# The Triple Helix

*"I did not feel that I was in a race with Watson and Crick. . . . They felt that they were in a race with me."*

**by Thomas Hager**

**Most of the former contestants in the Caltech-Cambridge DNA duel gathered at a Caltech protein conference in September 1953 (this is about a third of the group). Pauling and Corey stand at right in the front row; John Kendrew at left. Wilkins is in the second row at the left behind Kendrew (no, they are not twins); Rich is second from left and Crick at far right. In the back row Max Perutz stands seoond from left, next to Schomaker, who is next to Watson, looming over Pauling's head. In 1962 Crick, Watson, and Wilkins won the Nobel Prize in physiology or medicine, while Perutz and Kendrew of the Cavendish Lab won it in chemistry. Pauling won the 1962 Nobel Peace Prize.**



*In James Watson's 1968 book,* The Double Helix, *he writes an irreverent account of the race to discover the structure of DNA—as seen from England, where the race was won in 1953. From the beginning, Watson and Francis Crick at Sir Lawrence Bragg's Cavendish Laboratory at Cambridge University, knew they were in a contest with Linus Pauling, "Cal Tech's fabulous chemist" for the prize, "the most golden of all molecules." Also involved in a somewhat uneasy collaboration on the English side were the x-ray crystallographers Maurice Wilkins and Rosalind Franklin at King's College in London.*

*Meanwhile, what was going on at Caltech? In his recent biography of Pauling, Tom Hager gives the view from Pasadena. While Watson and Crick were wringing their hands about what progress he might be making, Pauling wasn't giving it much thought at all. He certainly considered DNA within his own province, but initially had little interest in it; he was preoccupied by proteins, which he thought far more complex and interesting than deoxyribonucleic acid. When he was refused a passport to attend a meeting of the Royal Society in London in May 1952, he missed the chance to see Wilkins and Franklin's x-ray photos and have his mind changed. (But Pauling's close collaborator, Robert Corey, did see the photos, which takes the blame for Pauling's failure off the State Department.) Pauling's passport came through in July, in time to attend the International Phage Colloquium at Royaumont, outside Paris, and hear the proof that DNA was indeed the master molecule of genetics. He spoke with Watson at Royaumont, met Crick at Cambridge, but did not bother to take the opportunity to visit King's College, missing his chance a second time. Pauling's interest was, however, finally piqued.*

The real prize, the true secret of life, Pauling now knew, was DNA, and it was here that he next turned his attention.

On November 25, 1952, three months after returning from England, Pauling attended a Caltech biology seminar given by Robley Williams, a Berkeley professor who had done some amazing work with an electron microscope. Through a complicated technique he was able to get images of incredibly small biological structures. Pauling was spellbound. One of Williams's photos showed long, tangled strands of sodium ribonucleate, the salt of a form of nucleic acid, shaded so that three-dimensional details could be seen. What caught Pauling's attention was the obvious cylindricality of the strands: They were not flat ribbons; they were long, skinny tubes. He guessed then, looking at these black-and-white slides in the darkened seminar room, that DNA was likely to be a helix. No other conformation would fit both Astbury's x-ray patterns of the molecule and the photos he was seeing. Even better, Williams was able to estimate the sizes of structures on his photos, and his work showed that each strand was about 15 angstroms across. Pauling was interested enough to ask him to repeat the figure, which Williams qualified by noting the difficulty he had in making precise measurements. The molecule Williams was showing was not DNA, but it was a molecular cousin—and it started Pauling thinking.

The next day, Pauling sat at his desk with a pencil, a sheaf of paper, and a slide rule. New data that summer from Alexander Todd's

**Proteins were Pauling's primary interest in the early 1950s. This photo of Pauling and Robert Corey with a protein model appeared in the October 1951 issue of *Engineering & Science*, illustrating an article on "The Structure of Proteins."**

laboratory had confirmed the linkage points between the sugars and phosphates in DNA; other work showed where they connected to the bases. Pauling was already convinced from his earlier work that the various-sized bases had to be on the outside of the molecule; the phosphates, on the inside. Now he knew that the molecule was probably helical. These were his starting points for a preliminary look at DNA. He did not know how far he would get with this first attempt at a structure, especially because he still had no firm structural data on the precise sizes and bonding angles of the base-sugar-phosphate building blocks of DNA, but it was worth a look.

