

## Obituary



**Francis H.C. Crick (1916–2004)**

Francis Crick, one of the premier biologists of the 20th century, passed away on July 28, 2004 in San Diego, CA. At the age of 88, he was increasingly frail, his hair had thinned drastically from chemotherapy, and he wobbled on his cane unsteadily. But intellectually he was still one of the dominating leviathans of biology.

Most people in the biological sciences know that Francis Crick and James Watson (together with Maurice Wilkins and Rosalind Franklin at King's College, London) uncovered the structure of what sits in the middle of every cell in every living body on the planet: DNA. The double helix they deduced led rapidly to an unraveling of the secrets of the genetic code. It had long been known that you inherit traits from your parents—but no one had any good idea how your father's nose-shape and your mother's eye color were encoded in invisibly small molecules. By the 1960s, thanks largely to the work of Francis Crick and his circle of friends, the molecular basis of inheritance was worked out.

For the DNA work Crick, Watson, and Wilkins won the Nobel Prize in 1962 (Rosalind Franklin had died of cancer 4 years earlier). Few discoveries will match the basis of genetic inheritance, but that was only the beginning of Francis' story. Francis went on to blaze trails in molecular biology, laying the groundwork for everything that would happen in that field over the next half-century. At a rate more rapid than even he would have guessed, unsolved problems in molecular biology

were cracked wide open. The biologist Jacques Monod said of Crick, "one man dominates intellectually the whole field [of molecular biology], because he knows the most and understands the most."

When Francis died, the popular media offered depictions they thought the public would appreciate, declaring, for example, that the work of Dr. Crick laid the groundwork for genetically engineered tomatoes. While such tomatoes can indeed trace far-away roots to Crick's discoveries, the journalists were digging in the wrong place: Crick cared about the deeper questions, the questions about life itself.

And thus, when he had wrapped up most of the answers to his questions in molecular biology, he turned his voracious intellectual appetite to what he described as his second goal: an understanding of the brain. In 1977 he moved to the Salk Institute in La Jolla, California. Above all, Crick wanted to know how the brains produced consciousness. At that time, in the field of neuroscience, consciousness was forbidden territory. The zeitgeist had been dominated by decades of the Behaviorist school of thinking, spearheaded by the American psychologist B.F. Skinner, which asserted that consciousness was an unimportant illusion in a stimulus–response machine. It took someone with the gravitas of Francis Crick to establish consciousness as a real scientific problem. It *feels* like something to have pain. It *feels* like something to see the color indigo. Somehow, these

conscious perceptions are underpinned by neural activity—but how, where, what?

Francis Crick and Christof Koch, who was to become his long time collaborator, suggested that some aspects of the consciousness question would be too difficult to tackle head-on. So they proposed a different tack: they would seek clear examples wherein people (or monkeys) were either aware or not aware of a stimulus, and then look for brain areas that correlated with that awareness. The neurons, populations, or patterns discovered this way could then be identified as neural correlates of consciousness. Correlates were not equivalents, but they were a strong start.

To Crick and Koch, vision seemed like the natural place to begin: much more was known about the anatomy and physiology of the visual brain than any other modality. And one could straightforwardly make and manipulate visual stimuli. With this in mind, Crick asked penetrating questions, rallied researchers around the globe to perform experiments, and inspired hundreds in his quest. From his meditative ocean-view office at the Salk, he opened up new research directions. Browse any issue of *Vision Research* and you are likely to find several papers discussing visual awareness. Pre-Crick, that was far less common.

His mission was to tie theory firmly to the neural substrate. But he knew that when it came to human brains, the neural substrate was thin on data. He once lamented over lunch that ‘the psychologists say that when it comes to neurons, everything is connected to everything—but the situation is far worse than that.’ By ‘worse than that’, he meant that the pattern of connectivity among brain cells contains crucial specificity that we do not currently see. In 1993 he co-authored a *Nature* paper entitled ‘The backwardness of human neuroanatomy’, with which he brought attention to the fact that theory could only progress a limited amount without a richer knowledge of the details of the microcircuitry of the human brain. Through letters, phone calls, and personal conversations, he always worked to rally the troops to fill in the unknown details of human neuroanatomy.

