Through a magic casement

John Cairns

What Mad Pursuit: A Personal View of Scientific Discovery. By Francis Crick. *Sloan Foundation Science Series/Basic Books: 1988. Pp. 182. $16.95. To be published in Britain in Spring 1989 by Weidenfeld & Nicolson.*

CRICK's autobiography starts off as the straightforward story of an intelligent boy, brought up in a Protestant environment, who finds himself drawn to atheism, and thence to physics, in the face of his family's unquestioning religious beliefs.

When the war ended in 1945 he was 29 years old and, as a physicist, had successfully designed acoustic mines that were believed to have sunk many hundreds of ships — hardly, one would think, the ideal preparation for a Nobel prize in medicine. The government wanted him to continue designing weapons, but the curiosity of the agnostic was a stronger force and Crick decided that the most interesting subjects were "the borderline between the living and the nonliving, and the workings of the brain". At this point, he received a lot of advice from such a distinguished list of people that the reader comes to realize that Crick must have done remarkably well in his wartime work at the Admiralty, though this is something he modestly glosses over. After receiving the experts' conflicting opinions, he spent two years fruitlessly studying the physical properties of cytoplasm. Finally, in his thirties, he went to join a new Medical Research Council unit, set up in Cambridge for the study of protein structure by X-ray diffraction.

Now, at last, his career was underway, and the tale moves from one excitement to the next — from protein structure to DNA structure, and from there to the coding of protein synthesis. It is, by now, a well-known story. The double helix is the hero, of course, and what we are being given is yet another version of the leaf-fringed legend that haunts about its shape (for, if Crick can choose to take his title from Keats's *Ode to a Grecian Urn*, I too should be allowed to rummage about in the same poem). Finally, the sedges of Cambridge wither, and he retreats to California and the Salk Institute to wrestle with his other chosen subject — the brain.

That is the simple synopsis. But the book is much more than an autobiography. Its primary concern is with the place of ideas and theory in the biological sciences. Watson and Crick were impelled forward by an Idea. Crick points out that, even before they saw the meaning of the structure of DNA in 1953, Watson had coined the phrase "DNA makes RNA makes protein"; the magnitude of that leap in understanding will become clear if you look at a contemporary review of protein synthesis such as Borsook's article in the 1953 volume of *Advances in Protein Chemistry*. Even as they were wrestling with the structure of DNA, Watson and Crick were starting to wonder how *base sequence* could be translated into *amino acid sequence*; to see this in its proper context, you should remember that when Itano and Pauling described the electrophoretic abnormality of sickle cell haemoglobin, in 1947, they concluded simply that the mutant gene was "through some series of reactions. . . introducing the modification into the hemoglobin molecule that distinguished sickle cell anemia hemoglobin from the normal protein".

A youthful Francis Crick — given time to think.

Once the structure of DNA became clear, Crick's attention turned to the coding problem and he was led to propose the Adaptor Hypothesis, several years in advance of the actual discovery of transfer RNA. Before any part of the genetic code had been deciphered, Crick and Brenner had shown it was a commaless, non-overlapping triplet code, Brenner had demonstrated that there were chain-terminating signals, and the two of them had deduced the existence of messenger RNA.

Much of the book is devoted to the important part played by speculation in the history of molecular biology. This aspect was largely missing from Watson's two best-sellers on the subject — *The Molecular Biology of the Gene* and *The Double Helix*; in the first, Watson gave a dazzling account of what might be called the inventorial view of molecular biology, and in the second he wrote almost exclusively about the personalities and scandals and the quest for fame and fortune. Crick describes what now most interests him about those few years in the 1950s, when a small group found themselves in the happy position of being the first to think usefully about the storage and control of biological information. It was one of those rare moments when there is a revolution in our understanding of the world around us.

In terms of the history of science, the sequence of thoughts behind each of the discoveries was as interesting as the actual discoveries themselves. Crick points out that most of the ideas they had about the coding problem proved to be wrong, and this leads him into a discussion of the continuous, delicate interplay between hypotheses and facts — what class of hypothesis is needed for each particular occasion, and how one should decide which facts are important and which are misleading. He goes on to describe what he thinks is the key difference between successful theories in biology and in physics. "Biologists must constantly keep in mind that what they see was not designed, but rather evolved. Physicists are all too apt. . . to concoct theoretical models [in biology] that are too neat, too powerful and too clean."

Here perhaps he could again have gone back to Keats, who wrote that the true mark of intelligence is an unwillingness to fill in the many gaps in our understanding with a set of irrational beliefs. Keats called it "negative capability". I wonder if that is not the essence of Crick's brilliance and clarity of thought. Certainly, it would account for his atheism and for his present distaste for much of what is called cognitive science.

Part of Crick's interest in that brief period of intense theorizing may relate to his current preoccupation with the brain and the problem of consciousness. The human brain finds things out by blundering around between various possible hypotheses. On certain rare occasions, a group of scientists suddenly find themselves looking, with a wild surmise, at some uncharted sea, and that is a time when their thoughts have to run far ahead of the facts. So perhaps there is something special to be learnt from the successes and failures of all those theories of the 1950s. Is Crick possibly thinking about a theory of theories, that might lead to another way of thinking about consciousness? ▶

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Autobiography is a treacherous undertaking. The more you cover up, the more you are likely to reveal. Someone once wrote that he had never seen Francis Crick in a modest mood; it was a memorable phrase. Now, at long last, we are hearing from the man himself. Only in one respect do I think him misleading and immodest. He makes it all seem too easy. I have watched him at several Cold Spring Harbor symposia. He would sit in the front row, listen intently to every talk, interrogate, dominate, and end the week in a state of exhaustion. It seems for him there is nothing between rest and overdrive. This capacity for prolonged and intense concentration is one side to his character that does not appear in the book.

