Introduction

Lucky or not, Watson was
a highly privileged young man.

Peter Medawar

It was a typical early spring afternoon at Cold Spring Harbor Laboratory (CSHL) when a long black limousine, with James and Elizabeth Watson in the back seats, behind its dark windows, turned from the driveway of Ballybung house — the Watsons residence at the northernmost tip of the CSHL campus — onto Bungtown Road, and continued southward. It was driving slowly, majestically, by the *Time Spirals* sculpture, a stylized version of the double helix model erected on a mound near Ballybung. The limo passed Olney house on the right, serving as campus security headquarters (if a visitor strayed near Ballybung, within seconds a security car would pull up out of nowhere, offering help). The limo continued on the semi-dirt road, becoming a paved surface amongst laboratory and residential structures. Every building had its own history and the Watsons left their marks on every one of them. As the limo continued further south, the Beckman Laboratory and more conspicuously the Hazen Tower could be seen on the right at a distance. The two together gave the impression of a modern cathedral. What could not be seen from the

Spirals Time – Time Spirals: Double helix sculpture by Charles A. Jencks at Cold Spring Harbor Laboratory with the Watsons' residence in the background (photo by the author).

Beckman Building at Cold Spring Harbor Laboratory (CSHL) with the Hazen Tower in front of it (photos by the author).

Bungtown Road was that each side of Hazen Tower had a lowercase letter carved into it, a, c, g, and t, for the four bases of DNA, adenine, cytosine, guanine, and thymine. A bit further down on Bungtown Road, the limo passed Blackford Hall with its cafeteria where, long ago, in the late 1940s, Jim Watson used to earn his keep by serving meals to the participants of summer courses. It was also at Blackford Hall where he first reported the double helix structure of DNA at a meeting in June 1953. Finally, the limo passed Grace Auditorium dominating the scene on the right whereas on the left, at a distance, Carnegie Library could be glimpsed at, which holds the Watson archives and memorabilia. Leaving the campus, the limo turned right onto Road 25A of Long Island, merging smoothly into the light afternoon traffic, and changing gear, it sped away in the eastern direction; it was out of sight in a second. Everyone on both sides of Bungtown Road knew that Jim and Liz were heading into the City for a book launch and some also knew that they would spend some time with their older son whose chronic illness necessitated another painful hospital stay.

Whether being director, president, or chancellor, CSHL has been Watson's territory, and a long way from his humble environment in Chicago where he was born on April 6, 1928. He is most famous for his discovery, jointly with Francis Crick, of the double helix structure of DNA in 1953, in Cambridge, England. Watson and Crick, together with Maurice Wilkins, were awarded the 1962 Nobel Prize in Medicine.

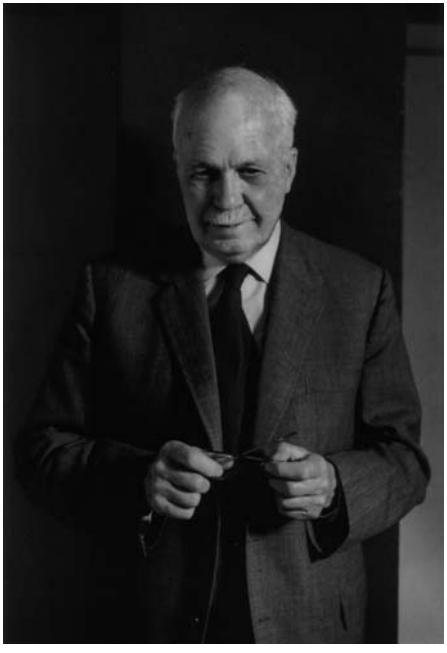
The 25-year-old Watson was thrust into world fame and he has been looming over larger than life ever since. Seldom has a scientist remained at the top of science for so long after a seminal discovery and Watson's stamina is the more remarkable because he was so young when the discovery happened. As an individual, he has become emblematic of an era when the image of the lonely scientist is giving way to large and often faceless teams. Watson described the story of the discovery in his acclaimed and popular book, *The Double Helix*, to which an emblem of a previous era, William Lawrence Bragg wrote the Foreword.

