Twists in the Double Helix

The 21st anniversary of the discovery of DNA's structure provokes some intriguing reflections on that epic scientific race

by Kendrick Frazier

"We wish to suggest a structure for the salt of deoxyribose nucleic acid (DNA). This structure has novel features which are of considerable biological interest."

With such teasing understatement began a one-page report in the April 25, 1953, issue of the British journal NATURE. It was the announcement by James Watson and Francis Crick of their discovery of the double-helix structure of DNA, the molecule of heredity. Biology would never be the same again.

Peter Medawar has called the breaking of the genetic code "the greatest achievement of science in the 20th century." Jacob Bronowski in *The Ascent of Man* calls it "the adventure story of science in the 20th century." And Jacques Monod groups it with Mendel's defining the gene as the bearer of heredity, Avery's chemical identification of it, and Darwin and Wallace's theory of natural selection as "without a doubt . . . the most important discoveries ever made in biology."

NATURE (Vol. 248, p. 765) recently celebrated the 21st anniversary of the Watson-Crick announcement by publishing nine articles—some personal and anecdotal, some formal and philosophical—about the discovery and the way molecular biology has been affected. "One thing has become clear," NATURE observes. "A central contribution of the magnitude of Watson and Crick's stirs up the culture of science to a quite remarkable degree, and it is a change in the cultural climate, perhaps more even than the actual discovery itself, which breathes new life into science."

James Watson himself altered the climate of science a bit more in 1968 when he published his book *The Double Helix,* his brash and iconoclastic account of the discovery, portraying the struggles and ambitions of him and his colleagues (and competitors) with a warts-and-all candor that brought a welcome breath of fresh air to the musty archives of scientists' accounts of their achievements.

Who can ever forget his classic opening sentence: "I have never seen Francis Crick in a modest mood." Well, apparently not Francis Crick.

Crick and Watson just after publication of their manuscript on the double helix.

For among the least important but most amusing tidbits in NATURE's recent retrospective is the disclosure by Crick that he once considered writing his own account of the discovery. He planned to title it *The Loose Screw,* and he says he even went so far as to compose what he hoped was a catchy opening: "Jim was always clumsy with his hands. One had only to see him peel an orange. . . ." But then, says Crick, "I found I had no stomach to go on."

In a somewhat similar vein is biochemist Erwin Chargaff's slightly pained response to one of Watson's characterizations of him. In *The Double Helix* Watson wrote: "Chargaff and I glanced at each other in Paris. A trace of a sardonic smile was all the recognition I got when we passed in the courtyard . . . of the Sorbonne." Future science historians take note that Chargaff has a mild disclaimer: "I felt far from sardonic: I was looking for a toilet; but whatever door I opened, there was a lecture room and the same large portrait of Cardinal Richelieu."

Chargaff, dismayed by Crick and Watson's brashness and admitted ignorance of chemistry, jotted down afterwards: "Two pitchmen in search of a helix."

There are some poignant moments in these recollections, such as Linus Pauling recalling his erroneous conception of a three-chain helix structure for DNA. "In hindsight, it is evident that I made a mistake on Nov. 26, 1952, in having decided to study the triple helix rather than the double helix." The error sealed Pauling's fate as the loser in the great race to decipher DNA and win the Nobel Prize. But Pauling believes he probably would have lost the race anyway: "I myself think that the chance is rather small that I would have thought of the double helix in 1952, before Watson and Crick made their great discovery."

Crick acknowledges that the structure would not have remained unrevealed indefinitely. "I doubt myself whether the discovery of the structure could have been delayed for more than two or three years."

Pauling settles on about the same time scale. "It is my opinion that if Watson and Crick had not carried on their persistent effort . . . the discovery

of the double helix, which has led to such great developments in molecular biology, might well have been delayed for several years."

However, some have argued, as Crick notes, "that if Watson and I had not discovered the structure, instead of being revealed with a flourish it would have trickled out and that its impact would have been far less."

Crick doesn't totally go along with the argument: "Rather than believe that Watson and Crick made the DNA structure, I would rather stress that the structure made Watson and Crick. After all, I was almost totally unknown at the time, and Watson was regarded, in most circles, as too bright to be really sound. But what I think is overlooked in such arguments is the intrinsic beauty of the DNA double helix. It is the molecule which has style, quite as much as the scientists."

Crick also provides some interesting sidelights on the writing of the landmark paper announcing the discovery. Apart from its second sentence, quoted at the beginning of this article, and another phrase referring to their proposal of "a radically different structure," its significance would be easy to miss. However, one short sentence added toward the end hinted at the ramifications: "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

Why the sentence was included, and why it was so restrained, illustrates some of the problems scientists have to consider when announcing new results. Crick says the sentence was a compromise. He wanted a full discussion of the genetic implications. Watson did not. Watson feared, periodically, that their structure might be wrong. If so, he didn't want to come off any sillier than necessary. Crick deferred, but insisted that something be added, "otherwise someone else would certainly write to make the suggestion, assuming we had been too blind to see it. In short, it was a claim to priority."