*And this was what the central problem had reduced itself to in his mind: a question of phosphate structural chemistry.*

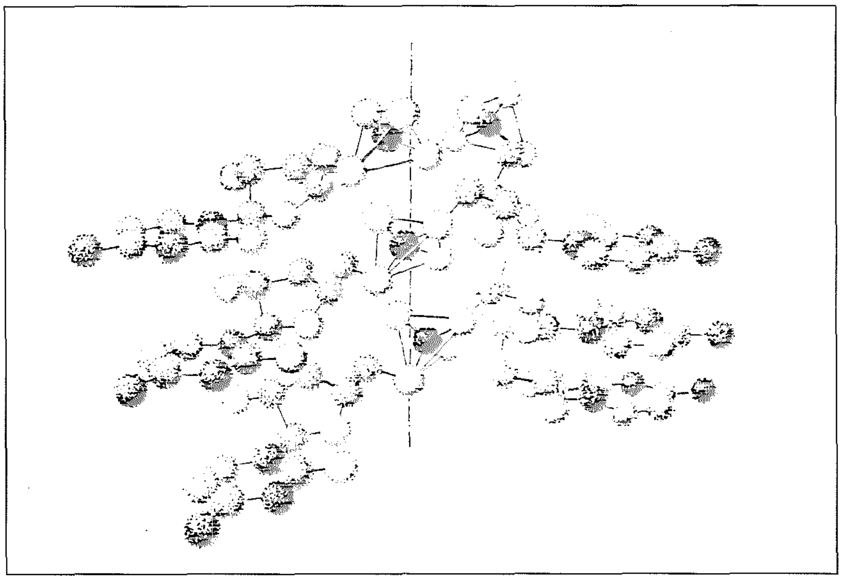
Pauling quickly made some calculations to determine DNA's molecular volume and the expected length of each repeating unit along its axis. Astbury's photos showed a strong reflection at 3.4 angstroms—according to Pauling's calculations, about three times his estimated length of a single nucleotide unit along the fiber. Repeating groups of three different nucleotides seemed unlikely; a threefold chain structure would explain the repeat more easily. His density calculations indicated that three chains would need to pack together tightly to fit the observed volume, but that was all right. In crystallography, the tighter the packing, the better. After five lines of simple calculations on the first page of his attack on DNA, Pauling wrote, "Perhaps we have a triple-chain structure!"

He was immediately captivated by the idea: three chains wound around one another with the phosphates in the middle. Sketching and calculating, he quickly saw that there was no way for hydrogen bonds to form along the long fiber axis, holding the windings of the chain in place, as in the alpha helix. Without them, what held the molecule in shape? One place that hydrogen bonds could form, he saw, was across the middle of the molecule, from phosphate to phosphate. That was a surprise, but everything else seemed to be working out. After six pages of calculations, he wrote, "Note that each chain has . . . roughly three residues per turn. There are three chains closely intertwined, and held together by hydrogen bonds between $PO_4$'s." The only problem was that there did not seem to be quite enough space in the center of the molecule, where the phosphates came into closest contact. He put down his pencil for the night.

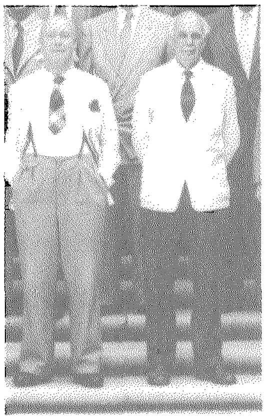
Three days later, he came back to the problem. According to Astbury's figures, DNA was a relatively dense molecule, which implied tight packing at the core. But trying to jam three chains' worth of phosphates into Astbury's space restrictions was like trying to fit the stepsisters' feet into Cinderella's glass slipper. No matter how he twisted and turned the phosphates, they wouldn't fit. *"Why are the $PO_4$ in a column so close together?"* he wrote in frustration. If Astbury's estimates on distances could be relaxed a bit, everything would fit, but Pauling could not do that without deviating too far from Astbury's x-ray data. Pauling next tried deforming the phosphate tetrahedra to make them fit, shortening some sides and lengthening others. It looked better, but still not right. He stopped again.

Next, he had an assistant go back through the literature in the chemistry library and pick up everything he could find on the x-ray crystallography of nucleic acids. There was not much to go on besides Astbury's work and that of Sven Furberg, a Norwegian crystallographer who had studied under Bernal and had found that the bases in DNA were oriented at right angles to the sugars. There was not one detailed structure of any purine or pyrimidine, much less a nucleotide.

On December 2 he made another assault, filling nine pages with drawings and calculations. And, he thought, he came up with something that looked plausible. "I have put the phosphates as close together as possible, and have distorted them as much as possible," he noted. Even though some phosphate oxygens were jammed uncomfortably close in the molecule's center, not only did it all just fit, but Pauling saw that the innermost oxygens packed together in the form of an almost perfect octahedron, one of the most basic shapes in crystallography. It was very tight, but things were lining up nicely. It had to be right. It had been less than a week



**This perspective model of DNA appeared in Pauling and Corey's paper, "A Proposed Structure for the Nucleic Acids," published in the *Proceedings of the National Academy of Sciences* in February 1953. The phosphate tetrahedra are in the center, connected by the sugar rings into chains with the purines and pyrimidines (here represented by purine only) attached on the outside.**



**Sir Lawrence Bragg (right), Nobel laureate, cofounder of x-ray crystallography, and director of the Cavendish Laboratory, was Pauling's great rival. He chaired one of the sessions of Pauling's protein conference here in September 1953. At left stands William Astbury of Leeds University, on whose x-ray data Pauling based his DNA model.**

since he first sat down with the problem.

