The structure of DNA: Cooperation and competition

During the early 1950s, the intellectual journeys of a bird biologist, an expert on the structure of coal, a designer of underwater mines, and a nuclear physicist intersected, resulting—not in a submarine explosion of feathers, as one might expect—but in a discovery that offered a glimpse of the molecular mechanisms that underlie all life, paving the way for a revolution in molecular biology. The insight, innovation, and persistence of James Watson, Rosalind Franklin, Francis Crick, and Maurice Wilkins led to a detailed understanding of the structure of DNA, the stuff that genes are made of (Fig. 1). This discovery brought together information from many disciplines and many researchers to answer one of the most fundamental questions in life science: How do living things pass on traits to their offspring?

Fig. 1. Clockwise from top left, James Watson, Francis Crick, Maurice Wilkins, and Rosalind Franklin. Center, Image B 51, a key piece of evidence in the discovery of the structure of DNA.

This case study highlights the following aspects of the nature of science:

- Science can test hypotheses about things that are too small for us to observe directly.
- Science relies on communication within a diverse scientific community.
- Scientists are expected to give credit where credit is due.
- Scientific discoveries lead to ongoing research.

The right timing

Scientific discoveries may seem like sudden breakthroughs—the work of a genius who just "sees" the answer—but new findings don't come out of nowhere. Each breakthrough is made possible by the work that came before it. Some scientific discoveries are a bit like putting together the pieces of a puzzle. Many different researchers discover important bits of evidence—pieces of the puzzle—and the sudden breakthrough arises when one group or person sees how the puzzle pieces logically fit together. And sometimes—as in the case of DNA—new findings and technological advances have made so many new puzzle pieces available that the odds of *someone* putting them together seem quite high. Making this final leap often involves a brilliant insight—but it's important to recognize all the clues which made that insight possible.

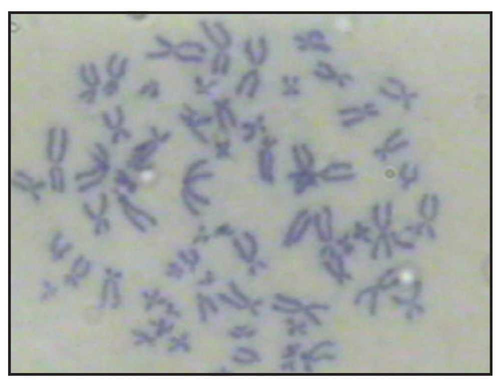

Fig. 2. Human chromosomes magnified 1000 times.

In the 19th century, the Austrian monk, Gregor Mendel, discovered basic patterns of inheritance. Traits pass from parent to offspring in an organized and predictable way. Although the scientists that followed in Mendel's footsteps had no concrete understanding of what caused these distinct patterns, they knew that the explanation of inheritance would have to account for them.

By the 1940s and 50s, scientists were getting closer to a physical explanation of how parents pass on traits to their offspring. New technology had made it possible to observe smaller structures than ever before. Biologists had found that genetic instructions are carried on parts of the cell known as chromosomes (Fig. 2), and chemists had discovered that these chromosomes are made up of two components: proteins and DNA. Furthermore, experiments looking for the key molecule of life had zeroed in on DNA, and not protein, as the component that actually carries genetic information (Fig. 3).

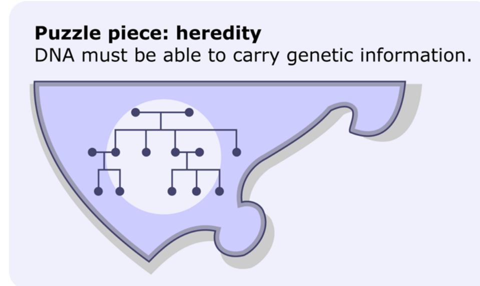

Fig. 3.

But exactly how could DNA carry all the information needed to make a new organism? The answer might be revealed by the molecule's three-dimensional structure—and some tantalizing clues regarding this structure were becoming available. Researchers already knew that DNA was a relatively simple molecule. It seemed to consist of an unremarkable chain of phosphates and sugars, in some way attached to a set of ring-shaped molecules called nitrogenous bases. These bases come in four "flavors": adenine (A), thymine (T), cytosine (C), and guanine (G) (Fig. 4). Somehow, these simple components would have to carry all the instructions necessary to make fruit flies, oak trees, humans, and the rest of life. Some early work suggested that the bases were arranged like a stack of pancakes in the molecule, each 0.34 nanometers apart from one another,[1] but other than that, little was known about exactly how a DNA molecule was put together.

To further complicate matters, researchers had discovered another intriguing—but perplexing—clue. DNA's bases always occur in the same special ratios: the amount of A is always equal to the amount of T, and C is always equal to G—though the ratio of A/T to C/G varies from species to species.[2] What this meant wasn't clear, but any hypothesis about DNA's three-dimensional structure would have to account for this strange observation.

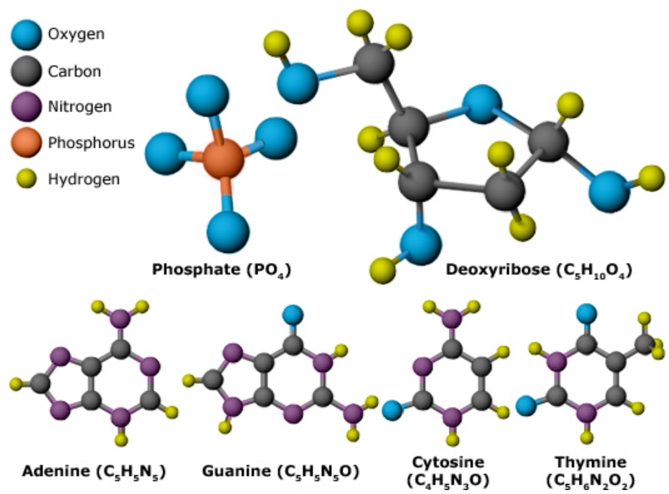

Fig. 4. The molecular components of DNA: phosphates, deoxyribose (a sugar), and the four nitrogenous bases, adenine, guanine, cytosine, and thymine.

Around the same time that these three puzzle pieces were discovered (Fig. 5), more and more physicists and chemists were becoming interested in applying their knowledge and skills to learning about the physical basis for life. To add further fuel to the fire, technological breakthroughs and refinements had recently offered scientists new ways to study the positions of atoms within molecular structures. Together, these factors were providing scientists with the tools and insights to put the DNA puzzle together. The stage was set for a breakthrough.

[1]Astbury, W.T. 1939. X-ray study of thymonucleic acid. Nature 141(3573):747-748.
[2]Chargaff, E. 1950. Chemical specificity of nucleic acids and mechanism of their enzymatic degradation. Experientia 6(6):201-209.

