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And the Award goes to…

For many, nanotechnology seems far removed from biology. There is none the less a sense in which nanotechnology was born of medicine.

The actress

Simone Signoret was an actress of striking appearance and ability. The eldest daughter of a French-born Jewish army officer and linguist who would later work in the United Nations. She was raised in Paris. Her film of 1950 was banned in the USA for immorality, and her portrayal of a prostitute in a 1951 movie won her a British BAFTA Award. Then in 1959 Ms Signoret won best actress awards throughout Europe and in the USA for her performance in "Room at the Top." Set in Yorkshire in the early 1950s, this film tells the story of a ruthless young former prisoner of war who quits his poor and dreary birthplace to take a job in the Treasurer's Department in a wealthy town. He meets a voluptuous older Frenchwoman and the daughter of a British millionaire at an amateur theatrical society production. He joins the society to pursue his worldly ambitions... In 1959 Simone Signoret became the first to receive an Oscar for best actress in a foreign film.

"The Train of the Stars"

Santa Fe Railway's world-famous Super Chief train was launched in 1936. Super Chief set a new standard for luxury rail travel in America and quickly became "the" ride from Chicago to Los Angeles. By 1937 Super Chief-2 could cover the entire distance in under 40 h, passing through places of stunning appearance on the way. Adding to Super Chief's mystique was its Hollywood clientele, which was growing rapidly with the motion picture industry from the mid-1940s. Star-studded Super Chief trains from Chicago let the celebrities disembark in Pasadena, well up-market of dingy Union Passenger Terminal in Los Angeles. The first jet service from New York to LA began in 1959, bringing Super Chief's grand era to an end but catapulting the surrounding area into the future.

Pasadena

In the 1950s Caltech was buzzing with achievement in biology and chemistry. Thomas H Morgan moved there in 1928 to head the Division of Biology. He wanted to distinguish his program from others by focusing on genetics, physiology, biophysics, and biochemistry. He would win the Nobel Prize in medicine or physiology in 1933 for his work on the genetics of the fly, *Drosophila*. Not long thereafter, it became widely recognized that improved knowledge of genetics would be important to medicine. George Beadle was a research fellow at Caltech from 1931 to 1936. In 1946 he became chairman of the Division of Biology. His study of the development of eye pigment in *Drosophila* led eventually to biochemical analysis of the genetics of the fungus *Neurospora*, work for which Beadle shared the Nobel Prize in physiology or medicine in 1958. Several years earlier, in 1954, Linus Pauling was awarded the Nobel Prize in chemistry for his work on chemical bonds. In 1949 Pauling and coworkers at Caltech had published the first proof that a human disease was associated with a change in a specific protein, hemoglobin, which transports oxygen in the blood. Their finding was the first demonstration of a specific protein associated with a human disease, sickle cell anemia, and the Mendelian inheritance of a change in that specific protein. In 1950 and 1951 Pauling and Dr RB Corey published papers in *Proceedings of the National Academy of Sciences* and *Journal of the American Chemical Society* on hydrogen bonded helical configurations of the polypeptide chain, the pleated sheet, and the polypeptide configuration in hemoglobin.

Cambridge

There must have been quite a bit of enlivened talk at Caltech in the 1950s about significant scientific breakthroughs being made in Europe. In 1953 James Watson and Francis Crick published in *Nature* their landmark work at Cambridge University on the DNA double helix. Elucidation of the structure of DNA provided a mechanistic explanation for the replication of DNA and genetic inheritance. Watson and Crick would win the Nobel Prize in medicine or physiology in 1962, the same year in which Max Perutz and John Kendrew of Cambridge would win the Nobel Prize in chemistry for determination by X-ray crystallography of the structure of hemoglobin and myoglobin. Kendrew published a 6 Å resolution model of myoglobin in 1957, and by 1959 the resolution was 2 Å – basically atomic. In 1959 Perutz determined the molecular structure of hemoglobin. Fred Sanger, also of Cambridge, was awarded the Nobel Prize in chemistry for his work for determining the complete amino acid sequence of insulin, a peptide hormone which is crucial for the regulation of blood sugar, in 1955. Such recognitions of achievement promised further discoveries in determining molecular causes of disease.

The actor

Richard P Feynman was happily rejected for service in the US Army for mental illness in 1946. He took up a professorship in physics at Cornell University at the invitation of Hans Bethe, the renowned physicist, but left for Caltech in 1950. He would remain based in Pasadena for the rest of his life. Feynman was born in 1918 in Queens, New York City. His parents were Jewish, and although they were not ritualistic in the practice of religion, they went to synagogue every Friday. Feynman gained a reputation for being a very smart buffoon, an extremely clever guy who could figure out hard problems but also did not take himself very seriously. Feynman's first wife, Arline Greenbaum, was his high school sweetheart. Their courtship continued when he left New York for undergraduate study at MIT and continued after he enrolled for graduate study at Princeton. During this time, Greenbaum was diagnosed with tuberculosis, an infectious bacterium. Feynman's parents tried to dissuade him from marrying Greenbaum, but he insisted that he must do it to provide the care she needed. She died in Albuquerque in June 1945, having moved there to be near Feynman while he was working on the Manhattan Project in nearby Los Alamos. Feynman used to hitchhike on weekends to visit her. In 1952 Feynman tried to settle down by marrying Mary Louise Bell, an instructor in the history of decorative art, whom he had met at Cornell, but the marriage ended after just four years.