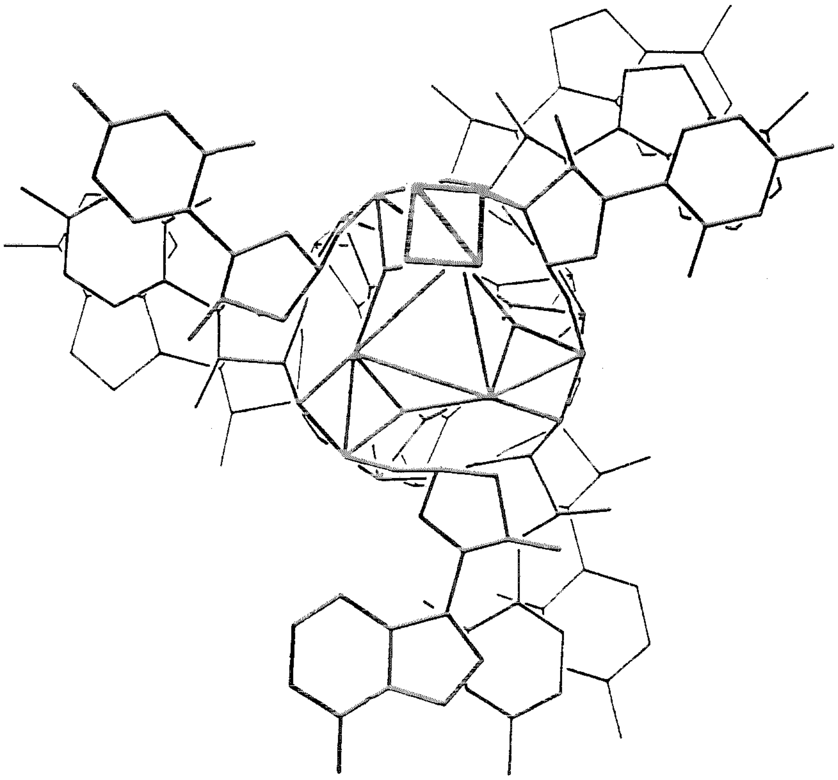
The next day, Pauling excitedly wrote a colleague, "I think now we have found the complete molecular structure of the nucleic acids." During the next several weeks he ran downstairs every morning from his second-story office in Crellin to Verner Schomaker's office, "*very* enthusiastic," Schomaker remembered, bouncing ideas off the younger man, thinking aloud as he checked and refined his model. He began working with Corey to pinpoint the fine structure.

Then came trouble. Corey's detailed calculation of atomic positions showed that the core oxygens were, in fact, too close to fit. In early December, Pauling went back to twisting and squeezing the phosphate tetrahedra. Someone brought up the question of how his model allowed for the creation of a sodium salt of DNA, in which the positive sodium ions supposedly adhered to the negative phosphates. There was no room for sodium ions in his tightly packed core, was there? Pauling had to admit he could find no good way to fit the ions. But that would sort itself out later. The other results were positive. Running the proposed structure through Crick's mathematical formula indicated that his model helix would fit most of the x-ray data, although not all of it. Schomaker played with some models on his own and found a way to twist the phosphate tetrahedra so that they were not quite so jammed, but for the moment Pauling saw no reason to change his ideas. The core phosphates were too neatly close-packed not to be true.

And this was what the central problem had reduced itself to in his mind: a question of phosphate structural chemistry. The biological significance of DNA would be worked out later, he thought; if the structure was right, the biological importance would fall out of it naturally in some way. At this point it was his business to get the structure, not the function. So he ignored the larger context surrounding the molecule and focused singlemindedly on one thing: finding a way to fit those phosphates into the core so that the resulting helixes fit the available data.

His faith in that approach had been justified by his success with the alpha helix. He had built his protein spiral from strict chemical principles, published it in the face of contradictory data, and later found the facts he needed to answer his critics. He was confident now about his ability to jump ahead of the pack, to use his intuitive grasp of chemistry to tease out a structure that felt right. If you waited for every doubt to be answered first, you would never get credit for any discovery. And his DNA triple helix felt right.