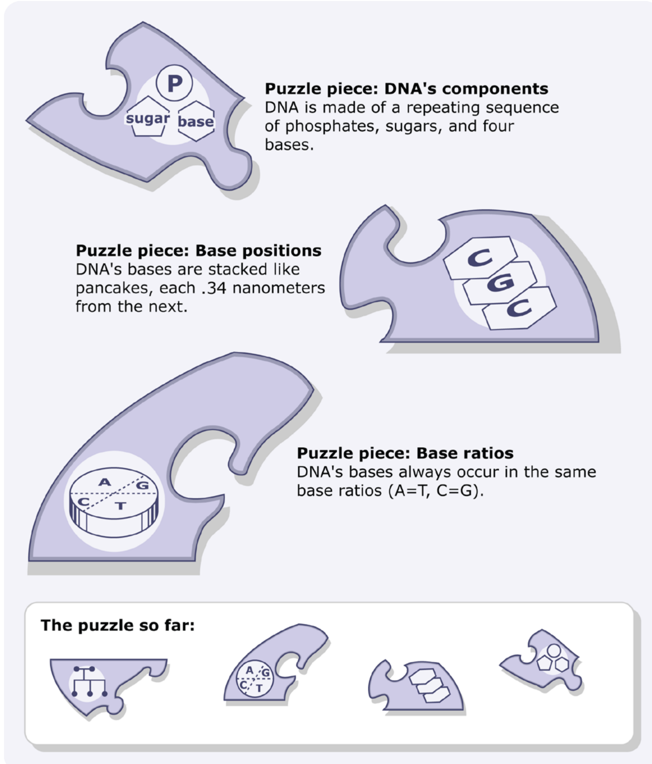

Fig. 5.

The great race

Onto the scene, from all different directions, came Wilkins and Franklin, then Watson and Crick (Fig. 6). Though their scientific backgrounds were diverse, all four recognized that understanding how the parts of a DNA molecule fit together would provide important information about the way life works. Each hoped to be part of the team that solved the puzzle first. Wilkins and Franklin worked together at the University of London, and Crick and Watson collaborated at Cambridge University—but they weren't the only scientists thinking about DNA. Several other groups also recognized that the three-dimensional structure of DNA was within reach, so the competition was stiff. Linus Pauling, a soon-to-be Nobel Prize winner who had already solved a complicated molecular structure found in proteins, led one of the groups working to identify DNA's structure. The number of people investigating the problem made it a race right from the beginning. The edges of the puzzle were laid out—but who would be the first to fill in all the pieces?

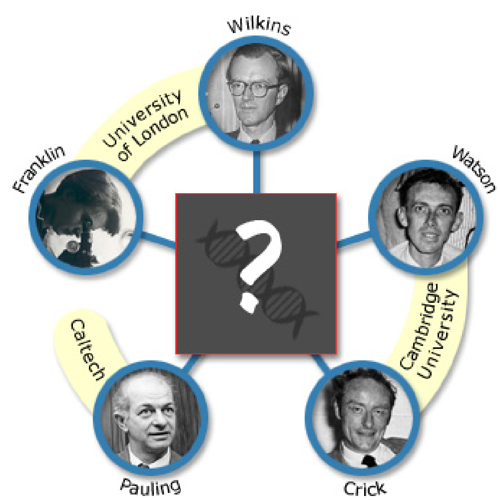

Fig. 6.

Atoms and X-rays: Seeing inside a crystal

Fig. 7. Raymond Gosling, a Ph.D. student in the lab at the University of London.

Maurice Wilkins, the nuclear physicist, entered the race for DNA based on a stroke of luck. After his work with the Manhattan Project on atomic bombs was completed, he wanted to switch to a more peaceful line of work and was inspired to investigate the physical basis for life. He turned to the fast-growing field of biophysics, taking up a position at the University of London. Early in his career there, he happened to attend a conference where a biochemist gave away samples of high-quality DNA. Wilkins was lucky enough to get a sample—though it might not have seemed that impressive at the time. It was so slimy and gooey that he later described it as "just like snot." Nevertheless, because it contained long, intact DNA molecules—which were hard to come by at the time—this slippery sample would turn out to be critical in uncovering clues to DNA's structure. Raymond Gosling (Fig. 7), a Ph.D. student in Wilkins' lab, suggested looking at the DNA with a new observational technique called X-ray diffraction.

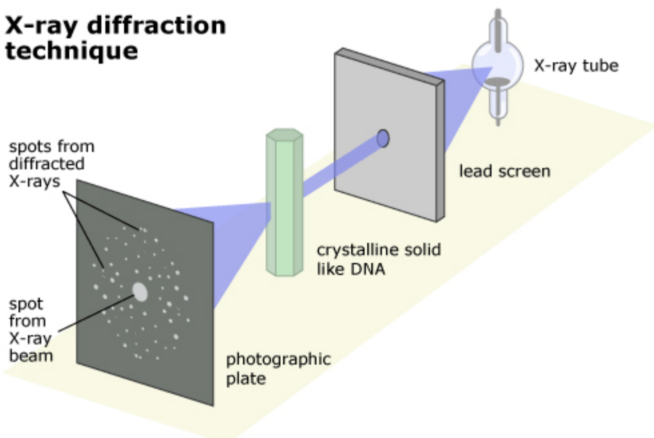

Fig. 8.

X-ray diffraction, developed in the first half of the 20th century, was one of the new technologies that made solving the structure of DNA possible. The technique works on crystals, a kind of molecule with a regular, repeating structure. When X-rays are aimed through a sample, they are bent or diffracted in different directions depending on the locations of the atoms in the sample, and the final direction of the X-rays can be recorded on film (Fig. 8). Because the X-rays must travel through many layers of atoms, it's important that the atoms always occur in the same crystalline arrangement. If they don't, the X-rays are bent into overlapping patterns, leaving the results a fuzzy, indistinct blur. However, if the structure has a repeating arrangement of atoms, they leave a pattern of sharp, clear spots. Different structures scatter the X-rays into different characteristic patterns.

Even though scientists couldn't directly observe the atoms within the crystal, they could work backward from X-ray diffraction patterns to reconstruct the three-dimensional structure that produced the scattering. This works a little like trying to figure out how tall a person is by looking at his or her shadow. Depending on the angle of the sun, the shadow might be longer or shorter, but if you could compare many pictures of their shadow at different times of day, you'd eventually be able to figure out how tall they were. Similarly, scientists compare many "shadows," or X-ray diffraction patterns, cast by a crystal to determine the arrangement of atoms within it.

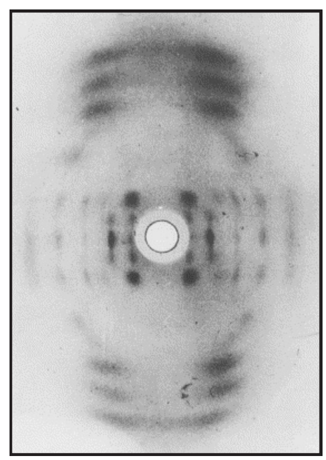

Fig. 9. This X-ray diffraction pattern photographed by Gosling and Wilkins in 1950 showed that DNA *did* have a crystalline structure.

Although the DNA didn't *look* very crystalline, Gosling wanted to try X-ray diffraction on the molecule anyway. Wilkins and Gosling knew DNA's structure might be too irregular to produce a clear, well-defined X-ray pattern, but as it turned out, the sample was sticky and stringy because it was made up of lots of long, thin molecules of intact, crystalline DNA. Over the summer of 1950, Wilkins and Gosling's patterns showed that DNA *did* have a regular structure—which meant that X-ray diffraction would be a critical tool in solving the structure (Fig. 9). The patterns even suggested what that basic structure might be. Despite a few confusing blurry spots, the images hinted that DNA might come in the form of a twisted spiral—better known as a helix—though it was still not clear how the phosphates, sugars, and bases were arrayed within that helix (Fig. 10).

