Francis Crick (1916-2004)

Francis Crick, one of the elder statesmen of modern biology, is no more. Crick passed away on July 28, 2004, another victim of cancer, barely one year after the worldwide celebration of the Golden Jubilee of the Double Helix. In a scientific career that spanned over fifty years, Crick’s intellectual contributions to modern biology were immense. Though he is best remembered for the elucidation of DNA structure along with James Watson, Crick’s other contributions include remarkable achievements such as his work on the genetic code, proposal of the Central Dogma of molecular biology, prediction of the role of the transfer RNA that act as adapters in protein synthesis, to name a few. His scientific interests ranged from origin of life to the complexity of the human brain and human consciousness, on which he spent the later part of his career.

Several outstanding obituaries of Crick have been penned by his peers, colleagues and collaborators that bring out all the wonderful aspects of Crick’s personality and his intellectual command over modern biology. They all project the image of an intellectual giant, who was at the same time a gentle, sensitive and considerate person. An insight into his creative nature can be gleaned from the autobiographical account of his scientific career, “What Mad Pursuit: A Personal View of Scientific Discovery” (reviewed in this issue). The witty and lucid account of the major scientific sojourns of his lifetime, presented in the book, is better than any eulogy that can be written by others.

A remarkable aspect of Crick’s career is that he was trained as a physicist, who later on chose to embrace biology, a common phenomenon among many physicists in the post World War II era. Major contributions to biology were made by these immigrants who came to biology in search of newer problems, ideas and challenges, encouraged by the thoughts of great physicists like Erwin Schrödinger and Niels Bohr.

Francis Harry Compton Crick was born in a modest middle class family in Northampton, England, on June 8, 1916, in the middle of the First World War. Neither his father, Harry Crick, who was a shoemaker, nor his mother Anne Elizabeth Crick, had any scientific background. Yet, young Francis was always curious and inquisitive about everything around him. Partly to satisfy his curiosity, his parents presented him with a Children’s Encyclopedia series. Francis was particularly fascinated by the science topics in the encyclopedia and was even afraid that he may run out of scientific questions to study when he grew older! Though his parents were “religious in a rather quiet way”, Crick lost his religious faith at an early age, much to the dismay of his mother particularly. From
that point in time, Crick was a "skeptic, an agnostic with a strong inclination towards atheism". His quest for reason was a strong motivating force in his scientific career.

After early schooling from the local "Grammar" school, Crick completed his schooling from the Mill Hill Public School in North London, where he received thorough grounding in the basic sciences and mathematics. At age twenty-one, Crick obtained a second-class Honors degree in physics from the University College, London. Crick claims in his autobiography that the physics he was taught there could be more appropriately called "historical physics", with only very brief introduction to emerging topics like quantum mechanics and group theory. With financial support from his uncle, Crick started his research career at the University College under the guidance of Neville da Costa Andrade on the determination of viscosity of water under pressure. In Crick's own words, this was one of the "dullest problems imaginable". The only challenge was the construction of the necessary apparatus for making the measurements.

Crick's studies were interrupted by the Second World War. During the war, he worked as a scientist in the British Admiralty, designing mines of different types, magnetic and acoustic. After the war, Crick did not have to go back to the boring problem of viscosity measurements, as by "good fortune", a bomb had destroyed much of the lab and equipment that he had painstakingly built. He continued to work for the Admiralty as a civil servant for two more years while thinking about what career to pursue in the future. The fact that he had no doctorate degree or research publications did not discourage him. His training was in somewhat old-fashioned physics and mathematics. Yet, Crick felt that this was an advantage as he could explore new areas of research. With this positive outlook, he settled on two possibilities; the study of the borderline between the living and the non-living (what we now call molecular biology) or the study of the brain and its functions or neurobiology. After much deliberation, he took up a studentship at the Strangeways, working on a problem related to the physical properties of cytoplasm. After a couple of publications and serious reading and thinking for two years, Crick joined the newly established MRC Centre at the Cavendish Laboratory in Cambridge, under the overall supervision of the famous crystallographer, Sir Lawrence Bragg.

Biophysics was an emerging area of research where physical methods such as X-ray crystallography were being applied to solve structures of bio-molecules like proteins. Max Perutz and John Kendrew at Cavendish were leaders in the area. There were also a few other groups, J D Bernal at the Birkbeck College, London, who founded the field of
protein crystallography, Linus Pauling in the United States, John Randall and Maurice Wilkins at the King’s College, London, to name a few, working on similar problems. One of the central problems in biology was to explain how genetic information is replicated and transmitted from generation to generation. Proteins that come in all sizes and varieties were thought to be the obvious candidates to perform this task also, just as they perform most other tasks in the cell. This belief was despite the demonstration in 1944 by Oswald Avery and his colleagues MacLeod and McCarty at the Rockefeller Institute, New York, that DNA is the “transforming principle” that can bring about genetic change from the rough to smooth form in bacteria. But by the late 1940’s, the role of DNA as the carrier of genetic information was reasonably well established. This was to a great extent aided by the pioneering biochemical work of Erwin Chargaff, who showed that different organisms had different base compositions. DNA was after all, not a dull molecule as originally thought to be and could carry information. The brilliant but uncelebrated result of Chargaff’s work was the finding of the molar equivalence of adenines and thymines, cytosines and guanines in DNA, that later played a major role in the elucidation of the double helix.

