In an interview, Linus Pauling said:

the gathering of further evidence. Or, publishing a plausible hypothesis may save other scientists needless work on a problem and productively focus
constructing all the plausible alternative hypotheses that need to be considered. Publication may stimulate another scientist to devise a
may publish a hypothesis and stimulate another scientist to design a crucial experiment to test it. A single scientist may not be good at
marketplace of scientific ideas. The person who conceives the hypothesis may not know the best methods for testing it. One scientist
at the time, the hypotheses that later failed were plausible. Publishing a plausible hypothesis plays the important role of placing it in the
None of the errors of these famous scientists was due to fraud or misconduct. Given the theories and evidence available to the scientist
acknowledged the success of the alternative experimental method and accepted the code that the biochemists deciphered. His genetic
wrong” (Judson 1996, p. 314). Crick attempted to test his own, admittedly theoretical, hypothesis with genetic experiments, with little
this work, said of the comma-free code: “an idea of Crick’s that was the most elegant biological theory ever to be proposed and proved
The Italian physicist Enrico Fermi received the Nobel Prize in 1938 for two aspects of his work: the slow neutron technique and the
"discovery" of "transuranium elements." These two aspects suffered quite different fates. The slow neutron technique proved useful in
future work. However, the "transuranium elements" that he thought he had detected were misinterpretations of his experimental results.
Instead of creating new elements, heavier than uranium, he was splitting the uranium atom, thereby producing smaller, lighter elements.
Other physicists soon sorted out the mistake, leading to the discovery of fission, the process used to make the atomic bomb (Weart
1983). Fermi accepted the reinterpretation of his results and went on to contribute to further work leading to the use of fission in the
atomic bomb (Segre 1970).
The famous American chemist, Linus Pauling, helped to found the field of structural chemistry with his important work on the nature of
the chemical bond, for which he received the Nobel Prize in 1954. His structural analysis of proteins, showing what he called an "alpha
helix structure," has proved to be an important structural component of proteins. In contrast, Pauling's model for another molecule--
DNA--was rapidly superseded. Pauling's three strand model of the structure of DNA (deoxyribonucleic acid, the genetic material),
proposed in 1953, was bested in the same year by James Watson and Francis Crick's two strand, double helix model. Pauling conceded
his mistake and corrected a small error in Watson and Crick's structure (Hager 1995).
The American James Watson and the Englishman Francis Crick received the Nobel Prize in 1962 for their double helix model of DNA,
built in Cambridge, England, in 1953. After the discovery of the structure of the genetic material, Crick went on to propose a "pretty,
almost elegant" version of the genetic code, called "the comma free code" (Crick 1988, p. 99). Horace Judson, chronicling the history of
this work, said of the comma-free code: “an idea of Crick's that was the most elegant biological theory ever to be proposed and proved
wrong” (Judson 1996, p. 314). Crick attempted to test his own, admittedly theoretical, hypothesis with genetic experiments, with little
acknowledged the success of the alternative experimental method and accepted the code that the biochemists deciphered. His genetic
own experiments later produced independent evidence for some of the details (Crick 1988).
None of the errors of these famous scientists was due to fraud or misconduct. Given the theories and evidence available to the scientist
at the time, the hypotheses that later failed were plausible. Publishing a plausible hypothesis plays the important role of placing it in the
marketplace of scientific ideas. The person who conceives the hypothesis may not know the best methods for testing it. One scientist
may publish a hypothesis and stimulate another scientist to design a crucial experiment to test it. A single scientist may not be good at
constructing all the plausible alternative hypotheses that need to be considered. Publication may stimulate another scientist to devise a
plausible alternative. Or, publishing a plausible hypothesis may save other scientists needless work on a problem and productively focus
the gathering of further evidence.

In an interview, Linus Pauling said:
This method works both for individual scientists and for the scientific community. Individual scientists consider alternatives prior to publishing and choose the one that is best supported by the evidence they have at the time. Publication then allows the wider scientific community to continue the same process (Darden 1991). Plausible ideas need to be published, subjected to debate, challenged with new evidence. If a hypothesis turns out to be bad, science throws it away. If it stands up in the face of further evidence, then the scientist who first published it receives the credit. Science as a whole benefits from timely publication and the scrutiny to which the hypothesis is subjected (Hull 1988).

Scientific inquiry is an ongoing process of error correcting—constructing plausible hypotheses, generating as many plausible rivals as possible, designing new experiments, correcting errors in hypotheses in the face of anomalies. Cycles of discovery and testing and revision characterize scientific change (Darden 1990; 1991).