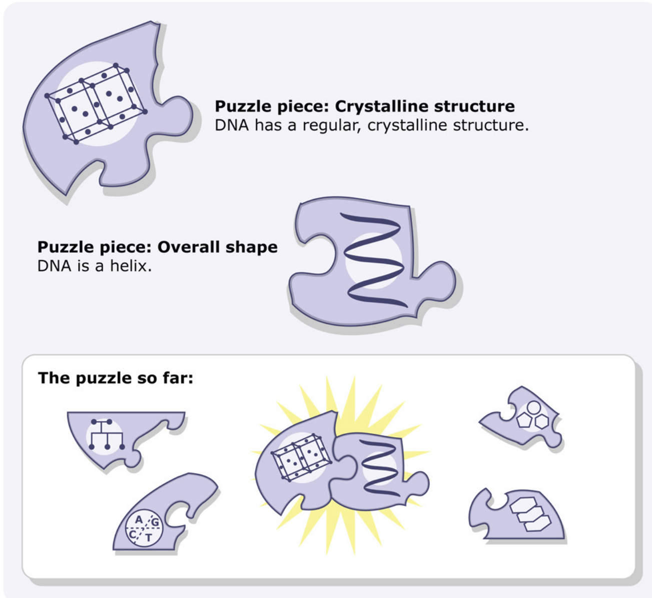

Fig. 10.

Passing puzzle pieces

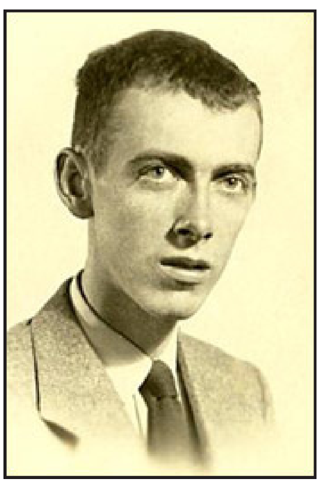

Fig. 11. James Watson, 1949.

Wilkins' and Gosling's results were intriguing enough to be communicated to the scientific community. Researchers regularly share their findings and ideas with one another so that others can evaluate and build upon them. Scientific conferences provide a direct way of doing this. In May of 1951, Wilkins set off to present the results at a conference in Italy. There, these tantalizing clues would inspire another scientist to join in the race for the structure of DNA.

James Watson (Fig. 11) was studying biochemistry at the Naples Marine Station—but he spent every spare moment reading about genes and the molecules they might be made of. Although Watson began his career studying birds, he had switched to genetics as a graduate student. He felt that understanding genes was essential to figuring out how life worked—and all the latest evidence suggested that genes were made of DNA. So when Wilkins presented his findings—the most detailed information then available on the structure of DNA—Watson was in the audience, watching with interest (Fig. 12). He could see from Wilkins' results that there was a repeating pattern to DNA's structure. If he could just figure out what caused that pattern, he thought he would be able to unravel the structure itself.

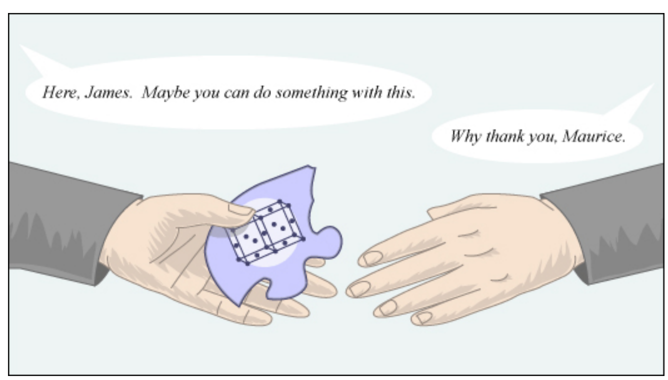

Fig. 12.

Watson photo courtesy of Cold Spring Harbor Laboratory Library and Archive, James D. Watson Collection

Fig. 13. Francis Crick and James Watson in the 1950s.

Inspired by this clue, Watson decided to devote all his time and energy to understanding the structure of DNA. At first, he wanted to join Wilkins' lab—but Wilkins didn't have any room. Instead, in the autumn of 1951, he joined another lab specializing in X-ray diffraction, at Cambridge University. There, he shared Wilkins' and Gosling's clue about DNA with someone who would soon join him in the race for the structure of DNA, Francis Crick (Fig. 13).

Like Wilkins, Crick had started out as a physicist. During World War II, he put his scientific training to work designing underwater mines. After the war, he got interested in studying the physical basis of life and joined a Cambridge biology lab. There, Crick launched into an investigation of protein structure—but his concentration on this project was soon to be interrupted by Watson's arrival in the lab.

Watson's enthusiasm for DNA was contagious. He was convinced by the published results suggesting that genes were made of DNA. And though he did not yet know that a helical structure had been suggested for DNA, he had seen the evidence from Wilkins' presentation indicating that the structure of DNA was simple enough to solve. Watson shared this evidence with Crick—who eventually decided to join the race himself (Fig. 14).

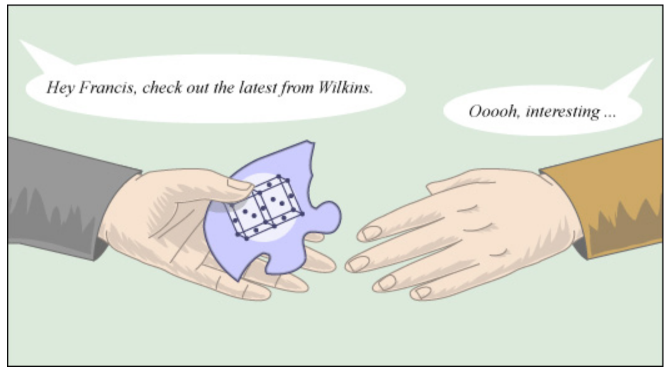

Fig. 14.

Franklin joins the fray

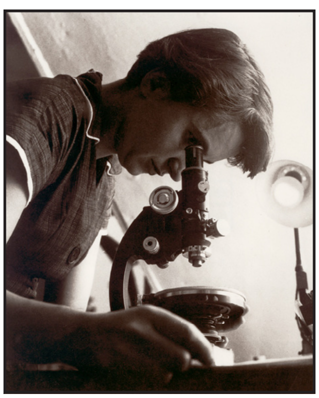

Fig. 15. Rosalind Franklin at work in 1954.

While Crick and Watson were joining forces at Cambridge, things were changing back in Wilkins' lab at the University of London too. The preliminary findings were exciting—they knew that DNA had a regular structure—but they still had to figure out what that structure was. Expert help was needed to improve and interpret the X-ray results. Luckily, Rosalind Franklin, a scientist who specialized in X-ray diffraction, had just joined the lab (Fig. 15). Franklin was used to working with messy materials that came from living things—she had just finished an important study applying X-ray diffraction to coal, the compressed remains of ancient swamp plants. She was asked to lend her expertise to the DNA project, and it soon caught her imagination.

Franklin began working with Raymond Gosling, the graduate student who had encouraged Wilkins to try X-ray diffraction on his DNA sample. Over the summer of 1951, she taught Gosling the exacting X-ray diffraction techniques she'd developed. They exposed the special high-quality DNA sample to a range of different humidities, from wet to dry. In the dry atmosphere, the strands appeared to thicken, and the X-ray patterns turned into a sharp scatter with many distinct spots. As they added moisture to the atmosphere, the strands stretched, and the X-ray pattern changed to a clear x shape (Fig. 16).