A week before Christmas, he wrote Alex Todd at Cambridge, "We have, we believe, discovered the structure of nucleic acids. I have practically no doubt. . . . The structure really is a beautiful one." Pauling knew that Todd had been working with purified nucleotides and asked him to send samples of x-ray analysis. "Dr. Corey and I are much disturbed that there has been no precise structure determination reported as yet for any nucleotide. We have decided that it is necessary that some of the structure determinations be made in our laboratory. I know that the Cavendish people are working in this field, but it is



**Another view of Pauling's model from his February 1953 paper shows the tightly packed phosphates in the middle with the nucleotide residues spiraling around the outside.**

such a big field that it cannot be expected that they will do the whole job." He then wrote his son Peter and Jerry Donohue that he was hoping soon to complete a short paper on nucleic acids.

But the structure still was not quite right. Everything would seem to fall into place when Corey came up with another set of calculations showing that the phosphates were packed just a little too tightly, their atoms jostling each other a little too closely to be reasonable. Pauling would readjust and tinker, bend and squash, so close to the answer yet unable to make it all fit perfectly.

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*{Two days before Christmas, professional FBI informer Louis Budenz named as concealed Communists 23 people, including Linus Pauling. An irate Pauling called him a liar, but Budenz was protected from prosecution for perjury by congressional privilege.}*

Depressed about this unexpected political attack, Pauling took the unusual step of inviting some colleagues into his laboratory on Christmas Day to have a look at this work on DNA. He was tired of the niggling problems with his model and ready for some good news. He got it from his small audience, who expressed enthusiasm for his ideas. Much cheered, Pauling spent the last week of the year working with Corey on the finalization of a manuscript.

On the last day of December 1952, Pauling and Corey sent in their paper, "A Proposed Structure for the Nucleic Acids," to the *Proceedings of the National Academy of Sciences*. This was, they stressed, "the first precisely described structure for the nucleic acids that has been suggested by any investigator"—thus positioning the work as the nucleic acid equivalent to the alpha helix. He went through his reasoning for the core structure. Most of the paper concentrated on precisely stacking phosphate tetrahedra, but there was a little biology, too. In Pauling's model, the bases, the message-carrying portion of nucleic acids, were directed outward, like leaves along a stalk, with room enough to be put into any order, providing maximum variability in the molecule and thus maximum specificity in the message. Astbury had already noted that the 3.4-angstrom repeat in nucleic acid was about the same as the distance per amino acid along an extended polypeptide chain, raising the idea that new proteins might be struck directly off a nucleic acid mold. Pauling noted that his model allowed the same thing to happen, with the sides of four adjacent bases along his chains forming a space just right for fitting an amino acid.

There was, however, an uncharacteristic tentativeness in the piece. This was "a promising structure," Pauling wrote, but "an extraordinarily tight one"; it accounted only "moderately well" for the x-ray data and gave only "reasonably satisfactory agreement" with the theoretical values obtained by the Crick formula; the atomic positions, he wrote, were "probably capable of further refinement."

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It was, in fact, a rush job. Pauling knew that DNA was important; he knew that Wilkins and Franklin were after it and that Bragg's group had already made at least one stab at it. He knew that it was a relatively simple structure compared to proteins. And he knew that whoever got out a roughly correct structure first—even if it was not quite right in all its details—would establish priority. That is what he was aiming for, not the last word on DNA but the first, the initial publication that would be cited by all following. It did not have to be precise. He wanted credit for the discovery.

The hurried haphazardness of the nucleic-acid paper can best be understood by comparison to Pauling's protein work. Pauling's alpha helix was the result of more than a decade of off-and-on analysis and thousands of man-hours of meticulous crystallographic work. Before he published his model, his lab pinned down the structure of the amino-acid subunits to a fraction of a degree and a hundredth of an angstrom. There was an abundance of clean x-ray work available on the subject proteins, allowing Pauling to scrutinize and eliminate dozens of alternative structures. Two years passed between the time he came up with the rough idea for his helix and the time he published it. Much of that interval was spent with Corey, overseeing and refining the precise construction of a series of elaborate three-dimensional models.

None of that went into DNA.

## *"The only doubt I have . . ."*

Crick and Watson were downcast by the news from Peter in late December that Pauling had solved DNA. Alternating between bouts of despair and denial—trying to figure out how he could have beaten them and then deciding that he certainly could not have without seeing Wilkins and Franklin's x-ray work and then thinking, well, of course, he is Pauling, so anything is possible—they continued working on the problem themselves. If they could come up with something independently before Pauling's paper appeared, at least they might share credit.

*There it was in black and white in a respected text: The phosphates had to be ionized. The book they were looking at was Pauling's* General Chemistry.

