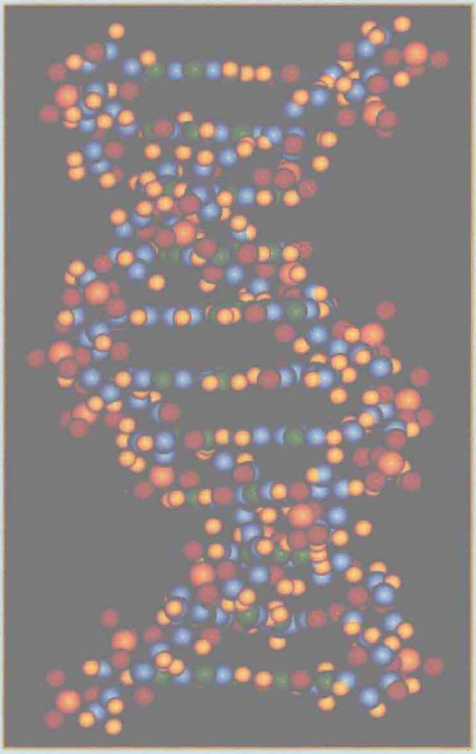
The Double Helix

A Personal Account of the Discovery of the Structure of DNA

James Watson



Edited by Gunther S. Stent

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JAMES D.

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A Personal Account of the Discovery of the Structure of DNA

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Edited by

GUNTHER S. STENT
UNIVERSITY OF CALIFORNIA, BERKELEY

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Preface

The fantastically rapid progress of scientific research in the past decades has had one important, as yet not fully appreciated, cultural by-product: there are now alive many scientists who can look back on their own early work, and that of their contemporaries, from a depth of historical perspective that for scientific disciplines flowering in earlier times had opened only after all the witnesses of the formative stages were long dead. Nowadays, for instance, merely middle-aged molecular biologists have available to them a retrospective view over their field whose range is comparable to that given to a late-eighteenth-century colleague of Joseph Priestley or Antoine Lavoisier who, by some miracle, would have been still active in chemical research and teaching in the 1930s, after atomic structure and the nature of the chemical bond had been fathomed. This deeper personal perspective has brought an existential dimension to the history of science, thanks to which feelings, social interactions, and irrational attitudes are seen to have a much more prominent role in the advancement of knowledge than had been the case previously. Admittedly, the role of "inspiration" in scientific discovery, such as Kékulé's vision in the fireplace of his lodgings of the formula of the benzene ring as a snake biting its own tail, has long been given its due. But the recognition that the very explananda of science, i.e., its "facts," are not objective givens but rather the creation of what Ludwik Fleck called "thought collectives" is a more recent phenomenon. Although Fleck developed this novel view of the history of science in the 1930s, it reached a wider public only in the 1960s, through the writings of Thomas Kuhn and Paul Feyerabend. But probably the book that contributed most to the demise of the traditional view of the scientific enterprise as an autonomous exercise of pure reason by disembodied, selfless spirits, inexorably moving toward a true knowledge of nature, was *The Double Helix*, James D. Watson's personal account of the discovery of the structure of DNA. That book was first published in 1968 and has been read by more than a million persons, including readers of foreign editions in at least seventeen different languages.

Although nothing could resemble less a treatise on the philosophy or sociology of science than Watson's autobiographical memoir, it nevertheless brought home, in a painless and enjoyable literary style, important insights into how the process of scientific discovery actually works. By now, *The Double Helix* has found its way into

many classrooms, as supplementary reading for courses on general biology, biochemistry, molecular biology, genetics, sociology, or history. In order, therefore, to increase its value in such academic contexts, I proposed to Watson to bring out the present "critical edition" of the book, in which his original text is accompanied by an overview of the scientific and historical setting in which the story is embedded, by retrospective views on the events described in the text by two other chief characters of the story (Francis Crick and Linus Pauling), by a selection of some of the most interesting reviews of the book in which other scientists comment and bring to bear their own experience and views on Watson's story, and by reproductions of the original scientific papers in which the double helical structure of DNA was first presented.

We thank the numerous authors and journals for permission to reproduce their articles and are indebted to Atheneum Press for granting us the right to reprint *The Double Helix*.