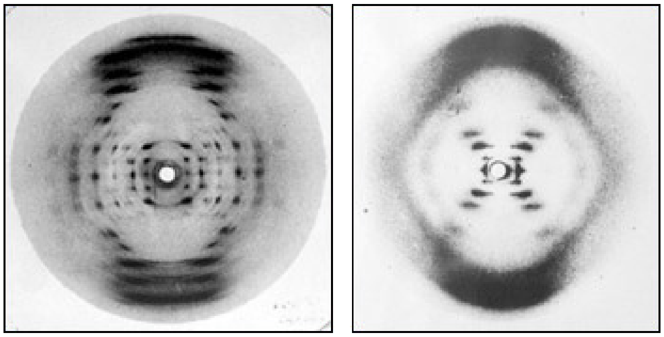

Fig. 16. X-ray diffraction patterns for the two forms of DNA; at left, form A, at right, form B.

The two different patterns demonstrated that DNA existed in two forms: the dry A form, which held less water, and the wet B form, in which water molecules cling to the DNA, causing it to stretch out (Fig. 17). The first X-ray images of DNA taken by Wilkins and Gosling (Fig. 9) had been sharp, but they had contained a few confusing blurry spots. Franklin and Gosling's new images explained why: the previous images were based on a blend of the two forms mixed together.

The University of London group had now uncovered several important clues to DNA's structure: it was crystalline, at least one of its forms took the shape of a helix, and many water molecules could cling to it. Franklin took things one step further, fitting together a few of the existing puzzle pieces. Based on the ease with which DNA took up water, she reasoned that the phosphates (which attract water) must be on the outside of the helix (Fig. 18). The London crew was off to a good start—but they would soon face stiff competition from another approach.

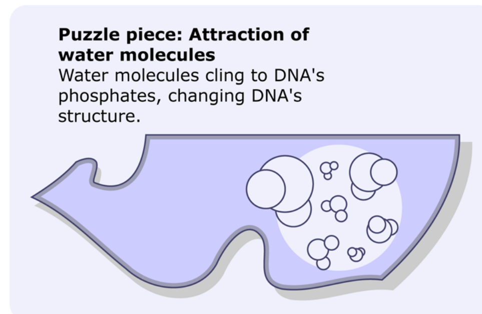

Fig. 17.

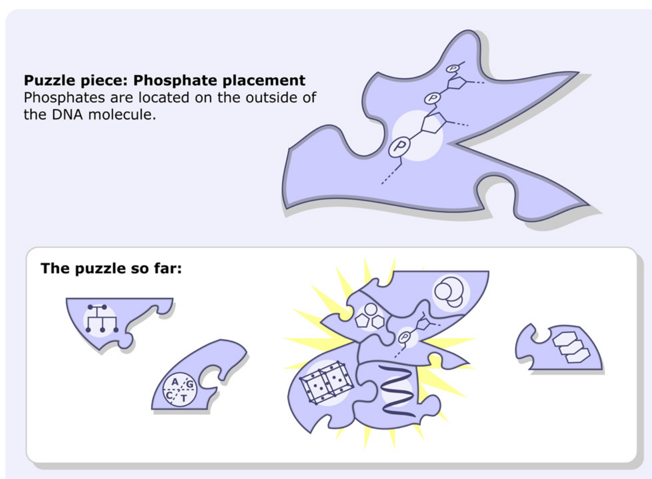

Fig. 18.

Diffraction patterns of Forms A and B of DNA courtesy of Cold Spring Harbor Laboratory Library and Archive, James D. Watson Collection

A model approach

Crick and Watson wanted to work on DNA's structure, but they couldn't approach it as Wilkins and Franklin were—through X-ray diffraction. First, Crick was a friend of Wilkins and didn't want to step on his toes. Second, Watson and Crick didn't have the high-quality DNA samples necessary for X-ray diffraction. But Watson and Crick had another way of working—they could form hypotheses about DNA's structure by building a physical model of how its atoms fit together (Fig. 19).

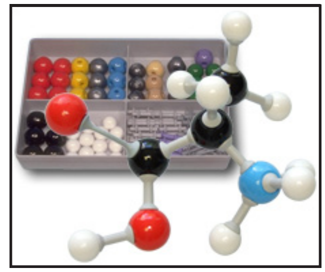

Fig. 19. One type of molecular modeling kit that is widely available today. The original Watson and Crick model was made using wire and pieces of flat metal, before good molecular model components became affordable.

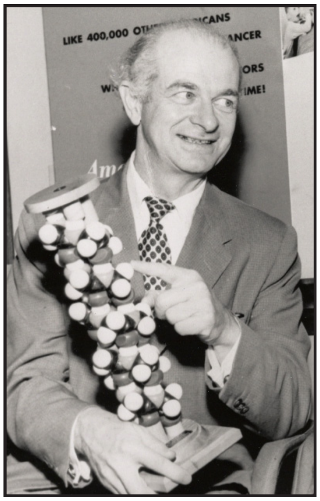

Fig. 20. Linus Pauling with a model of the helical structure exhibited in some segments of proteins.

Today, ball-and-stick models like the ones Watson and Crick used are available in most chemistry classes—but in 1951, they were found in only the best-equipped labs. In the first half of the 20th century, painstaking chemical work established the approximate sizes of atoms, the number of bonds they form with other atoms, and the angles at which these bonds form. The models Watson and Crick worked with incorporated all of this information. The flexibility and accuracy of the models allowed them to try out many different structures and quickly see whether they agreed with what was known about chemical bonding. This made the models a good way to form new hypotheses about the shape of a molecule—something too small to observe directly.

Watson and Crick were also encouraged by the fact that Linus Pauling (Fig. 20), a chemist who studied bond formation, had just used models to figure out the helices that are part of the structures of many proteins. Pauling came up with the solution by starting with X-ray diffraction data, then using ball-and-stick model-building as a shortcut. This approach had allowed him to find the solution much more quickly than he could have by using X-ray data alone. The success of his approach inspired Watson and Crick to try the same thing.

A false start

In order to try model building, Crick and Watson still needed data on DNA as a starting point. Molecular model-building works because it lets researchers explore different hypotheses about molecular structures and see which hypotheses fit well both with our knowledge about how atoms bond together and with evidence regarding the structure of a particular molecule like DNA. But evidence of DNA's structure came mainly from X-ray diffraction, Wilkins and Franklin's domain.

Fortunately for Crick and Watson, communicating evidence and results is a standard part of the process of science. They kept an eye out for any talks or papers related to DNA's structure, and as soon as they heard that Franklin was going to share her findings in a talk at the University of London, Watson made plans to go. At the presentation, Franklin showed X-ray diffraction patterns produced by DNA A and B, and discussed how the two forms seemed to be produced by surrounding the DNA molecules with different amounts of water. She also described the spacing between the atoms in DNA, based on the patterns in her diffraction images. Watson listened with interest (Fig. 21). Yet the next day, his memory failed him when he met up with Crick to discuss the evidence Franklin had shared. In particular, he couldn't seem to remember how much water Franklin had

Molecular model image from photos courtesy of Dave Barnes, Arbor Scientific (www.arborscientific.com); photo of Pauling with model courtesy of the Ava Helen and Linus Pauling Papers, Oregon State University Special Collections said surrounded the molecule. Nonetheless, Crick had experience in X-ray diffraction and thought he could put the pieces together. They decided that they had enough evidence to build a model of DNA's structure.