The previous spring, a few months after they had been warned off DNA and a few months before Pauling's visit to the Cavendish, Crick and Watson had been introduced to Erwin Chargaff, the acerbic and opinionated Austrian-born biochemist who had been using chromatography to analyze the chemical composition of nucleic acids. Chargaff was not impressed. "I never met two men who knew so little and aspired to so much," he said. "They told me they wanted to construct a helix, a polynucleotide to rival Pauling's alpha helix. They talked so much about 'pitch' that I remember I wrote it down afterwards, 'Two pitchmen in search of a helix.'" But this conversation was critical to Crick and Watson. Chargaff told them that there was a simple relationship between the occurrence of different bases in DNA, that adenine and thymine were present in roughly the same amounts and so were guanine and cytosine. One of each pair was a larger purine; the other, a smaller pyrimidine. It was the same relationship that he had told Pauling about during their Atlantic crossing in 1947 and that Pauling had ignored.

But it made all the difference to Crick and Watson. Franklin's criticisms had already pointed them toward putting the phosphates on the outside of the molecule; now they had the clue of a one-to-one relationship between the bases on the inside. They began thinking about helixes in which the purines and pyrimidines lined up somehow down the core of the molecule.

When Pauling's much anticipated DNA manuscript arrived via Peter in early February 1953, both researchers were surprised to see something that looked like their own abortive three-chain effort, only more tightly put together. A few minutes' reading showed that there was no room at the core for the positive ions needed to hold together the negatively charged phosphates. Crick and Watson were dumbfounded. Pauling's structure depended on hydrogen bonds between the phosphate groups, but how could there be a hydrogen there when the phosphates in DNA lost their hydrogens at normal pH? "Without the hydrogen atoms, the chains would immediately fly apart," Watson said. They had already been through this with their own model, but they checked it again, and there it was in black and white in a respected text: The phosphates had to be ionized. The book they were looking at was Pauling's *General Chemistry*.

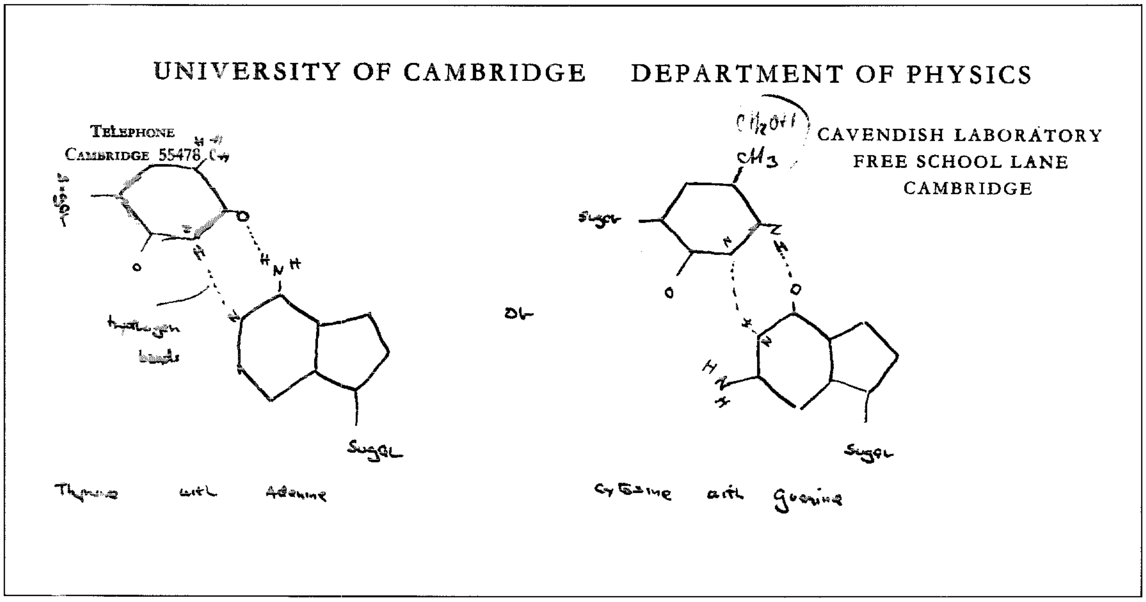
There was an immense feeling of relief. "If a student had made a similar mistake, he would be thought unfit to benefit from Caltech's chemistry faculty," Watson later said. He and Crick immediately went off to confirm their criticism with Cambridge's chemists. Before the day was out, Pauling's mistake was the talk of the college: Linus's chemistry was wrong.

Just as importantly for Watson, when he told Wilkins of Pauling's mistake and his idea that DNA was helical, he was given a reward: his first look at the more recent x-ray patterns Franklin had gotten from the molecule. She had found that DNA existed in two forms, a condensed dry form and an extended wet form the structure assumed when it drank up all that water. Astbury's photos, the ones Pauling had used, had been of a mixture of the two forms. Franklin's recent shots, much clearer and of only the extended form, immediately confirmed to Watson that the molecule was a helix and gave him several vital parameters for its solution.