**Lord Kelvin and the Age of the Earth**

William Thomson, Baron Kelvin of Largs (1824-1907), was knighted and later named a baron in recognition of his many accomplishments in engineering and science. He was instrumental in the engineering required for the first successful trans-Atlantic telegraph cable and he was honored for his work in thermodynamics and the theory of heat. He proposed a scale of absolute temperature which today is still measured in degrees Kelvin. He published over three hundred scientific papers and was regarded as one of the greatest physicists of his time. But in one of the major scientific undertakings of his life, Kelvin was in error. His calculations of the age of the earth were made obsolete by the discovery of radioactivity. Kelvin had based his mathematics on the earth's cooling from a molten mass, assuming only the sun as a significant energy source. Radioactivity was unknown until the very end of the nineteenth century; surprisingly, the earth was its own source of additional heat.

Kelvin was the son of a Scottish professor of engineering and mathematics. He graduated from Cambridge in 1845 and the next year became professor of natural philosophy at the University of Glasgow. He remained there for fifty-three years, becoming known as one of the greatest physicists of that time. His work on heat and thermodynamics led him to question several of the positions then held by geologists. In order to understand the nineteenth century and prevailing views about the sun, the earth and geology, we must remember that the existence of radioactivity was not known, not even suspected, until 1896. Kelvin and others puzzled over the world around them. Two questions were: What is the source of the sun's heat? How old is the earth? These questions were related because the earth was assumed to have cooled from a molten state with only the sun for an additional energy source. What was the sun using for an energy source? Kelvin was among those who even seriously considered the collision with meteors as a source of fuel for the sun and as impact energy for the earth. But calculations indicated that even the highest estimates of meteors hitting the sun would only sustain it for a few thousand years. And the impact of meteors could have only a minor effect upon the rate of cooling of the earth (Burchfield 1990). Kelvin suggested that the sun was slowly contracting and in that way producing heat (Thompson 1910, p. 537).

By the middle of the nineteenth century, most scientists had, in practice, abandoned Bishop Ussher's pronouncement that the earth had been created in 4004 B.C. and therefore was about 6000 years old. The geologists pondering the formation of the earth's features fell into two camps: the catastrophists and the uniformitarians. According to the catastrophists, the earth's surface had been shaped by a series of cataclysmic events: earthquakes, floods (they were willing to concede Noah's flood as the last of these, to the theologians) and volcanic eruptions. These events were assumed to have been far more destructive than similar events in remembered time. The uniformitarians, following the ideas of James Hutton and Charles Lyell, maintained that no events in nature other than what we now observe were needed--only the action of water, wind, occasional earthquakes and volcanoes, and an immense amount of time. Uniformitarian reasoning assumed that geological time could not actually be measured or calculated (Buchwald 1976, p. 383).

In 1859 Charles Darwin published *On the Origin of Species* in which he suggested that a struggle for survival among varying organisms was the mechanism for evolution. Darwin's theory of natural selection apparently required thousands of generations and hundreds of millions of years as a time span for the earth. Kelvin published several papers attacking the uniformitarian position. Many have speculated that Kelvin was actually opposing Darwin's theory but chose to challenge him indirectly, through questioning the age of the earth and hence the supposed time available for evolution to have taken place.

Beginning in 1862, and for thirty years after, Kelvin published papers arguing that, according to his calculations of the rate of the earth's cooling, the earth could not possibly be old enough for either Darwin's evolution by natural selection or for the uniformitarian scenario for the formation of the earth's features. The first of these papers was "On the Age of the Sun's Heat" (Kelvin 1862a); Kelvin stated that the energy of the sun is not inexhaustible, that it is coming from slight contraction of the mass of the sun, that the sun formerly was hotter, that it would have made the earth hotter than it is now, leading to more severe heat, storms and floods, and so the catastrophists were more likely to be right than the uniformitarians (Thompson 1910). Kelvin also included an opinion that the sun had not been illuminating the earth for as long as 100 million years and certainly not for 500 million years. In the second paper, "On the Secular Cooling of the Earth" (Kelvin 1862b) he said that considerations of temperatures beneath the earth's surface led him to calculate that the earth was not less than 20 million years nor more that 400 million years old. The uniformitarians, on the other hand, were considering possible time spans as great as thirty billion years (Thompson 1910, p. 539). Kelvin did not relent. In 1865 he presented a paper pointedly entitled "The Doctrine of Uniformity in Geology Briefly Refuted" (Kelvin 1865). In this and in an 1868 address to the Glasgow Geological Society, he reiterated that a fundamental assumption of uniformitarianism was contrary to natural laws. According to principles of thermodynamics, since the earth was a cooling body, it could simply not have been at the present temperature and with the present conditions for hundreds of millions of years. Over the next thirty years, as Kelvin refined his calculations, his estimates of the age of the...
earth went down, from 400 million years to 100 million to 50 million to 20-40 million years, in 1897 (Burchfield 1990, p. 43).