In their model, three long twists of the sugar-phosphate chain were held together by magnesium ions, and the bases flopped outward from this central backbone (Fig. 22). Watson and Crick excitedly invited Wilkins, Franklin, and Gosling to come see the model. When Franklin arrived, she quickly saw that Watson had remembered several things incorrectly—in particular, he had forgotten the amount of water that surrounded each strand. DNA crystals contained at least ten times as much water as their model allowed for, and there was no evidence that DNA contained any magnesium at all. If it did, all that water would cling to the magnesium ions, tearing the molecule apart. It was clear that the hypothesis Watson and Crick had formulated using their metal-and-wire models didn't fit the available evidence on DNA. It would have to be rejected.

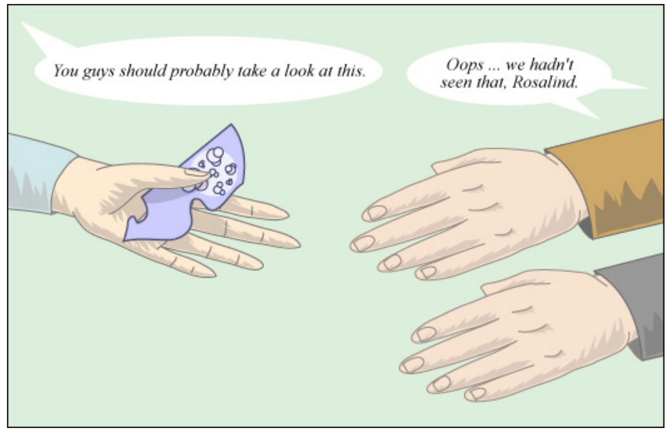

Fig. 21.

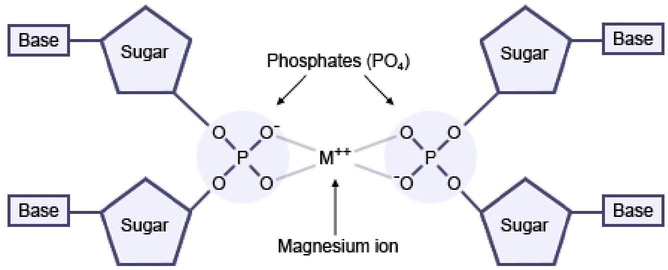

Fig. 22. Watson and Crick's model erroneously placed the bases on the outside of the DNA molecule with the phosphates, bound by magnesium or calcium ions, inside.

The accidental image

While Watson and Crick went back to their model building, Franklin continued to work on DNA by making X-ray diffraction images and analyzing these results. She and Gosling focused on DNA A, producing many clear images and uncovering more clues to its structure: the size of the repeating units that made up the molecule and the symmetry of these units. DNA crystals, it turned out, look the same when they are turned upside down and backwards (Figs. 23, 24).

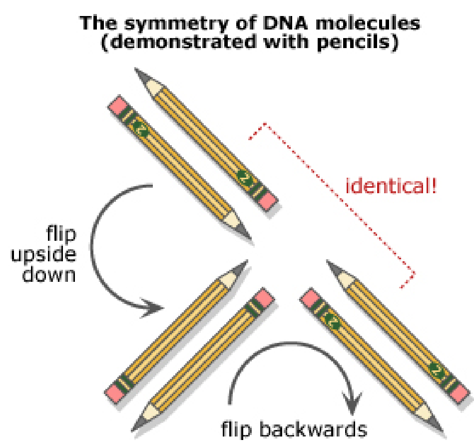

Fig. 23.

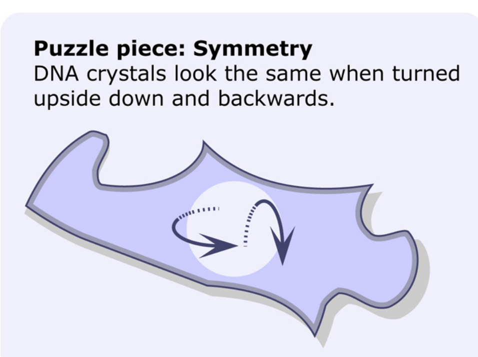

Fig. 24.

Each image took many hours of X-ray exposure to develop—sometimes up to 100 hours—so Franklin and Gosling occasionally exposed them overnight. On the morning of May 2nd, 1952, they returned to the lab to discover that the DNA had hydrated during the night and the image they had taken was actually of DNA B. It was unusually sharp—and illuminating. It showed an obvious x shape, a pattern that previous work associated with helical structures (Fig. 25). The image also confirmed the idea that DNA's bases were stacked pancake-style, 0.34 nanometers apart, and suggested that 10 of these layers occurred in every twist of the helix. It even delineated the width of the diameter of the helix: 2 nanometers (Fig. 26). Since it was the 51st image taken, they called it image B 51. They set it aside and decided to come back to it once they'd solved the structure of DNA A.

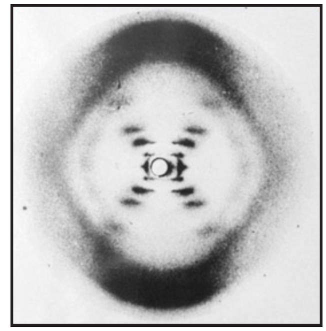

Fig. 25. X-ray diffraction image B 51 taken by Franklin and Gosling.

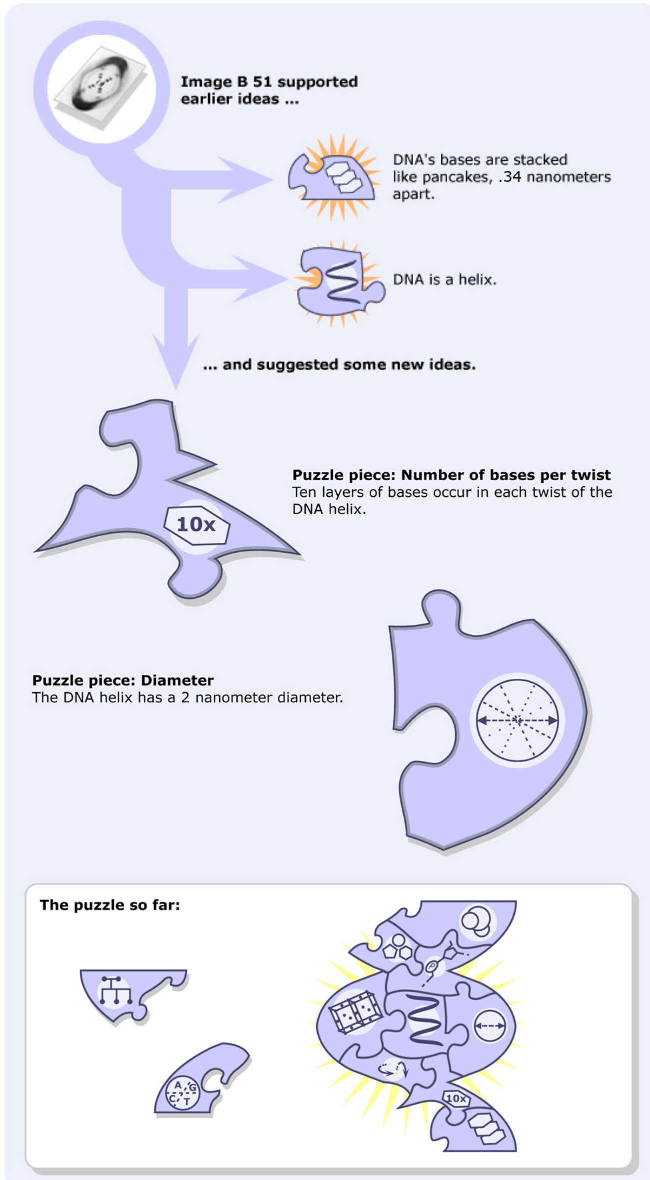

Fig. 26.