With obvious satisfaction, Crick, still smarting a bit from the coiled-coil affair *(a dispute over credit for a solution to the alpha-helix structure)*, wrote Pauling, to thank him for providing an advance copy of his nucleic acid paper. "We were very struck by the ingenuity of the structure," he wrote. "The only doubt I have is that I do not see what holds it together."

Pauling's apparent misstep pleased Bragg so much that he agreed to let Crick and Watson go back full-time to DNA. There was a window of opportunity here, and he wanted the Cavendish to take advantage before Pauling had time to regroup.

Pauling, however, had already moved on to a new project, a theory of ferromagnetism that he




**Watson's letter of March 12, 1953, to Max Delbrück contained this drawing at the top of the second page illustrating the last piece of the puzzle—the hydrogen bonds that form between thymine and adenine and between cytosine and guanine, making a ladder of paired bases across the double helix. At the end of his letter, Watson asked Delbrück, shown below in his Caltech lab in 1949, not to mention this latest solution to Pauling. But it was too good to keep quiet; Delbrück showed him the letter immediately.**

worked on through the spring. He also began making plans for a major international protein conference in Caltech the next fall and was drawn back to DNA only when Peter wrote him in mid-February about the English hooting at his structure. Corey had by now finally finished checking Pauling's atomic coordinates, some of which appeared again to be unacceptably tight. "I am checking over the nucleic acid structure again, trying to refine the parameters a bit," Pauling wrote Peter back. "I heard a rumor that Jim Watson and Crick had formulated this structure already sometime back, but had not done anything about it. Probably the rumor is exaggerated." In late February he finally tried Schomaker's suggestion of twisting the phosphate groups 45 degrees and found that it eased some of the strain.

Something was still wrong. When Pauling gave a seminar on his DNA structure at Caltech, the reception was cool; afterward, Delbrück told Schomaker that he thought Pauling's model was not convincing. He mentioned a letter he had gotten from Watson saying that Pauling's structure contained "some very bad mistakes" and in which Watson had added, "I have a very pretty model, which is so pretty that I am surprised that no-one ever thought of it before." Pauling wanted to know more. He quickly wrote Watson inviting him to his fall protein conference, mentioning that he had heard from Delbrück about his DNA work, and encouraging him to keep working on the problem. "Professor Corey and I do not feel that our structure has been proven to be right," he wrote, "although we incline to think that it is." In early March he drove with Ava Helen to the University of California at Riverside to examine a collection of organic phosphates there, finding candidates for structural analysis that would be similar to the phosphate groups in DNA, looking for models to tell him how much he could deform his tetrahedra. Crick's barb about what held the molecule together led him to gather chemical precedents for the existence of adjoining negative charges in the same molecule, and he began to reason to himself that perhaps the DNA core environment was a special one that allowed the phosphates to exist as he had proposed. It was still, to Pauling, a matter of phosphate chemistry. Meanwhile, Todd had sent him the requested samples of nucleotides, and Pauling started their x-ray analysis.

He was finally laying the groundwork for a reasonable structure. But it was too late.

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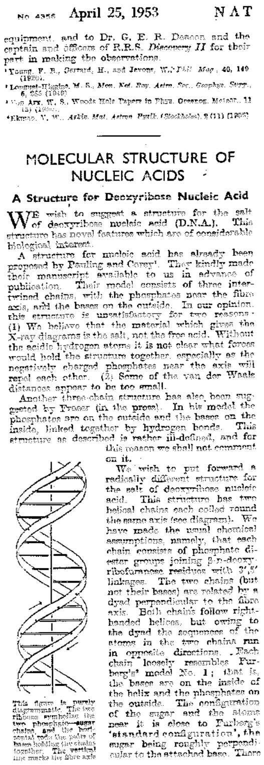
Given the go-ahead to return to DNA, thanks to Pauling's paper, Crick and Watson each began feverishly devising models, focusing more on two-stranded models now that Chargaff had gotten them thinking of bases somehow pairing with each other. The "very pretty model" of which Watson had written Delbrück was one attempt, but it was wrong, as Jerry Donohue pointed out.

Donohue's input turned out to be critical. A magna cum laude graduate of Dartmouth who had worked and studied with Pauling at Caltech since the early 1940s, Donohue knew structural chemistry inside and out. Hydrogen bonding


No. 4356 April 25, 1953 NAT

equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

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[2] Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, 5, 285 (1949).
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MOLECULAR STRUCTURE OF NUCLEIC ACIDS

**A Structure for Deoxyribose Nucleic Acid**

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There

This figure is purely diagrammatic. The two ribbons symbolize the two phosphate—sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

**The elegant structure of Watson and Crick's double helix, with its paired nucleotides forming a ladder through the center, left no doubt in anyone's mind by the time it was published in *Nature* in April 1953.**

*More than beautiful, the structure had meaning.*

had been a specialty of his, and he saw that Crick and Watson, chemical novices that they were, had been playing with the wrong structures for guanine and thymine. He set them right, switching the hydrogen atoms essential for cross-bonding into their correct positions, destroying their earlier model and pushing them toward the correct solution.