GUNTHER S. STENT

Introduction

I

GUNTHER S. STENT

The DNA Double Helix and the Rise of Molecular Biology

I learned in my history class at Hyde Park High School in Chicago that the Renaissance began on May 29, 1453, the day Constantinople fell to the Turks. On that date, so I thought, everybody suddenly found out that the Middle Ages were over and that the time had come to rediscover the arts and sciences of classical antiquity. Although I eventually managed to appreciate the absurdity of pinpointing the exact start of an historical era, I still hold that the era of molecular biology began exactly five hundred years—almost to the day—after the fall of Constantinople. That beginning came on April 25, 1953, when there appeared an article in the British scientific journal *Nature* by two young scientists, James Watson (formerly a student at Hyde Park High's rival, South Shore High) and Francis Crick, reporting the discovery of the DNA double helix. For as soon as the contents of that article became known—and they became widely known almost immediately—most biologists interested in the mechanism of heredity quickly realized that the time had come to think about genetics in terms of large molecules that carry hereditary information.

Just as the Renaissance sprang from the confrontation of the Christian West with the Muslim East, so molecular biology sprang from the confrontation of genetics with biochemistry. Genetics itself had begun in 1865, when Gregor Mendel published the results of experiments in which he had crossbred various strains of the common garden pea differing from each other in such hereditary characters as seed shape and flower color. Mendel had studied the manner in which these characters—round or wrinkled seed, red or white flower—were distributed among the resulting offspring plants. The outcome of his breeding experiments led Mendel to conclude that an organism carries and transmits to its offspring a set of hereditary elements, or *genes*. Each gene determines a single character, so that the overall appearance of an organism is governed by the total

set of particular genes which happens to have been passed on to it from its parents. Mendel's insights were, however, still too advanced for his times, and for the next thirty-five years they remained unnoticed by the community of biologists. Mendel's work was rediscovered in the year 1900, and during the first twenty years of this century, genetics developed into one of the most important frontiers of biological research. Thanks in large part to the work of Thomas H. Morgan and his associates, it became known that genes are arranged in a *linear order* on the chromosomes. [The chromosomes are thread-like bodies in the cell nucleus. Before each cell division, each chromosome splits in two, and during cell division the chromosomes are distributed in such a way that each of the two daughter cells is given its own complete chromosome set.] Furthermore, genes were found to be capable of undergoing sudden permanent changes, or *mutations*. A mutation results in a change of the particular hereditary character determined by the gene, such as the change from red flower color to white.

These insights made possible great advances in the understanding of life. On the theoretical plane, they provided a firm basis for understanding evolution. It could now be seen that gene mutation, being the prime source of biological novelty, is the motor that drives evolution. And it was realized that what the mechanism of natural selection put forward by Charles Darwin actually selects are organisms carrying novel genes, or novel combinations of genes, that confer greater fitness in the struggle for survival. On the practical plane, genetics brought tremendous benefits. In agriculture, it had become possible to design rational breeding procedures by means of which economically superior varieties of traditional crop plants and domestic animals could be produced. And in medicine, the recognition of the role of genes in many human diseases provided a rationale for taking measures for their prevention or relief. But throughout the first half of the twentieth century, while genetics had become the queen of the biological sciences, the physical nature of its central concept, the gene, had remained shrouded in mystery. No one knew of what the gene is made, how it manages to impose its character on the organism that carries it, or how it reproduces itself faithfully in cell division.

The mystery of the nature of the gene, and the possibility that the mechanism of its self-replication and governance of cell function might be explainable only in terms of hitherto unknown principles of physics and chemistry, attracted some physicists to genetics. The eventually most influential of these was Max Delbrück, a pupil of the great Danish physicist Niels Bohr. In 1935, at the age of twenty-nine, Delbrück made his debut as a biologist by publishing a speculative paper entitled "On the nature of gene mutation and gene

structure." Ten years later, the views expressed in Delbrück's rather esoteric and little-known paper were popularized in a widely-read book entitled *What Is Life?*, written by the physicist Erwin Schrödinger, then already very famous. In retrospect, the most important point made by Schrödinger was that the gene is to be thought of as an *information carrier*. And the only reasonable way in which genes could be imagined to carry their hereditary information is by embodying a succession of a small number of different repeating elements, or symbols, whose exact pattern of succession represents an encoded genetic message. Schrödinger illustrated the vast informational capacity of such a coding system with an example that used the two symbols of the Morse code—dots and dashes —as its repeating elements. Meanwhile Delbrück had already begun to attack the gene problem experimentally. In 1938, as a postdoctoral research fellow at the California Institute of Technology (Cal Tech) in Pasadena, Delbrück had taken up the study of bacterial viruses, or *phages*, as they are usually called. Although phages are very small and structurally rather simple, ultramicroscopic particles —less than one ten-thousandth of a millimeter in length—they are nevertheless endowed with the capacity for self-reproduction. As Delbrück found, each phage particle infecting a bacterial host cell gives rise to some hundred identical progeny phage particles within the half-hour. Thus the central problem of gene replication could be put in simple terms: just how does the parental phage particle manage to produce its crop of a hundred progeny during that half-hour? Two years later, Delbrück met Salvador Luria, then a recently arrived refugee from war-torn Europe, and Alfred Hershey of Washington University in St. Louis. This meeting brought into being the Phage Group, whose members were united by a single common goal—the desire to solve the mystery of the nature of the gene. In 1947, Luria, by then a professor at Indiana University, took on the nineteen-year-old James Watson as his graduate student and initiated him as a member of the Phage Group.