Photo of X-ray diffraction pattern courtesy of Cold Spring Harbor Laboratory Library and Archive, James D. Watson Collection

Personal personnel problems

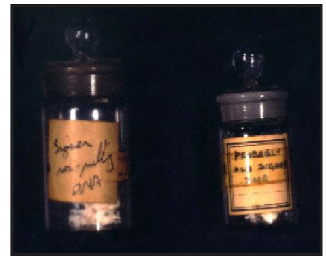

Fig. 27. Bottles containing the high-quality DNA samples that Franklin obtained from Wilkins.

With Franklin and Gosling gathering additional evidence, and Crick and Watson concentrating on generating new hypotheses, the puzzle of DNA seemed close to being solved. But a personal conflict would soon change the course of this discovery. From the time that Franklin started working in the lab, she and Wilkins had argued about which of them would get to work on DNA. Initially, their boss had asked Wilkins to hand the project over to Franklin—so Wilkins gave her all of the high-quality DNA sample (Fig. 27). Later, he decided he wanted to keep working on the problem anyway, but Franklin had already gotten started and didn't want to be pushed out. The resulting tension made both of them unhappy, and shortly after image B 51 was taken, Franklin notified her boss that she wanted to leave the lab. This left Gosling, her student, upset and without a Ph.D. supervisor. He decided to seek advice from Wilkins—and when he did, he took a critical piece of evidence with him: image B 51.

Wilkins had always been more interested in DNA B anyway, and he took special notice of the clear, informative image. Later that month, Watson came to London for another lab colloquium. After the talk, Wilkins had dinner with Watson and showed him the beautiful image of DNA B produced by Franklin (Fig. 28). Because Crick had helped Watson learn how to interpret the X-ray patterns produced by helices, Watson immediately recognized the tell-tale evidence of a helix—which he had suspected all along—as well as other clues that would help Watson and Crick put all the puzzle pieces together. Determined not to make the same mistake as before, Watson asked Wilkins for more details, and this time, he wrote everything down.

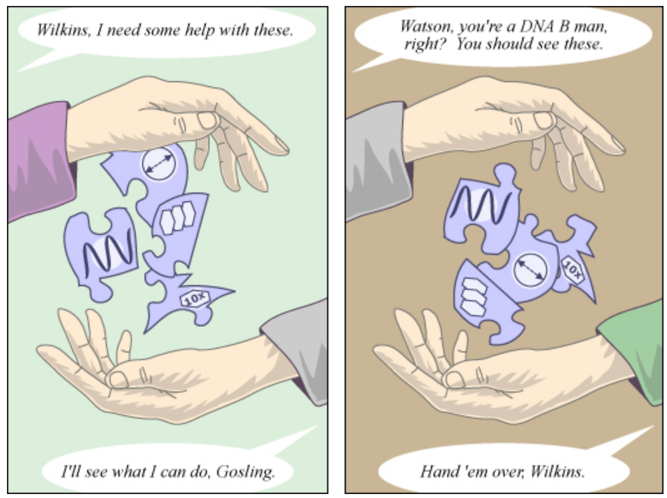

Fig. 28.

The race to discovery

When he returned to Cambridge, Watson shared the new results with Crick and they applied the information to their ball-and-stick models. Watson wanted to try making a model in which just two phosphate-sugar-base chains were linked together. He thought it made sense for genes to come in pairs, partly because most organisms have two parents. Watson and Crick also decided to try orienting the bases towards the center of the pair. Watson later recounted that they tried this approach simply because it was something they hadn't yet tried, though Franklin had previously given them good reason to think that the bases should be on the inside and phosphates on the outside of the molecule where they could attract water. Both of them were surprised by how well the new two-strand, bases-in model (Fig. 29) fit the clues Watson had scribbled down during his dinner with Wilkins. But Watson and

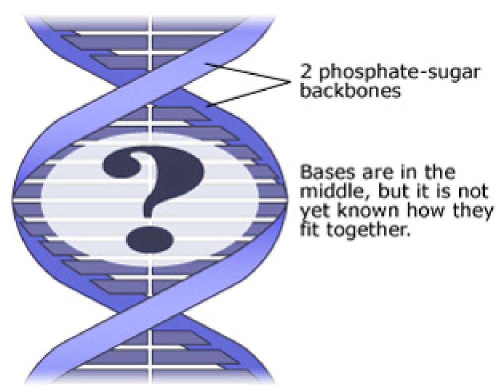

Fig. 29.

Crick weren't the only ones thinking about a double helix—Rosalind Franklin's notes from February 10th show that she started wondering if DNA B might be a two-chain helix around the same time.

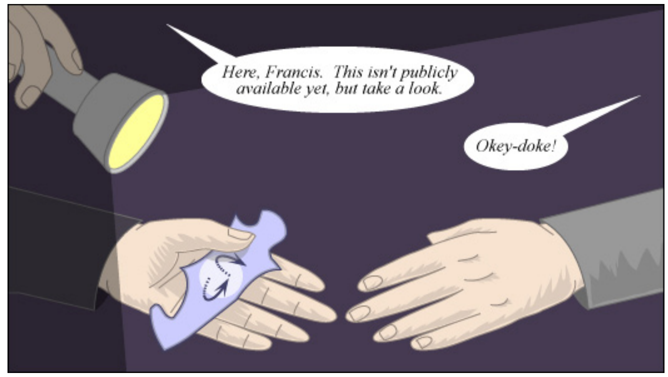

Fig. 30.

Of course, because she had produced the results, Franklin was the only one with all the data—and Watson and Crick needed more information to keep working. In science, researchers regularly share their findings with other scientists through journal publications, but Franklin's results were so new that they hadn't been thoroughly peer-reviewed and published. However, Watson and Crick were able to find out more about Franklin's work from another source. Her lab was funded by the Medical Research Council, which required grant recipients to report on their progress at the end of each year. All of the clues that Franklin had uncovered were summarized in that report. Such reports are supposed to be confidential, but Watson and Crick happened to know someone on the Medical Research Council who had a copy of the report and was willing to show it to them. When Crick saw the evidence in the report (Fig. 30), he recognized the type of crystal symmetry Franklin described, and realized something that she hadn't. If DNA crystals could be flipped upside down and backwards, and still look the same, the strands of the backbone must be identical, and they must run in opposite directions (Fig. 31).