With Donohue's corrections, Crick and Watson could now see hydrogen bonds forming naturally between specific pairs of purines and pyrimidines: adenine to thymine and guanine to cytosine. That was the last piece of the puzzle, and the result was dazzling. Matching a large with a small base not only smoothed the structure's outline but provided a simple explanation for Chargaff's findings. The resulting structure, a sort of ladder with base pairs as the steps and the sugar-phosphate backbone as the runners, formed easily into a helix that matched the x-ray data.

More than beautiful, the structure had meaning. Each strand was a complementary mirror image of the other; if separated, each could act as a mold for forming a new double helix identical with the original. This immediately provided ideas about replication that Pauling's model, with its bases facing out and unrelated to each other, could not.

On March 12, Watson sent Delbrück a letter, illustrated with rough sketches, discussing their new model. He warned his mentor not to tell Pauling about it until they were more certain of their results, but Delbrück, never one to keep secrets, immediately showed the letter around. Pauling's mind raced as he read it. He saw immediately that the Cavendish structure was not only chemically reasonable but biologically intriguing. "The simplicity of the structural complementariness of the two pyrimidines and their corresponding purines was a surprise to me—a pleasant one, of course, because of the great illumination it threw on the problem of the mechanism of heredity," he said. In it he could see echoes of many of the things he had been thinking and writing about complementarity since his 1940 paper with Delbrück.

The same day that Alex Rich *[who worked in Pauling's lab]* first heard about the Watson-Crick structure, he awoke in the middle of the night, got out of bed, went into his office, and began building a rough version of the Watson-Crick double helix out of the pieces of molecular models he had there. All he knew was that they had paired the DNA bases across the center of the molecule, but knowing that was enough. He quickly paired the correct bases, saw that it worked beautifully, and went back to bed shaking his head.

Pauling, while not yet ready to concede the race, was impressed. A few days after seeing Watson's letter, he wrote a colleague, "You must, of course, recognize that our proposed structure is nothing more than a proposed structure. There is a chance that it is right, but it will probably be two or three years before we can be reasonably sure. . . ." A few days later, he received an advance copy of the Watson and Crick manuscript, which started by attacking his DNA model and ended by thanking Jerry Donohue for his help. Pauling looked it over and wrote his son, "I think that it is fine that there are now two proposed structures for nucleic acid, and I am looking forward to finding out what the decision will be as to which is incorrect. Without doubt the King's-College data will eliminate one or the other."

He still had not seen any of Franklin's or Wilkins's recent x-ray photos and withheld final judgment until he did. His chance would come soon: He was planning to go to Brussels in April for a Solvay Conference on proteins and intended to stop off in England on the way to see the Watson-Crick model and the photos from Wilkins's and Franklin's laboratories. When he applied for a passport, his old nemesis Ruth Shipley *[head of the State Department's passport division]* again recommended denial, this time based on her belief that Pauling's Industrial Employment Review Board (IERB) testimony proved that he was refusing to be considered for top-secret clearance. After Pauling explained that he had been cleared for top-secret material

*He was amazed that this unlikely team, an adolescent postdoc and an elderly graduate student, had come up with so elegant a solution to so important a structure.*

**Watson (left) and Crick show off their DNA model, which they had wired together out of die-cut metal plates.**

in the past and would be willing to be again, but only if it was required for his work—and after he once more swore in her presence that he was not a Communist—his passport was approved.

In early April, a few days after Crick and Watson submitted their paper for publication, Pauling arrived in Cambridge. After spending the night with Peter, he walked into Crick's office and for the first time saw the three-dimensional model they had wired together out of die-cut metal plates. Crick chattered nervously about the features of the double helix while Pauling scrutinized it. He then examined Franklin's photo of the extended form of the molecule. Watson and Crick waited. Then, "gracefully," Watson remembered, "he gave the opinion that we had the answer."

It was a joyful moment for the two young men and a deflating one for Pauling. He was amazed that this unlikely team, an adolescent postdoc and an elderly graduate student, had come up with so elegant a solution to so important a structure. If they were right, his own model was a monstrous mistake, built inside out with the wrong number of chains. But he recognized now that the Cavendish team was almost certainly right.

There was only one thing left for him to do: Show the world how to handle defeat with style.