Bragg was somewhat younger than Watson when he and his father founded X-ray crystal structure analysis in 1912, and he also stayed in

James D. Watson in June 1953 at Cold Spring Harbor with a model of the double helix in his left hand (photo by and courtesy of Karl Maramorosch, Scarsdale, New York).

science for a long period. When Ernest Rutherford died in 1937, Bragg was thrust into the enormously prestigious Cavendish Chair of Physics at Cambridge University. While both were physicists, Rutherford was a chemistry Nobel laureate and Bragg a physics Nobel laureate. Bragg's Cavendish leadership was hampered by World War II, and when the war ended, the Cavendish supremacy in nuclear physics — Rutherford's principal field — also ended. "Rather than fight a rearguard action,"[5] Bragg encouraged the development of such non-traditional fields of research for the Cavendish as radio-astronomy and molecular biology. Both proved to be exceptionally fruitful and were eventually signified with Nobel Prizes. Nonetheless, Bragg never attained the worldwide influence in science that Watson later acquired. Both Bragg and Watson were about 25 years old when they did their principal

[5] Perutz, M., *Acta Cryst.* 1970, A26, pp. 183–185, p. 185.



William Lawrence Bragg (courtesy of the late David Shoenberg, Cambridge, UK).

discoveries, but that was not unique even in the history of 20th century science. Watson himself likes to quote his one time mentor and protector, Max Delbrück, who used to emphasize that Einstein as well as Werner Heisenberg did their best science when they were 25 years old.[6] Watson has noted repeatedly that he has been called the Einstein of molecular biology. He was never too shy to appreciate himself and his achievements even though he may have appeared physically withdrawn and spoken in a barely audible voice. When he wanted to see Salvador Dali, he sent him a note saying, "The second brightest person in the world wishes to meet the brightest."[7]

[6] Watson, J. D., "Afterword: Five Days in Berlin." In *Murderous Science: Elimination by Scientific Selection of Jews, Gypsies, and Others in Germany, 1933–1945*, ed. Müller-Hill, B. Cold Spring Harbor Laboratory Press, New York, 1998, p. 193.

[7] Watson, *Genes, Girls and Gamow.* Oxford University Press, 2001, p. 271.

Watson was not quite a child prodigy, but had an accelerated childhood, and was catapulted into adulthood by jumping adolescence. He started school at the normal age of six; left (Catholic) religion at 12; and completed high school at 15. In 1943, he was already a student of the University of Chicago whose maverick president Robert Hutchins encouraged early entrance and sent his students back to the sources rather than feeding them with the interpretation of the classics by intermediates. Hutchins' concept of education and the intellectual fervor that characterized the University of Chicago ideally benefited Watson while others criticized this approach as hopelessly idealistic.

While an undergraduate, Watson read Erwin Schrödinger's *What Is Life?* and became hooked with the genes for life. In 1947, he began graduate school at Indiana University — an odd choice for a future revolutionary of science — because he was declined by more prestigious schools. By happy coincidence, however, Indiana University was then, for a while, a world leader in genetics. There was H. J. Muller who had just been awarded the medical Nobel Prize in 1946 "for the discovery of the production of mutations by means of X-ray radiation." Watson chose as his mentor Salvador Luria who would later become a Nobel laureate and who was a co-founder of Max Delbrück's phage school. One of Watson's fellow students was Renato Dulbecco, also a future Nobel laureate. During his graduate studies, Watson not only experienced a rapidly advancing science, but was thrust into a cosmopolitan community. Delbrück was a non-Jewish German refugee from Nazism. Muller spent three and a half years in Moscow at the famous Russian biologist, N. I. Vavilov's invitation. With the rise of T. D. Lysenko, the ignorant and ruthless dictator of Soviet biology, Vavilov was to die in prison in 1943, but Muller left the Soviet Union in 1937. Luria was a Jewish-Italian refugee from Fascism; Dulbecco joined him after the war, after having studied with Professor Giuseppe Levi in Torino where Levi's other students, and in particular the future Nobel laureate Rita Levi-Montalcini had an important influence on his career.

Watson earned his PhD degree in 1950. His project was to see whether phages that had been inactivated by X-rays could be reactivated.

Jim Watson's mentors: left, Salvador Luria and his wife at CSHL in the 1950s (photo by and courtesy of Karl Maramorosch, Scarsdale, New York; note Leo Szilard on the right in the background); right, Max Delbrück (photo by and courtesy of Gunther S. Stent, Berkeley, California).

The most remarkable feature of his thesis was that he wrote it when he was only 22 years old. The lack of any exciting findings was compensated for by Delbrück telling him that this way there was no danger of falling into a trap of people wanting him to follow it up immediately. This way he would have the leisure to go on thinking and learning.[8] Watson left for postdoctoral studies in Europe where his stay in Denmark was not a great success. Then he joined the Cavendish Laboratory in Cambridge and stimulated Francis Crick to join him in their quest for the structure of DNA. Crick had been busy with writing up his PhD thesis on the structure of ox hemoglobin. There were tumultuous events preceding the discovery although they may have not appeared so significant at the time. In 1952, Watson gave a presentation — as a proxy — introducing the famous Hershey-Chase experiment, which yielded the same results as Avery *et al.*'s different (and more accurate) experiments in 1944, namely, that DNA is the substance of heredity. The scientific community was more

[8] Watson, J. D., "Growing Up in the Phage Group." In *Phage and the Origins of Molecular Biology*, Expanded Edition, eds. Cairns, J., Stent, G. S., Watson, J. D. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1992, pp. 239–245, p. 243.