No one had any better ideas. Kelvin's reputation was impeccable and his methods and calculations seemed above reproach. He used the best available data and the current laws of physics. As Kelvin's estimates of the age of the earth decreased, geological theories were less and less in agreement with them.

What Kelvin lacked as he did his calculations was the key to unlocking the puzzle of the earth's age--radioactivity. Radioactive elements within the earth's crust decay; they generate heat as they do so. This additional source of heat was unknown, even unsuspected, when Kelvin was making his calculations. Becquerel discovered the existence of radioactivity in 1896. In 1903 it was announced that radium is always hotter than its surroundings; it steadily gives off heat (Burchfield 1990, p. 163). By now Kelvin was in retirement but still reading widely. To him it seemed impossible that the heat was coming from within the radium, or any other radioactive element; that would be a violation of one of the natural laws, the law of conservation of energy. Kelvin argued for some external energy source.

Ernest Rutherford discovered that the source of radioactivity is disintegration of the atomic nucleus. As a radioactive element disintegrates it ejects particles (called alpha rays, beta rays and gamma rays, all invisible to the eye) and releases heat. Kelvin was not convinced but most other physicists were; the experimental evidence was strong. In Rutherford's memoirs is a humorous anecdote about Kelvin. In 1904 Rutherford was about to give a speech on radioactivity in which he disagreed with Kelvin's estimates of the age of the earth when he realized Kelvin was in the audience.

"... realized I was in for trouble at the last part of the speech... Then a sudden inspiration came and I said Lord Kelvin had limited the age of the earth, provided no new source of heat was discovered. That prophetic utterance refers to what we are now considering tonight, radium! Behold! The old boy beamed upon me." (Burchfield 1990, p. 164)

Rutherford concluded this speech, before the Royal Society, with a forthright statement of the new order of things.

"The discovery of the radio-active elements, in which their disintegration liberate enormous amounts of energy, thus increases the possible limit of the duration of life on this planet, and allows the time claimed by the geologist and biologist for the process of evolution." (Burchfield 1990, p. 164)

Kelvin never published any acknowledgment that radioactivity was supplying heat to the earth's crust and that thus his calculations of the age of the earth were not accurate. Indeed, in 1906 and 1907 he published several letters and papers denying that radium could be a source of heat within the earth or the sun. However, another physicist, J. J. Thompson, related in his own memoirs that "in private conversation Kelvin did concede that his theories had been overthrown" (Burchfield 1990, p. 56, note 52).

Kelvin was regarded as one of the greatest physicists of the nineteenth century. He received many awards and served a term as president of the Royal Society of London, the most august group in British science. His methods and calculations were admirable, but natural processes unknown to him made his estimates of the age of the earth far from accurate. "Radioactive dating...stretched the geological time scale by two orders of magnitude, from...20 million years, past Darwin's 300 million years, to the immense figure of three to five billion years" (Brush 1979, p. 148).

**Enrico Fermi: "Transuranium" Elements, Slow Neutrons**

Enrico Fermi (1901-1954) received the Nobel Prize in Physics in 1938 "for his demonstrations of the existence of new radioactive elements produced by neutron irradiation and for his related discovery of nuclear reactions brought about by slow neutrons" (Nobel Foundation). In his Nobel lecture, Fermi described the years of experimentation with slow neutrons and the bombarding of uranium; he named the new elements "ausonium" and "hesperium" (Segre 1970, p. 217). The atomic number of uranium is 92; ausonium and hesperium were thought to be numbers 93 and 94, respectively. Within weeks of the Nobel ceremony, the discovery of nuclear fission was announced. Uranium (92) had been split virtually in half; Fermi's supposed new elements were actually familiar ones--barium (56) and a mix of krypton (36) and other elements of similar weight (Hahn 1950, pp. 25-27). In contrast to Fermi's misinterpretation of the uranium experiments, the discovery of nuclear reactions brought about by slow neutrons proved fruitful in future basic research, as well as for practical applications in the nuclear power industry.

In 1926, prior to his Nobel prize-winning work, Fermi discovered "Fermi statistics" governing the behavior of particles now called "Fermions," and leading to the Fermi-Thomas statistical model of the atom (Segre 1970, p. 217). In 1927 he became the first holder of a chair in theoretical physics at the University of Rome. Throughout the next decade he was instrumental in the development of a modern school of physics there; a talented group of young scientists assembled. Fermi gained a worldwide reputation as a theoretical physicist, publishing in several different areas of physics. In the 1930s, Fermi decided to redirect his research to nuclear physics, leading to his work on both slow neutrons and transuranium elements.