Although the Phage Group made important contributions to clarifying what it is about the gene that is actually to be understood, the eventual identification of the physical nature of the gene came from an entirely different tradition. In the 1860s, Mendel's contemporary, the Swiss chemist Friedrich Miescher, had discovered that cell nuclei contain *nucleic acid*, a previously unknown substance rich in phosphorous. By the turn of this century biochemists had established the ubiquitous presence of nucleic acid in plant and animal cells and had shown it to be composed of four different kinds of nitrogenous bases, of a five-carbon sugar, and of phosphoric acid. One nitrogenous base, one sugar, and one phosphoric acid molecule turned out to be linked to form the basic nucleic acid building block, the *nucleo-*

tide, with the nucleic acid molecule being built up from many such nucleotides linked through phosphate diester bonds between sugar molecules. Nucleic acid is, therefore, a *polynucleotide chain*. By the 1920s it had been ascertained that there actually exist two different kinds of nucleic acid, one of which is called *ribonucleic acid*, or *RNA*, and the other *deoxyribonucleic acid*, or *DNA*. The chemical composition of these two kinds of nucleic acid is nearly identical, except that deoxyribose, the sugar molecule of DNA, has one less hydroxyl group than ribose, the sugar of RNA, and that uracil, one of the four nitrogenous bases of RNA, lacks a methyl group carried by thymine, the corresponding nitrogenous base of DNA. However, these two rather slight divergences in chemical structure turned out to have as their result a momentous difference in the biological function of DNA and RNA. The first intimation of this differential function was provided in the late 1920s by the finding that DNA is located almost exclusively in the chromosomes, whereas RNA is located mainly outside the nucleus, in the cytoplasm. And since by then Thomas Morgan's work had shown that the genes reside in the chromosomes, it did not seem farfetched to imagine that DNA plays some important role in heredity. But as the chromosomes contain even more protein than DNA, it was not necessary to infer that the genes are actually composed of DNA. In fact, the majority of informed opinion considered it virtually certain that the genes are composed of protein and that DNA merely plays some accessory, physiological role in hereditary transactions.

The first direct demonstration that DNA is, in fact, the genetic material was provided in 1944 by Oswald T. Avery and his collaborators at the Rockefeller Institute in New York. Avery had shown that upon addition of purified DNA extracted from normal *donor* bacteria to abnormal *recipient* bacteria that differ from the donor bacteria in one mutated gene, some of the recipient bacteria are transformed hereditarily into the donor type. Thus the normal donor gene must have entered the transformed recipient bacterium in the form of a donor DNA molecule and there displaced its homologous mutated gene. Hence it followed that the bacterial DNA embodies the bacterial genes. In 1944 this conclusion seemed so radical that even Avery himself was reluctant to accept it, until he had buttressed his experiments with the most rigorous controls. In fact, Avery's controls were evidently not rigorous enough for most contemporary biochemists and geneticists, and his discovery, though widely known and discussed, had little influence on thought about the mechanisms of heredity for the next eight years. Finally, in 1952, Hershey and his young assistant, Martha Chase, showed that when a phage particle infects its bacterial host cell, only the DNA of the phage actually enters the cell; the protein of the phage

remains outside, devoid of any further function in the reproductive drama about to ensue within. Thus it could be concluded that the genes of the parent phage responsible for directing the synthesis of progeny phages reside in its DNA. This second demonstration that DNA is the genetic material had an immediate and profound impact. From that time on, all genetic thought was focused on DNA.