Many readers will be struck by the thought that Crick belongs to a bygone age, when biologists were given time to think. What granting agency today would give several years of support to a young scientist who just wanted to build models? What 30 year old would now dare to embark on such a perilous pursuit? □

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"Amoebas at the start were not complex They tore themselves apart and started sex"

Mark Ridley

The Evolution of Complexity By Means of Natural Selection. By John Tyler Bonner. *Princeton University Press:1988. Pp.260. Hbk $40; pbk $13.95.*

WE DO NOT really know how many species are alive today. Until recently, the estimate was 'a few' million, a rough extrapolation from the fact that taxonomists have described about a million modern species. The latest estimate is a factor of ten higher, at about 3–4 $\times$ 10^7, the increase having been inspired by detailed sampling of the beetles in tropical trees.

Therefore, between the origin of life and the modern variety of forms, there must have been more than 30 million different lineages. It is difficult to estimate how many more. George Gaylord Simpson once guessed that 4 $\times$ 10^9 species have lived throughout evolutionary history. His estimate should probably now be revised upwards; but many of those species would have shared the same lineages, so the actual number of lineages must be between the total number of species that have ever lived and the total number alive today. Maybe 10^9 is a reasonable guess. Now, one *but only one* of those lineages runs through a long series of extinct forms from the origin of life to ourselves. A sure method of making many biologists hopping mad is to identify that particular lineage with the 'main line' of evolution or even with evolution itself.

Bonner is not one of those biologists. He is quite happy to talk about the evolutionary 'progression', of 'evolution from small to large' and 'evolution from simple to complex'. He is not interested in all the lineages in which evolution has gone from simple to simple, small to small (for the bacteria are still with us), or even from complex to simple, or large to small. All patterns can be found among the 10^9 lineages available. I therefore found myself repeatedly disagreeing with Bonner. The disagreement, fortunately, is mainly about words. Neither his argument, nor his evidence, concern 'evolution' as a whole; and if every time he says 'evolution' we substitute 'evolution down the one lineage in 10^9 that happens to run from the origin of life to humans beings' it usually makes equally good grammatical, and better biological, sense.

Bonner's first subject is size. From the origin of life onwards, the size of the largest kind of animal or plant present at any one time has increased. There were only unicellular organisms 3 $\times$ 10^9 years ago: now there are blue whales, and there were dinosaurs not so long ago. Bonner explains the trend by what he calls ecological 'pioneering'. If a niche in nature is unexploited, a pioneer ecological species will soon invade it. Likewise, over evolutionary time, species will tend to evolve into places where there is reduced competition. The niches for small organisms have been filled ever since the origin of life, and progressively larger forms have been able to pioneer the niches for larger and larger types. The process, as Bonner discusses, would have been speeded up when sexual reproduction evolved — which explains my titular quotation from Arthur Guiterman. The argument is a form of Darwin's 'principle of divergence', though Bonner does not mention it.

He then shows, in what is the main original result in the book, that the histological differentiation of living things is proportional to their body size. Bonner has compiled estimates of the number of cell types in various kinds of organism. Small, unicellular organisms have one cell type, mushrooms have about seven, squids and Diptera about 55, and vertebrates more than 120. Actually, there is no increase in the average body size between the forms with seven cell types and those with more than 120; but the trend is clear between the end points.

The number of cell types is Bonner's main criterion of organismic complexity. It, like size, will tend to evolve higher extreme forms by the principle of divergence, and Bonner argues that there are advantages in the division of labour too.

The book is not only about why more complex, and larger, forms have arisen later in evolution. Bonner discusses complexity in four areas of biology: genetics, embryology, ecology and animal behaviour. Behaviour is included as the pinnacle of complexity. Bonner likes analogies between principles in different fields, and he is interested, for example, in the abstract similarities between the development of behaviour and morphology. He does not, however, appear to have read J.W.S. Pringle's classic paper of almost 40 years ago (*Behaviour* **3**, 90–110; 1951). Pringle discussed the analogy between learning and evolution, both more deeply and more exactly than Bonner does. Pringle defined complexity in terms of information theory, and noticed that it is characteristic of learning to increase the complexity of an organism's behaviour patterns. Like natural selection, learning increases the frequency of otherwise improbable events and builds up biological complexity as it does so.

Bonner has aimed to write a synthetic work. He draws on a wide range of evidence from the four areas of biology, and almost any biologist will learn something new. It is hardly fair to demand that another whole subject should have been included, but palaeontology is an obvious gap. Bonner has not ignored the fossil evidence, but he has made no use of the modern palaeobiological ideas on long-term evolutionary trends. He discusses trends in size and complexity purely in terms of natural selection, but (as palaeobiologists have pointed out) trends can also arise when a character is correlated with speciation, or extinction, rates. A graph in the book suggests that more complex species have higher extinction rates, although it is difficult to be sure how much of the effect is a taxonomic artefact. If more complex forms do have higher extinction rates, the force of 'species selection' will tend to *decrease* the level of complexity in biological systems.

Bonner has a gentle style. *The Evolution of Complexity* is written for the general biological reader and each concept, such as speciation, is explained in elementary terms when it first appears. He does not go in for any cheap showing off: he only discusses things he is prepared to take seriously, and does not caricature his opponents, or make spurious claims to originality. I doubt whether the book contains any important new insights, but it makes pleasant reading and may direct somebody to a new line of thought on this apparently timeless problem of evolution. □

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