Pick up any book on the major scientific realignments of the past century and you’re guaranteed to find *F.H.C. Crick* in the index—but unlike other luminaries, he appears in *two* sections of the book—one on genes, the other on brains. He was one of the lucky few who went after the problems that interested him most, and who enjoyed the rare opportunity to redraw the map everywhere he stepped. But his intellectual passions did not end with genes and consciousness. He also published on memory, thalamus, dream sleep, the origin of life on Earth, and several other topics. Nothing was outside his intellectual ken. He once told me “the dangerous man is the one with only one theory, because he’ll fight to the death for it.”

James Watson famously opened his book *The Double Helix* with the line “I have never seen Francis Crick in a modest mood.” I have yet to find a more flawed opener. Francis Crick was always in a modest mood. He was one of the few people always willing to criticize his own ideas. He never filtered beliefs through his own ego, and never hesitated to applaud other people’s theories. He laughed freely and often. When asked about Watson’s meaning in the opening line, Crick smiled and said it merely reflected that he (Crick) always wanted to “get to the bottom of things.”

Even the scientific writer John Horgan, infamous for shredding people on the page after interviewing them, refrained from criticism after meeting Francis. “He was almost preternaturally jolly”, Horgan wrote, going on to describe him as the kind of scientist “who answers questions, who gets us somewhere. He is . . . singularly free of self-doubt, wishful thinking, and attachments to his own theories. His immodesty, such as it is, comes simply from wanting to know how things work, regardless of the consequences. He cannot tolerate obfuscation or wishful thinking.”

It seems that those who discover life’s secrets should be immune to life’s fatality. But in the end, Francis Crick was made only of the molecules he illuminated. He was the victim of uncontrolled cell division; he was consumed by the microscopic scales of which he was composed; the molecules he discovered were the sewn-in seeds of his own destruction. This description would appeal to Francis. His crusade was to teach that we are a vastly sophisticated network of trillions of cells—a tour de force of biological sophistication with no other magic in the machine. Some people worry that scientific understanding somehow diminishes the beauty of nature. To this Francis once answered, “It seems to me that what you lose in mystery you gain in awe.” What we have lost in Francis we gain in inspiration.

I first met Francis when I moved to the Salk Institute in 1999. He was quite a bit taller than I had expected. Beneath a head of silver hair he had sparkling eyes and an impish smile and the most impressively winged eyebrows I have seen to date. The first time I saw him in the auditorium during a talk, he sat alone in the front row. As the talk went on, his head began to sink and his eyes began to close. I felt the sad intuition that senescence was taking its toll on a great mind. But then the speaker made some seemingly innocuous interpretation of his results, and a small smile grew on the corner of Francis’ lip. He leisurely raised his hand, and in a rapid-fire Cambridge-accented karate-chop analysis the speaker was re-educated. I came to recognize this as a regular occurrence. Francis was never mean-spirited, just incisive. He detected microscopic flaws in logic. In a room full of smart scientists, Francis continually re-earned his position as the heavyweight champ.

He was an inspiration to all who knew him, a brainstorming intellectual powerhouse with a mischievous smile. He listened carefully, engaged ideas, loved vigorous debates, and hunted for the tough problems. At the age of 88 he continued to work every day on important unsolved problems in the field. He continued to publish major papers and he read all the journals in the field at an age when most people are playing bridge and intellectually melting away. He was working on a manuscript the day he died. As a scientist, thinker, author, mentor, friend, and colleague, one would be hard pressed to find someone who could outshine the twinkly-eyed Francis Crick. It will be some time before the world sees another like him.

### Selected publications

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