Why did Avery's announcement that DNA is the genetic material have so much less effect in the marketplace of genetic ideas in its day than the later Hershey-Chase experiment? The main reason, in my opinion at least, is that in 1944 the DNA molecule was still thought to consist of a regular iteration of its four types of component nucleotides. Thus it was very difficult to imagine how a DNA molecule, made up of monotonously repeating units, each containing one of the four types of nitrogenous bases—adenine, guanine, thymine, and cytosine—could be the carrier of genetic information. But that view had changed by 1952. More refined biochemical analyses of DNA, carried out by Erwin Chargaff at Columbia University, had shown meanwhile that DNA does not consist of a monotonous succession of nucleotides and that the four types of nitrogenous bases might follow each other in any arbitrary order in the polynucleotide chain. Since the relative abundance of the four bases was found to be different in DNA samples obtained from different biological sources, it could be envisaged at the time of the Hershey-Chase experiment that any given DNA molecule harbors its genetic information in the form of a precise sequence of the bases along the polynucleotide chain. In other words, the repeating elements of Schrödinger's proposed hereditary codescript could now be identified as the four different nucleotides carrying adenine, or guanine, or thymine, or cytosine. Upon the formulation of this idea, the fundamental problem posed by biological inheritance could be restated in terms of two separate functions of the DNA molecule. One of these, the autocatalytic function, consists of the replication of the precise nucleotide base sequence of the parental DNA to generate the genetic information to be passed on to the progeny. And the other, the heterocatalytic function, consists of the expression by the DNA of its embodied genetic information, by presiding over, or directing the biochemical reactions that make the organism what it actually is. But in order to work out how DNA performs these two functions, it turned out to be necessary to know not only its chemical composition but also the details of its three-dimensional structure.

Concurrent with the rise of the Phage Group there had also taken place a movement into biology of an entirely different group of physicists. In contrast to the Phage Group, whose efforts were motivated by the desire to understand the physical basis of the hereditary transmission of biological information, the interest of these other

persons was focused on the three-dimensional structure—that is, on the *form*—of biological molecules. This group of structural analysts, among whose interests genetics played at most a peripheral role, can be considered as having descended from W. H. Bragg and W. L. Bragg. The Braggs, father and son, had invented X-ray crystallography in 1912 and founded a school of cyrstallographers that made Britain the home of the study of molecular architecture. As success came to the determination of the structures of ever more complicated molecules, these crystallographers became sufficiently emboldened to train their structural methods also on some very complex molecules of biological importance. For they had embraced the idea that the physiological function of the cell cannot be understood in terms other than of the spatial conformation of its elements. Among the first of the Bragg pupils to engage in this line of work were W. T. Astbury and J. D. Bernal, who in the late 1930s began to tackle the structural analysis of proteins and nucleic acids. To designate this approach to the understanding of life processes, Astbury coined the term "molecular biology." Though for many years Astbury made vigorous propaganda in its favor, this neologism did not find wide acceptance. For instance, prior to April 25, 1953, no member of the Phage Group thought of or referred to himself as a "molecular biologist." But on that day, Delbrück's circle suddenly realized—just as suddenly as Molière's Monsieur Jourdain had realized that he was speaking prose—that what it had been doing all along was molecular biology.

The early work of Astbury, Bernal, and other Bragg pupils was to provide the foundation for many later advances. However, the first great triumph of structural molecular biology was not achieved by a member of the British school, but by Linus Pauling at Cal Tech, who, in 1951, discovered the basic structure of the protein molecule. Proteins are also long chain molecules, composed of an arbitrary succession of twenty different kinds of building blocks, or *amino acids*, one joined to the next via a chemical linkage called the *peptide bond*. Such an amino acid chain is called a *polypeptide*. Pauling had set himself the task of determining the spatial conformation of the polypeptide chain, that is, the shape of the backbone of the large protein molecule. He found that only a few different helical shapes are actually possible for the backbone, and predicted that one of these, called the α-helix, ought to play a dominant role in determining the shapes of protein molecules—a prediction that was not long in being confirmed. Pauling's success was due in part to a novel approach to structure determination, in which guesswork and model building played a much greater role than in the more straightforward, analytical procedures used by the British crystallographers. But however great Pauling's triumph was, the discovery of the α-helix did not immediately suggest to anyone very many new ideas