Martha Chase and Alfred Hershey at CSHL (photo by and courtesy of Karl Maramorosch, Scarsdale, New York). The Hershey-Chase experiment yielded the same result that Avery *et al.*'s experiment in 1944, namely, that DNA was the substance of heredity, but the scientific community was better prepared to accept these findings in 1951–1952 than it was in the mid-1940s.

perceptive in 1952 than in 1944 to accept the primacy of nucleic acids over proteins, and suddenly Watson and Crick's work received more urgency. Watson later remarked that Hershey and Chase's findings "spurred me even more into finding out what DNA looked like in three dimensions."[9] It was also in 1952 that Erwin Chargaff visited the Cavendish and met with Watson and Crick. Although Chargaff was dismayed by the lack of knowledge of chemistry by the two young researchers, he shared with them his seminal findings unselfishly that the purine and pyrimidine bases were in a one-to-one ratio in the DNAs of all organisms examined to date. Watson and Crick did not recognize the structural significance of Chargaff's findings at the time — and Chargaff did not either. Eventually, Chargaff's observations became a supporting evidence for the double helix model of DNA.

[9] Watson, *Genes, Girls and Gamow*, p. 17.

July 1952 meeting in Royaumont, France. James D. Watson is third from the right sitting in the front row; André Lwoff is the first, sitting on the right, second row; Alfred Hershey is standing first on the right; Max Delbrück is standing 11th from the left and François Jacob is 19th; Jacques Monod is kneeling in front of Delbrück; and Seymour Benzer is on his left (courtesy of Gunther S. Stent, Berkeley, California).

Even in *The Double Helix*, Watson appears as if almost downplaying the importance of Chargaff's discoveries. In contrast, 35 years later, in *DNA: The Secret of Life*, he mentions explicitely that he "read Erwin Chargaff's paper describing his findings that the DNA bases adenine and thymine occurred in roughly equal amounts, as did the bases guanine and cytosine. Hearing of these one-to-one ratios Crick wondered whether, during DNA duplication, adenine residues might be attracted to thymine and vice versa, and whether a corresponding attraction might exist between guanine and cytosine. If so, base sequences on the 'parental' chains (e.g. ATGC) would have to be complementary to those on 'daughter' strands (yielding in this case

TACG)."[10] Chargaff's visit with Crick and Watson further stimulated their thinking of the implications of Chargaff's observations with Crick giving it more importance than Watson.

The urgency of Watson and Crick's work was enhanced by Linus Pauling's joining what Watson later described as race although Pauling never admitted it as such. However, Pauling did not lack the competitive spirit. According to Watson, Pauling did not let him use the Caltech X-ray machine on an occasion because he considered Watson a competitor.[11] In any case, Pauling published a triple-helix structure in early 1953. Although Bragg did not think it gentlemanly for the Cavendish to compete with King's College of London for solving the DNA structure, Pauling's contribution made him feel imperative to let all British forces mobilized. In the course of a few weeks time, Maurice Wilkins showed Watson Rosalind Franklin's excellent X-ray diffraction pattern of the so-called wet B form of DNA and Perutz showed Watson and Crick the report of King's College, which contained Franklin's data, prepared for MRC inspection. Franklin's results much facilitated Crick and Watson's work.

Once the two-chain nature of the structure, their anti-parallel arrangement — consistent with two-fold (C_2) symmetry and complementarity — and base-pairing became evident, the structure of DNA was solved and duly reported. It was not only a beautiful construction; it also suggested "a possible copying mechanism for the genetic material."[12] The initial report was followed by more detailed papers, but the essence of the discovery remained the same.