In 1934 Frederic Joliot and Irene Joliet-Curie demonstrated that aluminum could be made artificially radioactive by bombarding it with alpha particles (two protons and two neutrons, the nucleus of a helium atom). What resulted was a radioactive form of phosphorus which then decayed into silicon. The suggestion was made that other particles could also be used for the bombardment (Latil 1966, pp. 56-58).

Fermi decided to irradiate every chemical element in the periodic table with neutrons, to see which would become radioactive. He and his group started with hydrogen but had no luck until they got to fluorine. After that, the radioactivity of many elements and the half-life of the radiation were recorded. Late in 1934 came the observations that led to the discovery of the effectiveness of slow neutrons. Repeated experiments with the same element did not give the same results. Something strange was going on. Fermi did experiments to exaggerate the unexplained variation; as part of these experiments he deliberately placed a screen of paraffin wax between the neutron source and the silver sample to be bombarded. The bombarding neutrons were slowed down in their passage through the paraffin and
In contrast to the slow neutron work, Fermi’s interpretation of the uranium bombardment experiments was soon discarded. In several papers in 1934, Fermi had suggested that neutron bombardment of uranium would produce an element one atomic number higher than the 92 of uranium. This hypothesis was plausible: other physicists had shown similar effects for other elements. When elements lower in the periodic table are irradiated, the resulting nucleus is a form of the next higher element. Fermi predicted that the expected new element 93 would have certain chemical properties, based on its expected location in the periodic table. His experimental results seemed to agree with this prediction: among the mix of radioactive products of the bombardment of uranium were some substances with the expected chemistry. These substances were not any of the elements from lead (80) up to uranium (92) in the periodic table. Because they were not below uranium in the periodic table and because they were not uranium, Fermi thought that they must be above uranium.

There was one voice of disagreement, to whom no one listened. Ida Naddock sent Fermi and his group a copy of a paper she published in 1934, suggesting that it was premature to talk of transuranium elements until tests were done to exclude all of the known elements, not just those close to uranium. Perhaps the nuclei were splitting into two parts to form elements of much lower atomic number (Segre 1970, p. 76). This suggestion was apparently taken as an appeal for rigor and thoroughness rather than as an alternate hypothesis; it was ignored (Turner 1940, p. 2). During the next several years, Fermi and others conducted many experiments to try to identify the many radiation products. A single neutron bombardment of uranium 92 would produce a mixture of several radioactive products having differing half-lives and differing chemical properties. Most physicists accepted the hypothesis that they were looking at transuranium elements. Some physicists had some doubts but could not give any other interpretation of the experimental results.

The Nobel ceremony honoring Fermi for slow neutrons and transuranium elements was December 10, 1938. On December 22, Otto Hahn and Fritz Strassmann sent their paper to the German journal Die Naturwissenschaften, announcing the definite presence of barium (56) after irradiating uranium (92) (Segre 1970, p. 99). Unlike the lower elements that absorbed the bombarding neutrons, the uranium nucleus had split almost in half.

The hypothesis that the uranium nucleus would split into two or more fragments simply had not occurred to most physicists. The theoreticians knew that some theory permitted it (the liquid-drop model of the nucleus; Weart 1983, p. 113) but didn’t think it actually would happen, while the experimentalists saw it and didn’t believe it was what they were seeing, because they thought it was not possible theoretically. In a letter to Lise Meitner that December, Otto Hahn wrote, “Perhaps you can propose some kind of fantastic explanation. We ourselves know that [uranium] cannot really burst apart into barium” (Weart 1983, p. 112). The original manuscript of the Naturwissenschaften paper included the phrase “contrary to all previous laws of nuclear physics”; apparently upon becoming familiar with the liquid-drop theory, Hahn changed the proofs of the article to “contrary to all previous experience in nuclear physics” (Weart 1983, p. 113).

(In fact, Fermi’s experiments had probably produced very small amounts of transuranium elements. It is now known that bombardment of uranium is how one makes neptunium (93) and plutonium (94). However, given Fermi’s techniques, the quantities would have been too minute to detect. What he was measuring, but misinterpreting, were the products of fission, the splitting of the uranium atom (Latil 1966, p. 82)).

After Fermi learned of the correct interpretation of his experiments and accepted it, he went on to be a major player, using the correct interpretation, in developing the atomic bomb. Fermi and his wife Laura and their two children went to Stockholm in December of 1938 for the Nobel ceremony. From there they proceeded to New York City without returning to Rome. Fermi and Laura had decided that if he were to be awarded a Nobel Prize they would emigrate to the United States immediately. The fascist anti-Semitic laws were becoming increasingly repressive; Laura was Jewish (L. Fermi 1954).