Crick had already spent considerable amount of time thinking about the problem of heredity. The arrival in Cambridge of the young biologist James Watson from the United States was indeed a turning point. The two were strongly convinced that if one could work out the structure of DNA, it would go a long way in understanding heredity and most other central problems in biology. The wisdom and expertise of Crick (he had already established his credentials in protein structure studies) combined with the passion and desire of Watson created a winning combination. In Crick’s own words, “Jim and I hit it off immediately, partly because our interests were astonishingly similar”.

By “gentlemen’s agreement” between Bragg and Randall, the problem of DNA structure was to be left strictly to the King’s College group lead by Maurice Wilkins and his newly appointed colleague, Rosalind Franklin. But this did not stop the pair from thinking about the problem. Their strategy was primarily to approach the problem of DNA structure through model building, a method perfected by Linus Pauling. Their initial attempt at building a model of DNA was disastrous as they primarily used the parameters based on memory of a talk given by Franklin that Watson attended at the King’s College. After the failure, they were admonished not to work on DNA by Bragg. But the burning desire to solve the problem did not let them stop thinking about it. Despite the preemptory order, Crick and Watson continued with their model building exercise that
was looked down upon by Rosalind Franklin. Due to rather tragic circumstances (see Resonance, March 2004), Franklin was asked to leave King’s College, though she had made good progress on the project that included taking an absolutely wonderful X-ray photograph of the moist (B) form of DNA that unequivocally showed the helical nature of the molecule. Crick’s friendship with Wilkins enabled them to exchange ideas and Watson had the opportunity to see Franklin’s data. The helical structure that was apparent in Franklin’s photograph provided crucial confirmation of the model that Crick and Watson had built. This was particularly critical after their disastrous earlier failure. By February 28, 1953, they could complete the model and announce it to the world.

As Crick notes, it was not the double helix per se that was important, but the complementarity of the base-pairing, suggested by Chargaff’s biochemical findings, that allows replication and information transfer. Their model was thus the result of the creative synthesis of ideas and experimental data from diverse sources. Interestingly Crick notes that the base pairing was not arrived at logically from Chargaff’s rule but by accident! Chance favours the prepared mind!

Under the mediation of Bragg and Randall, the three groups published their results in the same issue of the journal Nature on April 25, 1953 (the Watson-Crick paper is reproduced in the Classics Section). Like most outstanding contributions, this paper also elicited only a lukewarm response from the community initially. One is rather surprised at the modest nature of the initial statement and the rather subdued and understated concluding observation about the implications of the model. As Crick observes, this was a compromise formula to safeguard against the possibility of the model being wrong and at the same time staking a claim of priority on its implications. Once the Wilkins and Franklin papers were published, emboldened by the experimental confirmation of their model, Crick and Watson published another paper in May the same year that had additional details that were only alluded to in the first one.

One person who right away accepted their model and thought about the next step was the physicist George Gamow. Gamow initiated the problem of the genetic code: how does the cell translate the information present within the DNA sequence into protein sequence? The “Coding Problem” as it came to be known became a major intellectual exercise involving many top brains on both sides of the Atlantic (see Resonance July 2004). Crick’s genetic approach paid dividends: it could be established unequivocally
that the code is a non-overlapping triplet. In other words, three contiguous nucleotide bases in the DNA specified an amino acid on the protein. The concept of mRNA and tRNA was to follow. Today every high school student is familiar with the Central Dogma of Molecular Biology: information flows from DNA to RNA to Protein. It is this constraint of the living systems that makes it difficult for them to inherit acquired characters. No molecular mechanism exists that can convert the information from phenotype to genotype. In 1962, Crick shared the Nobel Prize for Physiology or Medicine with Watson and Wilkins. Rosalind Franklin's life was tragically and prematurely cut short by cancer by that time.

While Watson progressed to science administration after the double helix, Crick continued his intellectual pursuits. After three decades of path breaking work in the area of molecular biology of which he was one of the creators, Crick moved on to his other passion in biology – neurobiology, at the Salk Institute. Though he continued in this area trying to understand the basis for human consciousness, his success was not uniform. Many feel that if he had embarked on the problem thirty years ago, he may have made considerable progress. He continued his work in the field till his death.

In the words of another giant in modern biology, Jacques Monod, "No one created molecular biology. But one dominates intellectually the whole field because he knows and understands the most – Francis Crick". It is sad that today, the quote has to be converted to the past tense.

**Suggested Reading**


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