After the discovery, Watson did postdoctoral work at the California Institute of Technology; he became engaged in the study of the structure of RNA and the search for the messenger RNA. The "returns" were so much less significant than the discovery of the double helix that eventually he moved away from direct research and became an

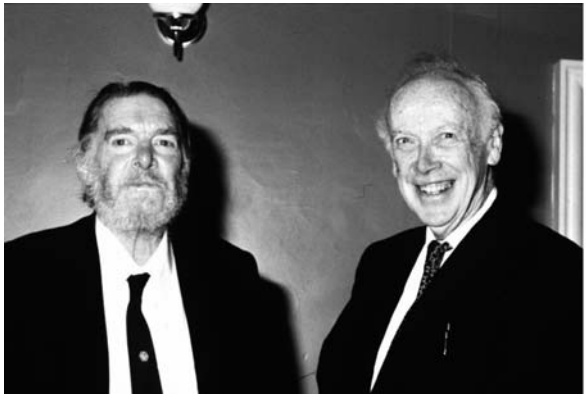
[10] Watson, J. D. (with A. Berry), *DNA: The Secret of Life*. William Heinemann, London, 2003, p. 49.
[11] Benzer, S., "Some Early Recollections of Jim Watson." In *Inspiring Science: Jim Watson and the Age of DNA*, eds. Inglis, J. R., Sambrook, J., Witkowski, J. A. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 2003, p. 17.
[12] Watson, J. D., Crick, F. H. C., "A Structure for Deoxyribose Nucleic Acid." *Nature* 1953, April 25, pp. 737–738, p. 737.

architect of science on an ever growing scale. From 1956 he had a position at Harvard University, and it was during his Harvard years that he launched his innovative textbook writing. He produced the first texts in molecular biology, starting with the *Molecular Biology of the Gene*, then, the *Molecular Biology of the Cell,* and forever changed the style of successful texts in this and related fields. His textbook was soaked in the chemistry that he so much lacked before. From 1968 to 1993 he was Director of Cold Spring Harbor Laboratory, at first parallel with his Harvard professorship, then, from 1976, full time. He was also the Director of the National Center for Human Genome Research of the National Institutes of Health between 1989 and 1992.

From time to time, Watson returned for sabbatical leaves to England, the locale of his initial and tumultuous success, and was enormously gratified when he was made into an Honorary British Knight in 2002. There were though limits to the British recognition; while former New York City Mayor Rudi Giuliani was handed the same honor directly by Queen Elizabeth II in London, Watson received it from the hands of the British Ambassador in Washington, DC. Domestic honors also came his way. Jimmy Carter awarded him the Presidential Medal of Freedom in 1977, and he received the National Medal of Science from Bill Clinton in 1997.

Fifteen years after the discovery of the double helix, Watson published *The Double Helix*,[13] which has become a classic. He stated in its Preface: "I am aware that the other participants in this story would tell parts of it in other ways, sometimes because their memory of what happened differs from mine and, perhaps in even more cases, because no two people ever see the same events in exactly the same light. … Here I relate *my version* of how the structure of DNA was discovered."[14] (italics added) We are reminded of Leo Szilard when he contemplated putting together a history of the Manhattan Project, writing down the facts, not for having it published, but merely for

[13] Watson, J.D., *The Double Helix: A Personal Account of the Discovery of the Structure of DNA.* The New American Library, New York, 1969.
[14] Ibid., p. ix.




Left: Jim Watson with Peter Pauling who wrote the Foreword to *Genes, Girls, and Gamow* (by permission from Sir John M. Thomas, Cambridge, UK); right: Jim Watson autographing *Genes, Girls, and Gamow* at CSHL in 2002 (photo by M. Hargittai).

God to know about them. When a colleague noted that God might know the facts, Szilard said that this might be so, but "not *this version* of the facts."[15] (italics added)

Watson's negative portrayal of Rosalind Franklin in *The Double Helix* triggered a re-examination of Franklin's role in the 1953 discovery, and has led to its wider recognition.[16] As a result, today it is known that Watson and Crick used Franklin's experimental observations without her knowledge. She died a few years later, in 1958, without ever learning the whole truth about this incident.

Almost 35 years after the appearance of *The Double Helix*, its sequel appeared, *Genes, Girls and Gamow*.[17] In our first conversation, Watson mentions it as having already been written but not yet published. At that time he was having difficulties finding a publisher for it, which surprised me in view of his excellent record with books. It is

[15] *Leo Szilard: His Version of the Facts. Selected Recollections and Correspondence.* Edited by Spencer R. Weart and Gertrud Weiss Szilard. MIT Press, Cambridge, Massachusetts, and London, England, 1978, p. xvii.

[16] Klug, A., "The Discovery of the Double Helix." *J. Mol. Biol.* 2004, 335, pp. 3–26; and references therein.

[17] Watson, *Genes, Girls and Gamow.*

a detailed account of the first few years of Watson's life after the discovery of the double helix. A review in *Nature* called the book "tedious."[18] However, Watson thought that if he was to believe the comparisons of him with Einstein and the like, 100 years from now every detail of his life should be of great interest.

[18] Judson, H. F., "Honest Jim: The Sequel. Further Misadventures of One of the Most Influential Scientists of Our Day." *Nature* 2001, 413, October 25, pp. 775–776.