA in cells was found in ribosomes, *that* had to be the sought-for messenger between DNA and proteins. An early triumph, and tribute to Crick's knowledge of, and faith in, the rules of steric chemistry was the prediction that there had to be an adaptor in order to ensure that the message in a triplet actually led to a specific amino acid being incorporated into the protein. Here the remark, made in a different but related context apropos Schrödinger's *What is life*, is of interest: '... like many physicists, he knew nothing of chemistry.' Somewhat unexpectedly, Crick says that he is reasonably sure that he would not have solved the structure of DNA by himself. Rosalind Franklin could have: she was only two steps from the solution. But she was a bit too cautious, lacking Watson's overriding interest in getting the answer, and moreover in getting it as quickly as possible. As mentioned in the review of S. Chandrasekhar's book (see *Curr. Sci.*, **59**, 284), the mathematician Harish-Chandra had something very apt to say about such situations: '... Knowledge, by advocating caution, tends to inhibit the flight of imagination. Therefore a certain naiveté, unburdened by conventional wisdom, can sometimes be a positive asset.'

One section of particular interest deals with Crick's attitude to the possibility of non-conventional structures of DNA. His feeling is that the measurements of linking number in circular DNA molecules have put to rest any claim for attention that side-by-side models might have possessed. One wonders whether future experiments will continue to justify the validity of this belief, considering that none of the polymorphic DNA structures put forward hitherto affect the fundamental realities of base pairing and antiparallel strands; surely not all naturally occurring forms of DNA have been examined. The story of the structure of collagen, on which pathbreaking work was done by G. N. Ramachandran and associates, is contrasted with the story of DNA: 'Its discovery had all the elements that surrounded the discovery of the double helix. The characters were just as colourful and diverse, ... yet nobody has written even one book about the race for the triple helix. This is surely because, in a very real sense, collagen is not as important a molecule as DNA.'

The latter part of the book contains mention of an excursion into developmental biology which was pulled up short by the realization that while gradients were all very well, there seemed to be no clue (luckily not true any more) as to what they were made of. Then there are references to brief but illuminating forays into contemporary molecular biology and, in some detail, discussion of a continuing active interest in brain mechanisms and perception, especially visual perception. The book ends with two very short appendices on the basis of molecular biology and an outline of the genetic code.

As already mentioned, the theme of natural selection provides an underlying thread of unity to this book. This is explicitly stressed at times, but more often it comes into play in the form of a short but telling aside. Crick draws implicit attention in these asides to what Dobzhansky has asserted: Nothing in biology makes sense except in the light of evolution. This is a profound statement and, like all profound statements, can be discussed at many levels. At its heart is the fact that life as we know it is the result of an enormous series of accidental steps. Each step represented an unpredictable, minor, tentative attempt on the part of a living creature to hazard a guess as to the best possible course for it to take to improve 'itself' by producing progeny better able to cope with the environment than it could. But the challenges posed by the environment—both living and non-living—keep changing with time (in large part as a consequence of evolution itself). Because of this all living forms of today contain within themselves, irreversibly frozen in their genetic makeup, solutions to problems which no longer exist. This historical baggage manifests itself as complexity of a staggering order. The simple evolutionary step which forms part of an eventual complexity contains within it no ultimate sense of purpose or meaning. All evolution can do is to provide short-term solutions to immediate problems, solutions that are compatible with what is already present—not solutions that are optimal or ideal or innovative. In the words of Francois Jacob, evolution is a tinkerer. What decides *which* solutions exhibit a relative advantage in the short run, and so prevail in the long run, is natural selection. On top of this, we have sufficient evidence today to reasonably conjecture that accidental catastrophes have often reset the stage for further evolution. Clearly, any attempt to explain the design of a living creature by applying to it criteria such as elegance and aesthetic beauty which are said to fulfil an important role in theoretical physics (because they are born out of the 'necessity' of physical nature to conform to deep mathematical laws) is unlikely to be useful. In fact the three-dimensional structure of a folded polypeptide might even be described as 'ugly'; the reason is that 'Elegance, if it exists, may well be more subtle and what may at first sight seem contrived or even ugly may be the best solution that natural selection could devise.' An interesting distinction is made with regard to this. There are 'simple' structures, like DNA or the α-helix, which must have arisen very early in evolution and which would therefore be '... nearer to physical chemistry than biology. At that level there are few alternatives for evolution to work on.' It is this that explains the 'intrinsic beauty of the double helix'. On the other hand, structures at higher levels are necessarily more complex because of evolution; the clues to understanding them must lie (in a sense) in their biology, not in their physics or chemistry. Now I must quote extensively: 'What gives biological research its special flavour is the long-continued operation of natural selection.' However there is a curious paradox. 'It might be thought, therefore, that evolutionary arguments would play a large part in guiding biological research, but this is far from the case ... evolutionary arguments can be used as *hints* to suggest possible lines of research, but it is highly dangerous to trust to them too much.' This leads Crick to the role of theory. 'To produce a really good biological theory one must try to see through the clutter produced by evolution to the basic mechanisms lying beneath them, realizing that they are likely to be overlaid by other, secondary mechanisms.... If elegance and simplicity are, in biology, dangerous guides to the correct answer, what constraints can be used as a guide through the jungle of possible theories? ... a deep and critical knowledge of many different kinds of [experimental] evidence is required, since one never knows what type of fact is likely to give the game away.'