At Caltech the first woman to earn a doctorate graduated in the mid-1950s; as at many other institutions, women were not admitted for undergraduate study until the 1970s. While on travel abroad in 1958, Feynman met Gweneth Margaret Howarth, a domestic servant from Yorkshire. Aged twenty-four, she was sixteen years his junior. Feynman convinced her to move to America to work for him as a housekeeper. The two fell in love and were married in 1960. Their marriage was a happy and tranquil one. They had a son together.

Feynman is sometimes called "the great explainer." He wrote a mere 37 scientific research papers during his career but shared the Nobel Prize in physics in 1965 for his work in quantum electrodynamics. He had a great passion for teaching. He took great care in explaining a matter to students, striving to make his subject accessible. He felt that he understood a topic if he could explain it to freshmen in a lecture. His students have said that his lectures were an electrifying experience. The stage was his. He commanded attention. He was in motion, like the atoms he loved to talk about. He strutted about like a dancer, making elaborate and graceful gestures with his arms and hands, amplifying the meaning of his words, which rose and fell to make a point. It was like watching a thespian on Broadway. Physicist Freeman Dyson has described his automobile trip with Feynman from New York to New Mexico. Along the way Feynman took great pleasure in covering up his Long Island origins by imitating the local accent. He loved to entertain on the bongo drums. A story is told of Feynman's beating out a rhythm on the men's room wall while relieving himself in a urinal during a break at a international physics conference.

Biophysics

"It was right after Watson and Crick's discovery of the DNA spiral," says Feynman in his story, "A Map of the Cat?" "There were some very good biologists at Caltech because Delbrück had his lab there, and Watson came to Caltech to give some lectures on the coding systems of DNA. I went to his lectures and to seminars in the biology department and got full of enthusiasm." Max Delbrück was a greatgrandson of the famous German chemist, Justus von Liebig. Delbrück trained as a physicist only to find his interest in biology aroused by the physicist and Nobel laureate Neils Bohr, who speculated that the complementarity principle of quantum mechanics might have applications in other fields, especially the relationship between physics and biology. The Bohr effect, which describes the effect of pH on the affinity of hemoglobin for oxygen, is named after Neils Bohr's father, a physician who was the first to describe it. Delbrück left Germany in 1937 and came to the USA. He was awarded a Rockefeller Foundation fellowship and chose Caltech for its strength in *Drosophila* genetics. Delbrück soon turned his attention to bacteriophages, however, a type of bacterial virus which unlike cells reproduces in "one step," because he believed bacteriophages were simple enough to understand in terms of physics and chemistry. The work on bacteriophage infection was a model for other types of infection. Delbrück's work on the genetic basis of bacterial resistance to bacteriophage infection would take him to Stockholm in 1969 to collect a Nobel Prize in medicine or physiology.

"(Plenty of) Room at the Bottom"

Feynman's famous talk of this title, which is often described as "the" origin of nanotechnology, was given in the context of an American Physical Society meeting at Caltech on 29 December 1959. He speaks apparently prophetically about the willful manipulation of matter on the molecular and submolecular length scales. Feynman would not have used the term 'nanotechnology' per se, which probably was not coined until the 1970s, but there can be no doubt that he foresaw the 1960s as a decade of significant new scientific and technological achievements. Perhaps unexpected for the work of a theoretical physicist, "(Plenty of) Room at the Bottom" makes various references to biology. Some are obvious, some are not. "The principles of physics, as far as I can see, do not speak against the possibility of maneuvering things atom by atom." How could physics prevent such a thing? Did not tiny structures in cells, called enzymes, replicate DNA? Had not such tiny structures been discovered by Arthur Kornberg and colleagues in 1955, work for which he shared the Nobel Prize in medicine or physiology in 1959? Might it not be possible to stand Sanger's work on its head and find a way to synthesize a peptide amino acid residue by residue, to make any desired peptide structure? Methods of chemical peptide synthesis were already known and being exploited in the 1950s. Bruce Merrifield would win the Nobel Prize in chemistry for development of solid-phase methods of peptide synthesis in 1984. "I am inspired by biological phenomena in which chemical forces are used in repetitious fashion to produce all kinds of weird effects (one of which is the author)," said Feynman in his 1959 talk. "The problems of chemistry and biology can be greatly helped if our ability to see what we are doing, and to do things on an atomic level, is ultimately developed—a development which I think cannot be avoided." X-ray crystallography was providing one way of seeing things at the atomic level. The resolution of electron microscopy was improving. Techniques such as atomic force microscopy were in the mind's eye but would not be developed until much later. "At the atomic level, we have new kinds of forces and new kinds of possibilities, new kinds of effects." The world is made of atoms, and individual atoms do not behave like collections of atoms. "Atoms at a small scale behave like nothing on a large scale." "Now, you might say, 'Who should do this and why should they do it?' Well, I pointed out a few of the economic applications, but I know that the reason that you would do it might be just for fun." Why not for fun, and economic applications? "What would happen if we could arrange atoms one by one the way we want them?" What if we could manipulate the structure of DNA to engineer enzymes to carry out novel chemical reactions, to make novel structures by building a molecule at a time? Could we learn from biological organisms how to go about it? What if such knowledge could be useful for medicine? What if it could be used to cure a disease? To save a life?