The matter was made academic a few weeks later when Watson and Crick received supporting X-ray evidence from Maurice Wilkens and Rosalind Franklin at Kings College and decided to write a full discussion of the genetic implications in a more speculative paper, published in NATURE on May 30, 1953.

Still, the entire biological community didn't immediately embrace the new ideas, and that also says something about the way science works. Instead, a small but influential group of active scientists took up the task of converting the nonbelievers. "My memory of the early days, says Sydney Brenner of the MRC Laboratory of Molecular Biology in Cambridge, "is that of a small and rather select evangelical movement which often experienced great difficulties in convincing the disbelieving heathen."

"This," observes NATURE, "conforms to a classical view of a seminal idea's acceptance—first accepted by the few, later sweeping all before it." NATURE contrasts it with the revolution in the earth sciences in the late 1960's and early 1970's. "There a whole army was waiting to pick up the central dogma of plate tectonics and make it their own."

And what has been the impact? As Brenner says, the double helix brought the realization that information in bio-

What has science become? A critical view

Not all scientists agree the changes in the cultural climate of science in recent decades have been for the better. As part of its 21st anniversary observance of the discovery of the structure of DNA, NATURE *published an essay by Columbia University biochemist Erwin Chargaff lamenting many aspects of what he considers "the scientific mass society" of today. Excerpts follow, by permission of* NATURE *and Chargaff.*

No one who entered science within the past 30 years or so can imagine how small the scientific establishment then was. Science was small; it was cheap; it was wide open. One could still do experiments in the old fashioned sense of the word. Now, everybody is working away at 'projects' the outcome of which must be known in advance, since otherwise the inordinate financial investment could not be justified. Papers, however, continue being written in the old way, as if the discovery had come after the search.

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The number of very significant scientific discoveries made in the interval between the two world wars was truly enormous. The impulse persisted, or even increased, in the United States up to about 1950 or 1955, and then slackened perceptibly, almost in reverse proportion to the number of new scientists entering the several disciplines.

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It was easy to open new fields and to go on cultivating them; there was no fear of immediate dispossession as is bound to happen now. There were relatively few symposia, and those that existed were not attended almost exclusively by hungry locusts yearning for fields to invade.

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The illusion that what is new is true has distorted the very sense of scientific research. The urge to be 'with it' is incompatible with the search for truth about nature. If the vaunted self-purification of science has broken down some time ago, this is only in part a result of the ever-increasing complexity of ever more poorly described experiments. It is even more a consequence of the pressed and driven mood in which research often is performed now.

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Another consequence of the restricted dimensions of our scientific knowledge at that time, before it was overwhelmed by multiple massive explosions of facts, many of them of the utmost triviality, was that it was still possible to comprehend the essentials of one or even of several sciences. This bucolic security has, I believe, ended: Out of swimmers we have all turned into floaters.

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Before, the biological sciences had each their characteristic faces and their distinct spheres of interest into which they drew different types of scientists. Now, when I go through a laboratory, be it of virology or of developmental physiology, there they all sit before the same high-speed centrifuges or scintillation counters producing the same superposable graphs. There has been very little room left for the all-important play of scientific imagination. *Home ludens* has been overcome by the seriousness of corporate finances.

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[Those who did some of the early basic research on nucleic acids] did their work before the strip-mining of nature had become so prevalent, before researchers had become alienated from the objects of their study. In the tower of forlorness, which the House of Science has become in my time, the inhabitants all speak the same language, but do not understand each other.

. . . Double Helix

logical systems could be studied in much the same way as matter and energy. "It turned genes into chemical objects whose structure and function could be analysed and understood in terms of biochemical machinery."

Suddenly the biological sciences had new elegance and glamour. "The double helix fundamentally changed the image of biology," notes Brenner. "To most young people of my generation the biology taught in universities was a most unattractive subject. It seemed to consist in learning long, dusty lists of Latin names punctuated by cutting up frogs or carrots in long, dusty laboratories. DNA changed all that and turned biology into an exciting, intellectually attractive subject."

This brought bright new students and explosive growth to molecular biology, including massive expansion of government support for science and education, particularly in the United States. Says Brenner: "Watson and Crick may have invented it [molecular biology] but Uncle Sam certainly fueled it."

As for Crick, he says he "enjoyed every minute of it." To convey his own feelings about his participation in such a momentous event in science, Crick quotes the painter John Minton: "The important thing is to be there when the picture is painted." □