By this time, Franklin had also concluded that DNA was a two-chain helix, composed of two intertwined sugar-phosphate backbones. Figuring out the shape of the backbones, though, still left the bases an open question. She knew from details in her X-ray images that the phosphates were on the outside of the helix, which meant that the bases must point toward the center. But how did they fit together? Each base is a slightly different size, but the smooth twists of the sugar-phosphate chain never varied. How could the bases fit inside the chains without touching and repelling one another? She was sure there was a clue in DNA's unique base ratios—one of the puzzle pieces discovered before Franklin had even begun to study DNA—but she still wasn't sure exactly what that clue meant. By February 23rd, her notes show that she realized that if A were physically interchangeable with G, and C with T, then the amount of A would have to equal T, and likewise for C and G. She was getting close—but she had yet to put the pieces together into a complete hypothesis. Meanwhile, back in Cambridge, Watson and Crick were working on the same problem …

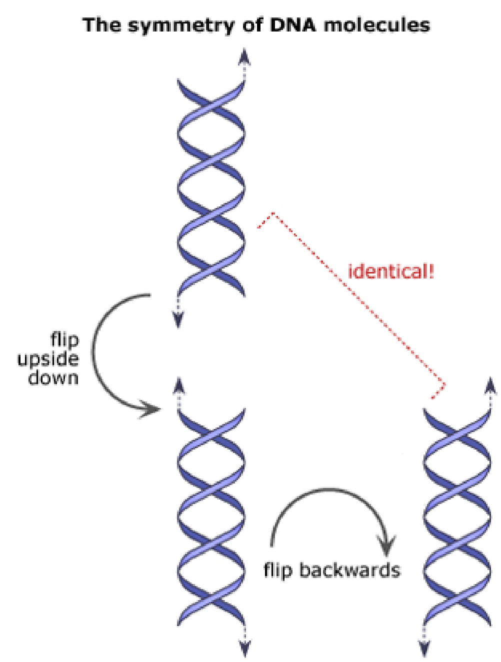

Fig. 31.

The finish line

Watson and Crick were also stuck on what to do with the bases. At first, Watson thought they paired together A-A, C-C, T-T, G-G—but because of the different sizes of the bases, the hypothesis had to be discarded. It would have required a sugar-phosphate backbone that wiggled in and out, rather than winding around in smooth twists. Then, Watson and Crick got a key piece of evidence about the shapes of the bases from a visiting American chemist, Jerry Donohue. At that time, most chemistry textbooks reported a particular placement of hydrogen on the bases. That placement made it impossible to match A to T, or G to C—they just didn't fit. Donohue told Watson that the textbooks were outdated. More was now known about the shapes these bases might take: one of the hydrogen atoms could be attached to the base in another location (Fig. 32). In fact, based on a few different lines of evidence, Donohue thought that the bases likely took shapes that Watson had not yet tried (Figs. 33, 34).

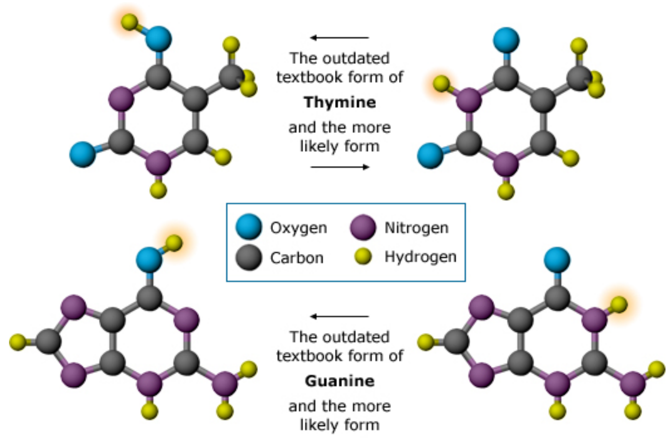

Fig. 32. The visiting American chemist, Jerry Donohue, provided a key piece of evidence when he revealed that the forms given for thymine and guanine in most textbooks were wrong. Note the changes, indicated by the glowing hydrogens.

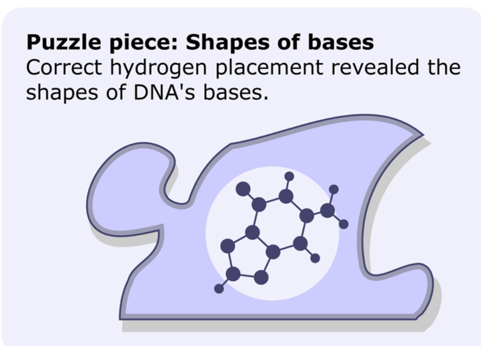

Fig. 33.

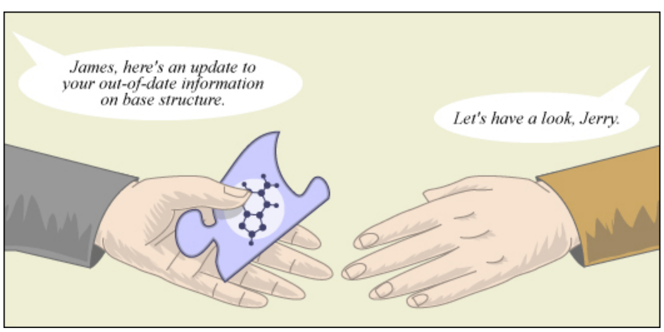

Fig. 34.

Watson tried to fit the new shapes into the two-chain model he and Crick had developed. On February 28th, he was playing with paper cutouts of each base when he suddenly saw the answer. The A fit with T, and G fit with C. Plus, the A-T pair had the exact same molecular length as the G-C pair! Bonded together like this, the bases wouldn't bump and repel one another. Crick realized that if the bases paired up like this, it would explain the mysterious base ratios: A=T, G=C (Fig. 35). Suddenly, it made perfect sense that the base pairs must be in the center of the molecule, and that the two sugar-phosphate strands wound around them. It even suggested how one strand could be used to copy the other. Because each base always matches up with the same partner, the order of bases on one strand could determine the exact order of bases on a new strand. Within a week, Watson and Crick had worked out the details of their hypothesis about the molecular structure of DNA.

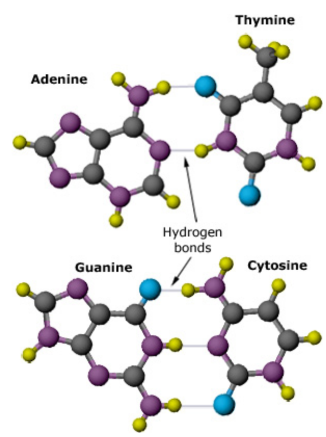

Fig. 35. Given the correct forms for the bases, Watson was able to figure out how adenine-thymine and guanine-cytosine pairs matched up, and formed weak hydrogen bonds with one another. Watson and Crick originally suggested that there were two bonds between guanine and cytosine but later it was found that a third existed.

Credit and debt


April 25, 1953 NATURE

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

Fig. 36.

Watson and Crick published their proposed structure for DNA in April 1953 in the journal *Nature*[3] (Fig. 36).In the same issue, Wilkins, Franklin, Gosling, and their colleagues presented the evidence they'd collected, which supported Watson and Crick's two-chain helix hypothesis.[4] In this way, the evidence and hypothesis relating to the structure of DNA entered the scientific literature and became available for other researchers to build on.