Fermi became Professor of Physics at Columbia University. A few weeks after his own arrival Fermi went down to the dock to welcome another new immigrant, Niels Bohr. From Bohr he learned of the discovery of barium in the irradiation products and therefore the discovery of nuclear fission by O. Hahn and F. Strassmann. The news was circulating among scientists in Europe but the journal article was still in press. Upon hearing from Hahn of the presence of barium, Lise Meitner and her nephew Otto Frisch had reasoned that the nucleus had split apart into two pieces whose charge would still total that of uranium. They calculated the huge energy that would be released. In January of 1939 they sent a paper to Nature; to Meitner and Frisch we owe the word “fission” (Hahn 1950).

Fermi and many other physicists immediately recognized the possibility of a chain reaction. When the uranium atom split, not all the neutrons would become part of the barium and krypton. At least two neutrons were always left over. If these neutrons could be made to collide with other uranium atoms, instead of being absorbed by something in the surroundings, each of those atoms would split and release two neutrons, and so on: a self-sustaining nuclear reaction.

Fermi directed the completion of the first such self-sustaining atomic pile on December 2, 1942, underneath the grandstand at Stagg Field at the University of Chicago. In this and later as part of the group of scientists at Los Alamos, he was a rare combination of theoretical physicist and experimentalist. His efforts proved important to both the development of the atomic bomb and the peaceful uses of nuclear power.
Pauling applied his prodigious talents to many problems in chemistry, with numerous successes and failures (Hager 1995).

No straightforward method exists to determine the three-dimensional arrangements of atoms in complex molecules. In the early twentieth century, European and British physicists developed the technique of x-ray crystallography. Molecules are x-rayed and the photographs, though complex, provide clues as to the three-dimensional structure. A. A. Noyes at the California Institute of Technology saw the promise of this new technique for chemistry. When Pauling arrived in 1922 at Cal Tech as a graduate student, x-ray crystallography was the most important chemical research technique there (Hager 1995, p. 88). After receiving his Ph.D., Pauling remained at Cal Tech on the faculty. In addition to learning x-ray crystallography, Pauling traveled in Europe to learn about new developments in quantum physics. He pioneered the application of new ideas about atoms from physics to chemistry. His book *The Nature of the Chemical Bond* (1939) became a standard textbook (Hager 1995). Pauling developed the method of combining evidence from x-ray data and knowledge of chemical bond angles and distances to build plausible structural models of molecules, which were then tested against further evidence. Because the x-ray data alone were insufficient to show the structure of complex molecules, model building and further testing proved a valuable method.

In the 1950s, Pauling applied his methods to large biological molecules--proteins and DNA--with very different results. In 1950, Pauling and his colleague Robert Corey published a paper in which they proposed a model for a structure found in proteins, the alpha helix. In 1953, they published a proposed structure for DNA, a triple helix. A helix is a spiral-like structure; the alpha helix was a single helix; Pauling's proposed DNA structure had three spirals. Additional evidence has ruled in favor of the alpha helix model as a component in proteins but against the triple helix model of DNA.

Pauling had hesitated to publish his alpha helix model of proteins for two years after coming up with the idea (1948-1950), because the model did not agree with one experimental result (technically: a strong spot on the x-ray photographs that seemed to indicate a repeat in the helix at 5.1 angstroms). Despite this one problem, additional evidence mounted in favor of Pauling's alpha helix model. He published despite not having an answer to the problem (Pauling and Corey 1950; Pauling et al. 1951). Proteins are composed of about twenty different smaller molecules called "amino acids." The primary structure of proteins is a linear chain of amino acids. The alpha helix is an arrangement of the chain of amino acids into a spiral-like pattern. The size and shape of the spiral was calculated, partially from the x-ray data, and partially from bonds and angles conforming to Pauling's chemical bonding theories.

Max Perutz was in a group of x-ray crystallographers at Cambridge University in England, which was often in rivalry with Pauling's Cal Tech lab. When Perutz read of Pauling's alpha helix, he immediately saw a way to test Pauling's model. He took additional x-ray photographs and found new evidence supporting the model. Publication, even in the face of some negative evidence, allowed other scientists to devise new tests of the alpha helix (Olby 1994, p. 293).

Later the problematic experimental result was explained away. It was shown to be the result of additional coiling of more than one alpha helix strand, a "coiled coil" (Crick 1988, p. 59). So, in retrospect, Pauling made a good decision to publish the alpha helix, despite knowing of one bit of negative evidence. That anomaly was later resolved without changing the alpha helix. It is a judgment call by an individual scientist at a particular time how to weight the importance of seemingly disconfirming evidence in the face of mounting positive evidence. The clarity of hindsight shows that Pauling made the right judgment about the alpha helix.