Pauling left Crick's office and met Bragg for lunch, during which Sir Lawrence vainly tried to restrain his ebullience. After so many years of coming in second, his team had finally beaten Pauling! Later, Pauling joined the Cricks at a pleasant dinner at their house at Portugal Place. Through it all he remained charming and funny and remarkably accepting of the new DNA structure, a true gentleman, both wise enough to recognize defeat and great enough to accept it with good humor. A day or two later both Bragg and Pauling went to the Solvay meeting—an occasional select gathering of the world's top researchers funded by a Belgian industrialist—where Bragg provided the first public announcement of the double helix. Pauling was generous in his support. "Although it is only two months since Professor Corey and I published our proposed structure for nucleic acid, I think that we must admit that it is probably wrong," he told the group. "Although some refinement might be made, I feel that it is very likely that the Watson-Crick structure is essentially correct."

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*[There was no shortage of opinions as to what had gone wrong—from ignoring the molecule's biological*

*function to ignoring others' results. Pauling himself blamed the x-ray photos he had used, his misreading of DNA's density, and his lack of knowledge about purines and pyrimidines.}*

Each excuse contained a measure of truth. But each was a symptom of a problem, not the problem itself.

There were two reasons Pauling failed with DNA: hurry and hubris. He rushed because DNA was the biggest prize around and if he did not crack it, someone else—probably someone in England—soon would. Although he later denied he was competing with the British researchers for the DNA structure—"I did not feel that I was in a race with Watson and Crick," he said. "They felt that they were in a race with me"—the fact was that he *was* in a race, perhaps not with the unknown Watson and Crick but certainly with Wilkins and Franklin and, above all, with his oldest rival, Sir William Lawrence Bragg. Pauling wanted to publish his DNA structure quickly in order to beat Bragg's group, and Wilkins, too, and he took a chance doing it without having done his homework.

*In certain cases he had to trust himself, not the experimental results. He had to trust his intuition, his nose for a good structure.*

Pauling had no precise structures for the nucleotide subunits. The x-ray photos he used, those that Astbury had done years before, were muddy and vague, and Pauling never attempted to make x-ray photos of his own prior to publication. He started with one idea, the phosphate-core model, and never deviated from it. No three-dimensional models were ever built. Pauling did not even have Corey check his figures a final time before sending in the paper. He wanted the credit for solving DNA, and to get it he had to publish first.

More importantly, he rushed because he thought he could get away with it. His success with the alpha helix had given him faith that he could jump ahead successfully. All of the basic assumptions that he had made in the late 1930s had been right; 15 years of further research had only proved it. He was right about hydrogen bonding and the planar peptide bond and the nonintegral repeat. As long as he stuck with what he knew about chemistry, he was always right.

The alpha helix had graced him with success and cursed him with overweening pride. After its solution, he believed he no longer needed to do the homework required by others. It was clear that he was the best person in the world at solving the structure of giant molecules—any molecules, for that matter. He knew that he had put together the correct basic structure of the alpha helix two years before he published it, two long years during which Bragg might have come up with the answer and beaten him to it. Pauling had hesitated then because of his doubts about the 5.1-angstrom x-ray reflection, an experimental observation that turned out to be irrelevant. The lesson was clear: In certain cases he had to trust himself, not the experimental results. He had to trust his intuition, his nose for a good structure. He knew that his triple-stranded DNA structure was very tight and that it begged the question of how the negatively charged phosphates could keep from repelling each other, but he believed that those matters would work themselves out, as the missing reflection in his alpha helix had worked itself out as a matter of coiled coils. The phosphate packing in the center of his model was too pretty, too clever not to be right.

He wanted the prize, he gambled, and he lost.

He regretted it, of course, the remainder of his life, although he was soon back to his usual cheerful self around the lab. Within a few months he could joke with Alex Rich about it, asking him how his new project on a special form of DNA was going, then adding, "You work hard on that problem, Alex, because I like *most* of the important discoveries to be made in Pasadena."

The encounter with DNA would become the stuff of legend in the literature that would spring up around its discovery. Watson and Crick would take center stage, with Pauling assuming the smaller part of an offstage voice, a legendary Goliath in a far land felled by two unlikely Davids. A year would rarely go by after 1953 without someone, a scientist or writer, asking him where he had gone wrong.

Ava Helen finally tired of it. After hearing the questions and explanations over and again, she cut through the excuses with a simple question. "If that was such an important problem," she asked her husband, "why didn't you work harder on it?" □

*Thomas Hager, who is director of the Office of Communications at the University of Oregon, wrote this biography with extensive cooperation from Pauling himself before his death in August 1994 at the age of 93. Pauling granted Hager hours of interviews and access to private papers, correspondence, and diaries; in addition to scores of interviews with Pauling's family, colleagues, and others, Hager also consulted previously unreleased FBI and State Department documents.* Force of Nature *can be ordered from the Caltech Bookstore (Mail Code 1-51, Pasadena, CA 91125) for $35.00; add $6.50 for shipping and handling.*