about proteins, about how they work or are made. It did not seem to lead to many new experiments, or to open new vistas to the imagination, except to show how very far one could go by use of the methods of structural analysis that Pauling had used. Meanwhile, in W. L. Bragg's laboratory in Cambridge, Max Perutz and John Kendrew had been working on the structure of the two oxygen-carrying proteins, hemoglobin and myoglobin. Their progress had been rather slow, since in view of the limited tools available at that time, the task they had cut out for themselves was immensely difficult and complex. Pauling's brilliant success came as a bit of a shock to the Cambridge group, but nevertheless it continued undeterred. The application of new analytical techniques and the availability of ever more potent computers for the mathematical analysis of their X-ray photographs finally allowed Perutz and Kendrew to work out the complete three-dimensional structure of their respective proteins, after nearly another ten years' labor. But Pauling's success in 1951 in working out the basic structure of the polypeptide chain, and a chance meeting with Maurice Wilkins, who was already carrying out X-ray crystallographic analyses of DNA in London, inspired James Watson, by then a new Ph.D. continuing his phage work in Copenhagen, to try to work out the structure of the DNA molecule. To gain the necessary skills in X-ray crystallography, Watson joined Kendrew in Cambridge. There Watson met Francis Crick, to whom it had also occurred that knowing the three-dimensional structure of DNA would be likely to provide important insights into the nature of the gene. Watson and Crick then began a collaboration which, in the spring of 1953, resulted in their discovery that the DNA molecule is a double helix, composed of two intertwined polyneucleotide chains. The DNA double helix is self-complementary, in that to each adenine nucleotide on one chain there corresponds a thymine nucleotide on the other, and to each guanine nucleotide on one chain there corresponds a cytosine nucleotide on the other. The specificity of this complentary relation devolves from hydrogen bonds formed between the two opposite nucleotides, adenine-thymine and guanine-cytosine, at each step of the double helical molecule.

On first sight, Watson and Crick's discovery of the double helical, self-complementary structure of DNA resembled Pauling's then two-year-old discovery of the α-helix, particulary since the formation of specific hydrogen bonds also plays an important role in Pauling's structure. But, on second sight, the promulgation of the DNA double helix emerges as an event of a qualitatively different nature. First, in working out the structure of the double helix, Watson and Crick had for the first time introduced genetic reasoning into structural determination by demanding that the evidently highly regular structure of DNA must be able to accommodate the informational element of arbitrary nucleotide base sequence along the two poly-

nucleotide strands. Second, unlike the protein α-helix, the discovery of the DNA double helix opened up enormous vistas to the imagination. It was to provide the highroad to understanding how the genetic material functions.

This brilliant wedding of structural and genetic considerations embodied in the DNA helix thus opened the era of molecular biology. But Watson and Crick had not only opened that era; they also dominated the next decade of molecular biological research. Most importantly, they were in the main responsible for formulating the *central dogma* of molecular biology that henceforth guided most studies on the nature of the gene. It is the existence of the central dogma that sharply distinguished the *Zeitgeist* of the molecular biology era from that which had preceeded it. For whereas the pre-1953 Phage Group had been groping for the still unimaginable, test and elaboration of the clearly stated central dogma were now the principal research agenda.

The central dogma represents a series of beliefs which give a coherent account of the mechanisms by means of which the DNA achieves the two fundamental autocatalytic and heterocatalytic functions. In its most abbreviated form, the dogma states that the autocatalytic function is a one-stage process, in which the DNA molecule serves directly as a template for the synthesis of its own DNA replica polynucleotide chain. The heterocatalytic function, however, is a two-stage process, in which the second type of nucleic acid, RNA, becomes involved. In the first stage, the DNA molecule serves as a template for the synthesis of an RNA polynucleotide chain onto which the sequence of nucleotides in the DNA chain is *transcribed*. In the second stage, the RNA chain is then *translated* by the cellular machinery for protein synthesis into polypeptide chains of the required structure. It is to be noted that an essential feature of the central dogma is a one-way flow of information from DNA to protein, a flow the direction of which is never reversed.

This view of the heterocatalytic function of DNA was predicated on an ancillary dogma, for which there was no proof whatever at the time it was embraced. This ancillary dogma, or "sequence hypothesis," states that the exact spatial conformation of a protein molecule, and hence the specificity of its biological function, is wholly determined by the particular sequence of the twenty kinds of amino acids which make up its polypeptide chains. Hence, the "meaning" of the particular sequence of the four types of nucleotides making up a sector of DNA corresponding to a gene could be nothing other than the specification of an amino acid sequence of some polypeptide chain.