Mounting evidence was pointing to DNA as the molecule carrying the genetic information. Chemically, DNA was known to consist of three types of molecules: sugars, phosphates, and "bases." The sugars and phosphates are chemically bonded in a chain called a "backbone." To the backbone are attached the "bases," four similar but slightly different molecules, usually abbreviated as the four letters A, T, G, C (for "adenine," "thymine," "guanine," and "cytosine"). However, the number of backbones and their arrangements in three dimensions was unknown. In 1951, a paper (Ronwin 1951) was published in the *Journal of the American Chemical Society* proposing a structure of DNA. When Pauling read Ronwin's paper, he immediately saw that it was wrong and he worked a bit then, in 1951, on the structure of DNA (Hager 1995, p. 399). Pauling had been interested in components of nucleic acid since 1933 and occasionally returned to the problem. He began model building in earnest in 1952 after seeing new electron microscope photographs at a seminar given at Cal Tech by a professor visiting from Berkeley (Pauling 1974). Pauling and Corey (1953) proposed a triple helix model of DNA, with three sugar-phosphate backbones on the inside and the bases sticking out. They based their "promising structure" on evidence from rather poor quality, published x-ray photographs of DNA, in addition to other specific chemical and structural evidence about DNA, and "general principles of molecular structure." Pauling and Corey had tried to take better x-ray photographs themselves, but the results were of poor quality (Pauling and Corey 1953, p. 84-85).

When the group at Cambridge saw Pauling's proposal for a triple helix model for DNA, they immediately saw its difficulties. Back in 1951, James Watson and Francis Crick had built their own triple helix model of DNA (explicitly using Pauling's model building techniques and his theory of chemical bonding). That model was not published because colleagues told them it was incorrect. Rosalind Franklin and Maurice Wilkins were x-ray crystallographers at King's College in London working on DNA. Watson and Crick invited them to view the 1951 scale model in Cambridge. Franklin immediately saw a difficulty with the triple helix structure (Watson 1968).

Pauling's publication of his own triple helix model in 1953 spurred Watson and Crick to new efforts to build a DNA model. Their productive modeling building was guided by their own and Pauling's incorrect models, which showed possibilities that would not work. The prior errors narrowed the remaining possibilities. They also had the advantage of access to Franklin's new x-rays photographs of DNA (Watson 1968). Their successful model building resulted in their double helix model, with two sugar-phosphate backbones on the outside of the helix (as Franklin had proposed) and the bases bonded in the middle (the key new discovery) (Watson and Crick 1953; Olby 1994; Judson 1996).
Pauling had not seen the new x-ray photographs. In 1953, Pauling visited Cambridge on his way to a conference in Brussels. After seeing Franklin’s photograph and Watson and Crick’s model, Pauling gracefully conceded defeat (Hager 1995, pp. 427-428). Although he attempted to refine his own model after returning to California, Pauling soon gave it up as hopeless (Hager 1995, p. 428).

Pauling later corrected a small error in the Watson and Crick model (Pauling and Corey 1956). Watson and Crick had proposed two chemical bonds between two of the DNA bases (guanine and cytosine). Pauling proposed a third. Watson (1968, p. 195), in a caption to a figure showing their original view of two bonds, said: “The formation of a third hydrogen bond between guanine and cytosine was considered, but rejected because a crystallographic study of guanine hinted that it would be very weak. Now this conjecture is known to be wrong. Three strong hydrogen bonds can be drawn between guanine and cytosine.” Pauling (1970, p. 1010) said: “This small refinement of the double helix was immediately accepted.”

The DNA story shows a common pattern in discovery: proposal of numerous plausible alternatives hypotheses (either unpublished or published), mounting evidence in favor of single one, acceptance of the correct one, further refinements to improve it. Interestingly in this case, the publication of incorrect models by others spurred both Pauling and Corey’s as well as Watson and Crick’s work on the DNA model.

Francis Crick: The Double Helix and The Genetic Code

Francis Crick (b. 1916) shared the Nobel Prize in 1962 with James Watson and Maurice Wilkins for their work on the structure of DNA. DNA is a large molecule in the chromosomes of the cell that carries the genetic information, in a coded form, for making the proteins in organisms, and thus, the genetic characteristics of organisms. Determining the structure of DNA and then deciphering the genetic code are among the most important achievements of twentieth century biology. Crick participated in both. He and Watson proposed the now-accepted double helix structure for DNA. However, the genetic code that Crick proposed, though elegant, was not confirmed by subsequent evidence.

