Comment

Fame is a bubble, but not for some

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The death of Francis Crick, who succumbed to colon cancer on 28 July at the age of 88, does more than mark the end of one of the most distinguished, and influential, scientific careers of the last century. It also helps mark the end of an era: the remarkable era when biology was transformed from a descriptive, largely organism-based science into a molecular one. Now we are living through another period of transformation, as genomics allied with molecular biology changes the subject into one that is more quantitative, more dependent on computational and engineering tools - and, perhaps, one that once again will put the whole organism, rather than just its parts, at the center of its world. It's rather a pity that Crick won't be around to see that through, because even if he didn't participate in it directly, he certainly would have had some pithy things to say about it.

Crick came to biology late - he started out in physics but fled that field after World War II, as did many other bright young physicists, perhaps in search of something more life-affirming. Whatever the motivations, the trend resulted in an influx of quantitative reductionists who were expert in doing very precise experiments, and they arrived at exactly the moment that biology was ripe for change. By the early 1950s, scientists had identified the major components, in molecular terms, of the cellular machinery and were just starting to develop and use sophisticated chemical and physical techniques that could reveal their structures and functions. Cambridge, England, was a Mecca for such people: in less than 20 years, Kendrew and his associates would use X-ray crystallography to produce the first atomic resolution structure of a protein molecule; Ingram and Perutz would characterize hemoglobin structurally and define the first molecular disease (the sickle-cell trait); Kendrew's collaborator Phillips would determine the first structure of an enzyme and propose a detailed explanation for its catalytic power; DeRosier, Caspar and Klug would lay the foundations for electron microscopy as a tool for structural biology and use it to unravel the structural principles of viruses; the molecular mechanism of muscle contraction would be proposed by Huxley; pioneering work on the antibody molecule by Porter would lead eventually to Millstein's development of monoclonal technology. And, of course, the structure of the genetic material would be determined.

It's interesting to speculate on what would have happened to Francis Crick had he not fallen in with a brash American postdoc (do the British think there is any other kind?) named James Watson and been introduced by him to the problem of finding the structure of DNA. At the time, Crick was a graduate student in his mid-30's, trying to deduce the structure of the protein hemoglobin by examining the autocorrelation function of its diffracted X-ray intensities (in projection, no less), a thesis project that seems in hindsight little short of lunacy. Ironically, he was to earn his PhD for this unsuccessful effort, not for the double-helical structure of DNA, which was only a side project and one that was not always sanctioned by his superiors.

By now, the story of how he and Watson (using fiber diffraction data 'borrowed' from the immensely talented crystallographer Rosalind Franklin without either her permission or her knowledge) deduced that the DNA molecule formed a self-complementary double helix has almost passed into the category of folklore, so there is no need to review it here. Ten years later, Watson and Crick were Nobel laureates, and Watson (after some very pretty work on viruses and an outstanding teaching career at Harvard) was on his way to becoming a full-time science administrator whose accomplishments included being one of the instigators of the effort to sequence the human genome. Crick, who eschewed administration as though it were a terminal disease (it often is), had by that time become the world leader in figuring out the implications of the DNA structure and, abetted by Cambridge colleagues like Sydney Brenner, had done much to chart the course of the fledgling field of molecular biology.

Brilliant, acerbic, not given to suffer much of anybody gladly, let alone fools, Francis Crick had enormous influence that

was not due to his having trained anyone but rather to his style (he made proposing detailed models for biological systems respectable) and high scientific standards. I suspect the desire on the part of his colleagues to uphold those standards had a lot to do with the exceptionally high quality of the research that flowed out of so many of the young scientists who flocked to the field he largely created. In the last few decades of his life his interests veered off into neurobiology, including such seemingly philosophical topics as the nature of human consciousness. My neurobiologist friends differ in their assessments of the quality and value of this work. From what I can make of it, I'd be surprised if it lived up to his earlier contributions. But then, if anyone in science ever deserved a free pass, it certainly would be Francis Crick.

Which brings me to the main point of this essay. I hadn't meant for it to be an obituary because, to be frank, his monumental accomplishments weren't the first thing I thought of when I heard the news of his death. My immediate reaction was that he was one of the few scientists in my lifetime who had managed to beat the "what-have-you-done-for-me-lately" syndrome that consigns so many senior investigators to the dustbin of history. Winning a Nobel Prize helps, to be sure, but how many of you who are chemists or studied chemistry have ever heard of W.F. Giauque, who won that very prize for liquefying helium? My guess is that at least half of the Nobel laureates are not recognizable names to a majority even of scientists in the same broad field. Immortality, it seems, can be pretty fleeting.

But not for a few, and Crick clearly was one of those. It helped that he was part of a revolution: paradigm shifts have a way of conferring name recognition that lasts a while. Regular readers of this column will know that I believe we are in the midst of another revolution: genomics is moving biology to a new era of data-mining, where the organism once again may take center stage. But this is a different sort of revolution, one that is currently driven more by advances in technology than by advances in understanding. We're generating a lot of data, but the unifying hypotheses and ground-breaking conclusions that must eventually spring from these data are pretty scarce at the moment. It's not clear that such times are as conducive to the anointing of larger-than-life figures.

One could argue, I suppose, that it takes a little historical perspective to recognize a special scientific generation, but I'm not convinced of that. People like Crick knew they were special, acted like they were special, and expected others to share that opinion, in part because the cosmic importance of their results was quickly apparent. A few of the fathers of the genomics revolution have those personality traits, but it remains to be seen whether their contributions will come to be associated with their names in the way the double helix will forever be linked with the names of Watson and Crick (so much so that in genome sequences the two strands are named after them).

Most of us, even the best of us, make our contributions, perhaps even win some prizes, and then our names are forgotten as a new generation or two comes along. The young have little respect for, or knowledge of, the history of their field. They take our contributions for granted, and they should. Their focus is not on our past, it's on their present and future, their ideas, their problems. The Francis Cricks of the world are pretty rare - not because smart, talented people are that rare but because few are fortunate enough to make a discovery that, quite literally, changes the world. He did, and for that reason he would be on most people's list of the five most important biologists since Darwin and Wallace. The rest of us live out our working lives in a scientific culture that only values us for what we've done lately, not for what we once did. That's the worst, and best, thing about it.