As far as the autocatalytic function was concerned, Watson and Crick proposed that the parental DNA molecule achieves its replication upon separation of the two helically intertwined, complemen-

tary polynucleotide strands. Each of the two parent strands then serves as a template for the ordered synthesis of its own complementary daughter strand, by having each nucleotide on the parent strand attract and line up for the polynucleotide synthesis the complementary free nucleotide. From the viewpoint of the central dogma, gene mutations can be seen as rare errors in this template-copy process, by means of which changes in the parental DNA nucleotide sequence arise. These changes evidently cause an alteration of the hereditary information encoded into the particular gene represented by the stretch of DNA in which the copy error had occurred. It took about five years to prove that this view of the autocatalytic function is essentially correct.

Detailed understanding of the heterocatalytic function, which from the very outset of its formulation appeared to be a more complex problem than the autocatalytic function, required a rather greater effort and a somewhat longer time. The central dogma and its ancillary "sequence hypothesis" had led directly to the belief that there must exist a *genetic code* that relates the nucleotide sequence in the DNA polynucleotide chain to amino acid sequence in the corresponding polypeptide chain. A simple consideration quickly revealed that this code could be no simpler than one involving the specification of each amino acid in the polypeptide chain by at least three successive nucleotides in the DNA. That is, four kinds of nucleotides taken three at a time provide $4 \times 4 \times 4 = 64$ different code words, or *codons*. Each of the twenty kinds of protein amino acids could then be represented by at least one such codon in the genetic code, though the greater number of available kinds of codons than of kinds of amino acids would allow also for the possibility that the code provides for the representation of one kind of amino acid by more than a single codon. These a priori insights into the nature of the genetic code had been reached soon after Watson and Crick's discovery of the DNA double helix and were first committed to print in 1954 by the physicist-cosmologist George Gamow. But it was not until 1961 that it was finally proven that the genetic code really does involve a language in which successive nucleotides in the DNA polynucleotide chain are read three-by-three in the polypeptide translation process. That proof came from purely formal genetic experiments carried out by Crick with mutant genes of phages.

It was all well and good to have demonstrated the formal, informational principles of the heterocatalytic function. But in order to really understand its molecular processes, it became necessary to employ the methods of biochemistry to open the black box containing the cellular hardware which actually effects the transcription-translation drama of the central dogma. One of the first insights then provided by the application of biochemical methods was the

identification of the *ribosome* as the *site* of cellular protein synthesis. The ribosome is a small particle present in vast numbers in all living cells. The mass of the ribosome is composed of about one-third protein and two-thirds RNA. But how is the information for specific amino acid permutations encoded in the gene made available to the ribosome in its polypeptide assembly process? In answer to this question it was proposed in 1961 by François Jacob and Jacques Monod that the RNA onto which, according to the central dogma, the nucleotide sequence of the gene is first transcribed, is a molecule of *messenger RNA*. This messenger RNA molecule is picked up by a ribosome, on whose surface than proceeds the translation of RNA nucleotide sequence into polypeptide amino acid sequence, codon by codon. In this translation process, the messenger RNA chain runs through the ribosome like a tape runs through a tape recorder head. It is to the clarification of the structure of the ribosome, the mechanism of formation of messenger RNA, and the translation of messenger RNA into proteins that Watson and his students eventually made many critical contributions. How the amino acids are actually assembled into the correct predetermined permutation by the messenger RNA as it runs through the ribosome had been envisaged by Crick in about 1958, before the concept of the messenger RNA had even been clearly formulated. Crick thought it unlikely that the twenty different amino acids could interact in any specific way directly with the nucleotide triplet on the RNA template chain. He therefore proposed the idea of a nucleotide *adaptor*, with which each amino acid is outfitted prior to its incorporation into the polypeptide chain. This adaptor was thought to contain a nucleotide triplet, or *anticodon*, complementary (in the Watson-Crick nucleotide pairing sense) to the nucleotide triplet codon that codes for the particular amino acid to which the adaptor is attached. The anticodon nucleotides of the adaptor would then form specific hydrogen bonds with their complementary codon nucleotides on the messenger RNA and thus bring the amino acids bearing the adaptor into the proper, predetermined alignment on the ribosome surface. No sooner had the adaptor hypothesis been formulated than students of the biochemistry of protein synthesis began to encounter an ensemble of specific reactions and enzymes that gradually resembled more and more the a priori postulates of that hypothesis. First, a special type of small RNA molecule, the *transfer RNA*, was discovered, which contains about eighty nucleotides in its polynucleotide chain. Each cell contains several dozen distinct species of transfer RNA, each species being capable of combining with one and only one kind of amino acid. This transfer RNA turned out to be Crick's postulated adaptor, since that transfer RNA species which accepts any given amino acid contains the anticodon nucleotide triplet in its polynucleotide chain which is complementary to the codon representing that same amino