In 1953, Watson and Crick (1953) determined the correct structure of DNA, a double helix. It resembles a spiral staircase, with two sugar-phosphate backbones forming the outer railings and four bases, joined in pairs across the middle, to make the stairs. Watson and Crick relied on chemical knowledge of the components of DNA, data from x-ray photographs of DNA taken by Maurice Wilkins and Rosalind Franklin (who died before the Nobel Prize was awarded in 1962), and the model-building techniques of Linus Pauling. One important piece of chemical knowledge was supplied by Jerry Donohue, who had worked with Pauling at Cal Tech but was visiting at Cambridge in 1953. The forms of the bases in chemistry textbooks were incorrect; Donohue showed Watson and Crick the correct chemical structures (Watson 1968).

The story of the discovery of the double helix model was told by Watson in his delightful book The Double Helix (1968). The book graphically portrays the many ideas they tried, and the failed models they considered, prior to their successful model building. Watson’s account leaves the reader somewhat amazed that these fellows had succeeded in finding a successful model where the famous Linus Pauling and the more experienced x-ray crystallographers had failed. Watson was an American postdoctoral fellow visiting at Cambridge, and Crick was a British physicist who had turned his attention to the study of biological molecules but had yet to finish his Ph.D.

After the discovery of the double helix model of DNA in 1953, Crick rapidly finished his Ph.D. in 1954, and turned his attention to other biological problems, including the genetic code. As Watson and Crick saw, the problem after discovering the structure of the genetic material was to understand how it functioned. Although DNA is the genetic material, most of the work in the cell is done by proteins. The genetic code specifies a relation between DNA and proteins. The coding problem was to decipher how the order of the bases along the DNA helix determines the order of amino acids that make up proteins. Because there are four different bases in DNA but twenty different amino acids in proteins, cracking the code meant determining how many and which bases correspond to which amino acids. If bases were taken two at a time, the sixteen possible combinations would not be enough. So the minimal number of bases needed to code for one amino acid appeared to be three.

Many different codes were proposed on theoretical grounds; some were published and some circulated in manuscripts but were never published. Some codes placed restrictions on which amino acids could be next to each other in proteins. Such restrictions allowed Crick to use the known sequences of proteins to test and eliminate some of the proposed codes (Judson 1996, Part II).

In 1957, Crick, along with colleagues Griffith and Orgel, published a paper in the Proceedings of the National Academy of Sciences (USA) entitled: “Codes Without Commas.” They stated the problem: “The problem of how a sequence of four things [DNA bases]...can determine a sequence of twenty things (amino acids) is known as the "coding" problem” (Crick, Griffith and Orgel 1957, p. 416). They discussed theoretical and empirical difficulties with previously proposed coding schemes, then opted for a code in which three bases determine one amino acid. “This,” they said, “confronts us with two difficulties: (1) Since there are...64 different triplets of four nucleotides, why are there not 64 kinds of amino acids? (2) In reading the code, how does one know how to choose the groups of three?...This second difficulty could be overcome by reading off from one end of the string of letters [now known to be how the code is read], but for reasons we shall explain later we consider an alternative method here” (Crick, Griffith and Orgel 1957, p. 417). They then
we learn how to learn as we learn. Science, as it has developed over the centuries, has improved its methods. As the philosopher of science Dudley Shapere (1984) puts it: "There are no accepted standards in the field. But peer review is not a guarantor of truth. No methods exist to guarantee truth. Nonetheless, peer review of scientific articles prior to publication serves as a check against hasty publication of results that do not conform to the accepted standards in the field. Science has developed a reward system of giving credit to the scientist who publishes first, which ensures open and free discussion of ideas. Peer review of scientific articles prior to publication serves as a check against hasty publication of results that do not conform to the accepted standards in the field. But peer review is not a guarantor of truth. No methods exist to guarantee truth. Nonetheless, science, as it has developed over the centuries, has improved its methods. As the philosopher of science Dudley Shapere (1984) puts it: "Theorists in biology should realize that it is almost essential if they are to succeed" (Crick 1988, p. 99).