These themes, the one of natural selection and the other of likely pitfalls in constructing theories in biology, are carried over into an epilogue containing an account of Crick's more recent work. He is worried that people who 'inflict' models of the brain are essentially interested only in the pretty results that computer programs can produce, not so much in whether the brain actually works in accordance with their model. 'Intellectual snobbery makes them feel they should produce results that are mathematically both deep and powerful and also apply to the brain. This is not likely to happen if the brain is really a complicated combination of rather simple tricks evolved by natural selection.'

This is a book to be read more than once; the beauty of its style masks much hard science and subtle thought. In spite of having heard it many times from others, the story of DNA as told by Crick still makes a marvellous read. A sense of clarity of thought combined with an equally strong sense of commitment and overlaid with the deep power of his thinking runs through the entire book. One sees that Crick possesses that all-important but dismayingly elusive knack of distinguishing what is significant from what is not. His confidence in the power of structural chemistry to unravel the functioning of biological molecules is unflagging. At the same time, warning signals sound constantly to keep possible evolutionary arbitrariness in mind. Both text and photographs give the impression of a gregarious personality who enjoys life as much as he enjoys doing science. A lightness of touch is present all along—no trace of ponderousness, no attempt at heavy philosophising. But there is self-assurance of a high order. On more than one occasion one is made to sit up with the thought that *this* is what Watson must have meant when he wrote his famous opening sentence in *The Double Helix*, but on the other hand, one feels strongly that the immodesty, if that is indeed how it appeared to Watson, was entirely justified. After all, the role of Francis Crick in the rise of molecular biology was both unique and unsurpassed.

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Advances in condensed materials

Recent Advances in Condensed Materials. Special Issue of the Journal of Scientific Research of the Banaras Hindu University. D. Pandey and A. V. Lagu eds. 1988. vol. 38. 148 pp.

The eighties have been witness to spectacular advances in condensed materials. If the discovery of quasicrystals in 1984 revolutionized our scientific understanding of the solid state, the discovery of high-temperature superconductors in 1986 promises technological advances of an unprecedented kind. This elegant volume under review captures the spirit of some of these advances through seven articles.

T. R. Anantharaman has written on 'New light alloys and composites through Rapsol technology'. Over a quarter century ago, he returned from the laboratories of Professor Pol Duwez and laid the foundation for the development of science and technology of rapid solidification in India. Though the tale has been told before, it is always refreshing to read how the employment of high rates of cooling of the order of a million degrees Kelvin per second bring about metastability in alloys. This paper reviews development of aluminium, magnesium and titanium alloys as well as metal matrix composites.

In the second paper, P. Ramachandrarao describes one particular metastable effect, namely the extension of solid solubility achievable through rapid solidification. He elucidates the thermodynamic and kinetic considerations and gives a particularly succinct description of solute trapping.

Quasicrystals were discovered just over five years ago by D. Shechtman and coworkers in rapidly solidified alloys of aluminium and manganese. They display crystallographically forbidden symmetries such as five-fold rotational axes and have thrown a major challenge to our understanding of the atomic configuration in the solid state. The Banaras school has made impressive contributions to this new and exciting field by synthesizing a new class of quasicrystals based on Mg–Zn–Al alloys. In their article on 'Quasicrystallography', Shrikant Lele and R. K. Mandal present an interesting and rigorous description of this subject. Higher dimensional periodic lattices give rise to quasiperiodic lattices in lower dimensions. The projection formalism is developed in a systematic fashion and used to illustrate their own outstanding contributions to the development of decagonal quasicrystals and vacancy ordered phases by projection of non-cubic lattices from six dimensions.

D. Pandey, V. S. Tiwari and A. K. Singh have chosen to deal with just one high-temperature superconductor, namely $YBa_2Cu_3O_{7-y}$. They describe the orthorhombic structure and draw attention to the occurrence of CuO_2 sheets as well as the Cu–O chains. Subtle features such as ordering of oxygen atoms, microtwinning and ordering of planar extended defects are emphasized. The paper also brings into context their own contributions of X-ray line profile analysis of ceramics prepared by a semi-wet or conventional route.

The phenomenon of polytypism has been a major research area of the Banaras school of physicists for over three decades. The pioneering researches of A. R. Verma and P. Krishna are well recognized for structural modelling and refined X-ray investigations. In D. Pandey's continuation of this tradition X-ray studies of the transformation among close-packed structures have been addressed. V. K. Kabra, representing the next generation of research scholars has written a powerful paper along with D. Pandey on the 'Kinetics of solid state transformation using Monte Carlo simulation studies'. They show that the 2H to 6H transformation in SiC can be successfully modelled using Kawasaki dynamics. In addition they stumbled upon a new state where long range ordering can occur without short range order correlations. It is to be hoped that the authors will further elaborate on this topic.

In a brief contribution, Lakshman Pandey describes the design of a sample probe for pulsed NMR studies on piezoelectric materials.

The final paper by Yashwant Singh is an exposition on the density-functional theory of freezing and the properties of ordered phases. It follows the innovative approach initiated by T. V. Ramakrishnan and M. Yussouff and applies it to the freezing of simple and complex fluids as well as glass transition.

In just under 150 pages the authors have covered a fascinating range of topics. All the articles are written in an authoritative fashion. The editors had indicated that they embarked on two experiments in fashioning this issue: the use of desk top publishing and the development of a focal theme. The appearance of the issue is pleasing and the focus is maintained. The Kulgeet rejoices that the Banaras Hindu University is the capital of all knowledge. It is to be hoped that future issues of the journal, will focus on other areas, where the Varanasi scientists have made prominent contributions. Indeed this thematic issue can serve as a model for publications brought out by other Indian universities. The editors are to be congratulated for their accomplishment.

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