But not everything that went into these papers came from freely available sources. Scientists often use others' data and ideas (Fig. 37), but they are expected to give credit to their sources. This allows science to grow by building on existing ideas, while rewarding individual scientists for their contributions. Crick and Watson's paper did give credit for much of the evidence they'd collected during their investigation of the structure of DNA. However, data inspiring some of their key insights came from Franklin's 1952 report to the Medical Research Council—which was supposed to be confidential information. Franklin never gave Watson and Crick permission to use that work, and in their paper—the scientific record of this discovery—they do not credit Franklin for supplying this evidence or for image B 51, which was so critical to their discovery. Retrospectively, both Crick and Watson acknowledged their debt. According to Crick, "all the really relevant experimental work on the X-ray diffraction patterns of DNA" came from Franklin's lab, and Watson later claimed that their discovery would not have been possible without the data collected by Franklin.

The failure to give full credit to important evidence is considered a serious infringement of scientific ethics. Crick and Watson have both had highly successful scientific careers, but the issue of whether or not they acted fairly has continued to follow them. In interviews and public appearances, they were—and are—frequently questioned about their choices and about Franklin's role in their most famous discovery, and have had to endure the scrutiny and judgment of the scientific community.

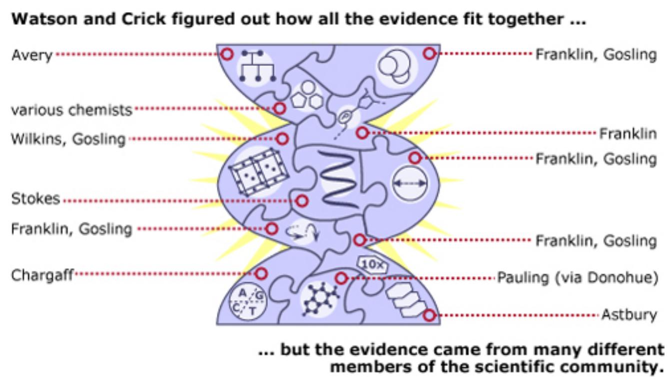

Fig. 37.

It's also worth noting that Franklin was a pioneer in terms of women's presence in the sciences. At the time Franklin was working on DNA, less than five percent of Ph.D.s in the physical sciences were awarded to women.[5] Franklin never reported specific examples of discrimination (aside from not being allowed to eat with her male colleagues in the senior common room), but she did worry that her work might not be taken seriously because of her gender. Though we can never know for sure, it's certainly possible that the discovery of DNA's structure—and the credit given for it—would have played out differently, had the social environment for women scientists been fairer.

[3]Watson, J.D., and F.H.C. Crick. 1953. A structure for deoxyribose nucleic acid. *Nature* 171:737-738.
[4]Franklin, R., and R.G. Gosling. 1953. Molecular configuration in sodium thymonucleate. *Nature* 171:740-741.
[5]In 2005, that number was closer to 30%. Ivie, R., and K.N. Ray. Feb, 2005. Women in physics and astronomy, 2005. American Institute of Physics. Retrieved July 3, 2008 from http://www.aip.org/statistics/trends/reports/women05.pdf

DNA then and now

After unraveling the structure of DNA, all four researchers continued to study genetics and molecular biology, although along their separate paths (Fig. 38). Wilkins, Watson, and Crick went on to collect additional evidence on DNA's structure, examine how DNA copies itself, and investigate the genetic code inherent in the DNA molecule. Sadly, Franklin's research was cut short when she died of cancer—just five years after the landmark *Nature* publication. This also meant that Franklin missed out on many of the honors awarded for their discovery, including the possibility of a Nobel Prize—which cannot be awarded posthumously.

Fig. 38. From left, Rosalind Franklin in 1956, James Watson in the 1980s, Francis Crick in the 1980s, and Maurice Wilkins in the early 1990s. Franklin died in 1958. Both Crick and Wilkins died in 2004.

Despite her early death, Franklin's work, along with that of the others, has earned a permanent place in our accumulated scientific knowledge (Fig. 39). Genetic researchers today still build on the foundation laid by these half-century old ideas and findings. If we trace the roots of today's cutting-edge technologies like DNA fingerprinting, genetic engineering, and genome sequencing back in time, we will find ourselves once again in the X-ray diffraction lab at the University of London and tinkering with models at Cambridge. And continuing even further back in time, we'll encounter the community of researchers who set the stage for this discovery by developing X-ray diffraction techniques and by uncovering those first puzzle pieces that inspired Wilkins, Franklin, Watson, and Crick to join the race and chase down the double helix. With many open questions involving DNA, its structure will continue to be a key piece of evidence in many new discoveries yet to come.

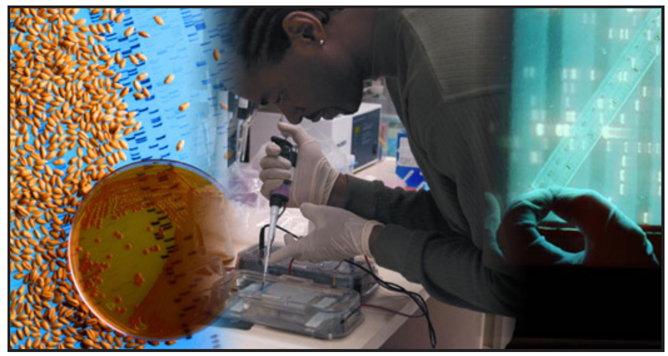

Fig. 39. The discovery of DNA's structure opened the door to an entire field of genetic research and application.

Though the discovery of the structure of DNA is frequently attributed to Watson and Crick, the story behind this discovery highlights just how indebted to other researchers they were (Fig. 40). Reliance on the clues discovered by others is a key theme, not just of this story, but of the process of science in general. Science is too big a job and involves too many complex ideas for any one person to tackle a problem in complete isolation. Even the few scientists who work alone on a day-to-day basis rely on the cumulative knowledge of the scientific community as a starting point and contribute their findings to this knowledge base so that others can build upon them. Because of science's collaborative nature, communication—sharing pieces of the puzzle—has played a critical role in many scientific discoveries. As we saw in the race for the structure of DNA, science works not solely through the brilliance and good fortune of a few individuals, but through the work of a diverse community.

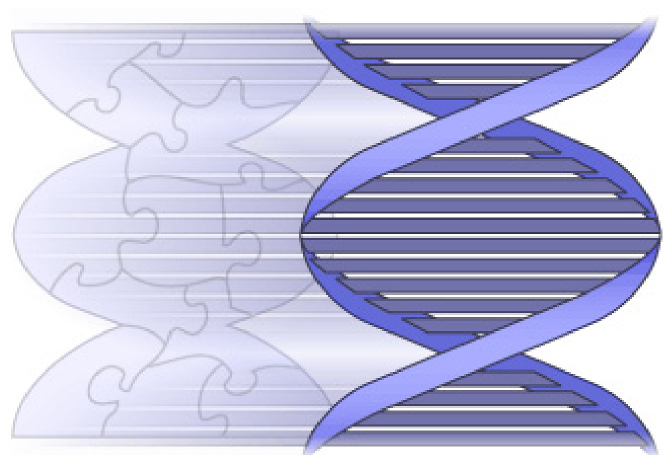

Fig. 40.

Photos of James Watson, Francis Crick, and Rosalind Franklin courtesy of Cold Spring Harbor Laboratory Library and Archive, James D. Watson Collection; Wilkins photo courtesy of TVNZ; grain genetics photo provided by USDA; researcher and PCR photos provided by NIH

Want to learn more? Check out these references

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