Reflecting on Crick's work, Horace Judson in his history of this period in molecular biology said:

"By 1966, he [Crick] had written two dozen papers related to the subject [of protein synthesis and the coding problem]. Six at least were of great and general importance. Two of those included experiments and were written with collaborators. One more paper [the Crick, Griffith and Orgel paper discussed above], of pleasing ingenuity, happened to be wrong: nature turned out to be less elegant than Crick's imagination." (Judson 1996, p. 288)

Reflecting back on this work himself, Crick said:

"if we were to image that the correct triplets were marked by commas (for example, ATC, CGA, TTC, ...), how did the cell know exactly where to put the commas? The obvious idea, that one stared at the beginning (whatever that was) and went along three at a time, seemed too simple [this is indeed how it happens], and I thought (quite wrongly) that there must be another solution." (Crick 1988, p. 99)

Crick extolled the aesthetic properties of their comma free code: "Naturally Orgel, Griffith, and I were excited by the idea of a comma-free code. It seemed so pretty, almost elegant. You fed in the magic numbers 4 (the 4 bases) and 3 (the triplet) and out come the magic number 20, the number of amino acids. Nevertheless I was hesitant. I realized we had no other evidence for the code, other than the striking emergence of the number twenty" (Crick 1988, pp. 99-100). They wrote an informal paper and circulated it among colleagues for comments. Crick noted that in spite of his worries, the new code attracted attention. After people began asking to quote the unpublished paper, they decided to publish and did so in 1957. "An account of it even appeared in a book for the general reader called The Coils of Life written by Ruth Moore [a journalist], though this was not published till 1961, by which time we had ceased to believe in the idea" (Crick 1988, p. 100).

Crick himself, always more a theoretician than an experimenter, began doing genetic experiments to try to obtain experimental evidence for the code. These were difficult experiments. No direct method for sequencing DNA was available at the time. Geneticists did not crack the code. Biochemists did. Marshall Nirenberg and J. H. Matthaei (1961) at the National Institutes of Health created a synthetic nucleic acid, put it into a experimental system for synthesizing proteins, and determined experimentally the first code for an amino acid (Nirenberg 1968). It was a possibility excluded by Crick's comma-free code, showing that Crick's elegant proposal was wrong, as Crick stated in his Nobel Lecture. "Comma-less triplet codes: All such codes are unlikely, not only because of the genetic evidence but also because of the results from the cell-free system" (Crick 1962, p. 211). Quickly the rest of the genetic code was deciphered by Nirenberg and other biochemists (Judson 1996, Ch. 8). Indeed there is a start signal and commas are not needed to separate the coding triplets. The idea that Crick had considered and rejected is how nature does it. Nature's code is less elegant than Crick's because some of the twenty amino acids are coded for by more than one triplet, a messy result excluded by Crick's comma-free code with its "magic number" of twenty.

Crick's genetic experiments, though they did not provide evidence for this comma-free code or provide the first breakthrough in cracking the code, did provide independent evidence for some aspects of the code. In particular, the genetic experiments provided evidence that the code is a triplet code, three bases code for one amino acid. Mutations showed different behavior when three bases, rather than two or three, were deleted (Crick 1962, p. 107; Crick 1988; Judson 1996, p. 467).

Crick, reflecting back on lessons learned from his theoretical work said:

"Theorists in biology should realize that it is unlikely that they will produce a good theory at their first attempt. It is amateurs who have one big bright beautiful idea that they can never abandon. Professionals know that they have to produce theory after theory before they are likely to hit the jackpot. The very process of abandoning one theory for another gives them a degree of critical detachment that is almost essential if they are to succeed" (Crick 1988, p. 142).

Conclusion

In all four cases of errors by well-known and successful scientists, their hypotheses were plausible at the time, given the evidence that they had available and the theoretical framework within which they were working. Further scientific work served to correct the mistakes.

It is a necessary part of scientific inquiry that alternative, plausible hypotheses be considered (Lederberg 1965). Sometimes an individual scientist constructs alternatives and does experiments to choose among them before publishing anything. At other times, the published scientific record is the forum for discussing competing alternatives. Subsequent published work sorts things out (Darden 1991).

Science has developed a reward system of giving credit to the scientist who publishes first, which ensures open and free discussion of ideas. Peer review of scientific articles prior to publication serves as a check against hasty publication of results that do not conform to the accepted standards in the field. But peer review is not a guarantor of truth. No methods exist to guarantee truth. Nonetheless, science, as it has developed over the centuries, has improved its methods. As the philosopher of science Dudley Shapere (1984) puts it: we learn how to learn as we learn.
Acknowledgments

Help from the following people is gratefully acknowledged: Spencer Weart of the American Institute for Physics for information about Kelvin and Fermi; the Niels Bohr Library of the American Institute for Physics for materials; Stephen Brush for information about Kelvin; Gregory Morgan and Bruce Buchanan for information about Pauling; Robert Olby for information about Crick; Natalie Robert for her work as my undergraduate research assistant; and Nancy Hall, as my graduate research assistant for her extensive work on the Kelvin and Fermi sections.

References


Copyright by Lindley Darden 1998

Available from: www.inform.umd.edu/PHIL/faculty/LDarden/

General permission is granted for non-commercial use; please acknowledge the author as copyright owner.

Questions, comments, and suggestions can be sent to darden@umd.edu.