What Mad Pursuit

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Candid, provocative, and disarming, this is the widely-praised memoir of the co-discoverer of the double helix of DNA.

What Mad Pursuit Details

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From Reader Review What Mad Pursuit for online ebook

Ipsita says

This is an exceptionally well written and invigorating work of one of the most ingenious minds in the fields of molecular biology, and science, at large. The entire book can be divided into four parts:

The first part focuses on Crick's decision to change fields from physics to molecular biology (he was interested in neurobiology as well, to which his interests return during his later years) and the discovery of the structure of proteins using X-Ray Crystallography by Crick and his seniors (Bragg, Perutz, Bernal, Kendrew, etc). Crick mentions the erroneous techniques, assumptions and inferences along with the correct discovery made by Pauling of the α-helix structure of proteins. The α-helix structure of polypeptide chains turns out to be one of the important contributors in the discovery of DNA structure.

> What attracted me to them was that each contained a major mystery—the mystery of life and the mystery of consciousness. I wanted to know more exactly what, in scientific terms, those mysteries were. I felt it would be splendid if I finally made some small contribution to their solution, but that seemed too far away to worry about.

The second part delves in depth regarding the discovery of the double helical structure of DNA by James (Jim) Watson and Crick (including experimental data provided by Wilkins and Rosalind Franklin). Moreover, there is an extensive but amusing review on a docudrama (*Life Story*) and the other denouements of the vital discovery (books, documentaries, movies, etc). The discovery is a fascinating account of acute observational skills, valid interpretation of data, certain intuitive skills and an authorative ruthlessness in approaching the 'correct' question. In the words of Crick himself,

> The main difference of approach was that Jim and I had an intimate knowledge of the way the α helix was discovered. We appreciated what a strong set of constraints the known interatomic distances and angles provided and how postulating that the structure was a regular helix reduced the number of free parameters drastically. The King’s workers were reluctant to be converted to such an approach. [...] I believe there were at least two others. Neither Jim nor I felt any external pressure to get on with the problem. This meant that we could approach it intensively for a period and then leave it alone for a bit. Our other advantage was that we had evolved unstated but fruitful methods of collaboration, something that was quite missing in the London group. If either of us suggested a new idea the other, while taking it seriously, would attempt to demolish it in a candid but nonhostile manner. This turned out to be quite crucial. [...] However, I don’t believe all this amounts to much. The major credit I think Jim and I deserve, considering how early we were in our research careers, is for selecting the right problem and sticking to it. It’s true that by blundering about we stumbled on gold, but the fact remains that we were looking for gold. Both of us had decided, quite independently of each other, that the central problem in molecular biology was the chemical structure of the gene. The geneticist Hermann Muller had pointed this out as long ago as the early 1920s, and many others had done so since then. What both Jim and I sensed was that there might be a shortcut to the answer, that things might not be quiteas complicated as they seemed. Curiously enough, I believed this partly because of my very detailed grasp of the current knowledge of proteins. We could not at all see what the answer was, but we considered it so important that we were determined to think about it long and hard, from any relevant point of view.

The third part would be the questions left to be answered after the knowledge and conclusive data after the revelation of DNA's structure and the pivotal role Crick played in these experimental and theoretical approaches. These include: the nature of the genetic code, the number of bases in a codon, the requirement of a messenger for protein synthesis (which turned out to be mRNA instead of rRNA after arduous experiments), the central dogma (turned out to be an inaccurate hypothesis later on), presence of an adaptor molecule in the protein synthesis machinery, and so on. Here, Crick mentions the blurring of distinctive boundaries between genetics and molecular biology (and biochemistry, to a certain extent). In his own words,

> I think that there is a lesson here for those wanting to build a bridge between two distinct but obviously related fields (a possible modern example would be cognitive science and neurobiology). I am not sure that reasoned arguments, however well constructed, do much good. They may produce an awareness of a possible connection, but not much more. Most geneticists could not have been easily persuaded to learn protein chemistry, for example, just because a few clever people thought that was where genetics ought to go. They thought (as functionalists do today) that the logic of their subject did not depend on knowing all the biochemical details. The geneticist R. A. Fisher once told me that what we had to explain was why genes were arranged like beads on a string. I don’t think it ever occurred to him that the genes made up the string!
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> What makes people really appreciate the connection between two fields is some new and striking result that obviously connects them in a dramatic way. One good example is worth a ton of theoretical arguments. Given that, the bridge between the two fields is soon crowded with research workers eager to join in the new approach.

He frankly cites his mistakes in some of his wrong assumptions and warns other researchers to be on the lookout for the same errors in the manner of thinking. Of particular brilliance are his words on the importance of knowing the distinction between a demonstration and a model for a theory.

> The path to success in theoretical biology is thus fraught with hazards. It is all too easy to make some plausible simplifying assumptions, do some elaborate mathematics that appear to give a rough fit with at least some experimental data, and think one has achieved something. The chance of such an approach doing anything useful, apart from soothing the theorist’s ego, is rather small, and especially so in biology. Moreover I have found, to my surprise, that most theorists do not appreciate the difference between a model and a demonstration, often mistaking the latter for the former.
> In my terminology, a “demonstration” is a “don’t worry” theory [...] That is, it does not pretend to approximate to the right answer, but it shows that at least a theory of that general type can be constructed. In a sense it is only an existence proof. Curiously enough, there exists in the literature an example of such a demonstration in relation to genes and DNA.

Finally, the fourth part would include his switch to neurobiology and cognitive science. The best part of the entire book is in those few pages of *Conclusion* where he delineates biology from other fields of Science; i.e., Mathematics and Physics. He states the limitations as well as the challenges in trying to establish a fundamental law in biology due to the constraints put by constant evolution and workings of natural selection.

> Physics is also different because its results can be expressed in powerful, deep, and often counterintuitive general laws. There is really nothing in biology that corresponds to special and general relativity, or quantum electrodynamics, or even such simple conservation laws as those of Newtonian mechanics: the conservation of energy, of momentum, and of angular momentum. Biology has its “laws,” such as those of Mendelian genetics, but they are often only rather broad generalizations, with significant exceptions to them. The laws of physics, it is believed, are the same everywhere in the universe. This is unlikely to be true of biology. We have no idea how similar extraterrestrial biology (if it exists) is to our own. We may certainly consider it likely that it too will be governed by natural selection, or something rather like it, but even this is only a plausible guess.
> What is found in biology is mechanisms, mechanisms built with chemical components and that are often modified by other, later, mechanisms added to the earlier ones. While Occam’s razor is a useful tool in the physical sciences, it can be a very dangerous implement in biology. It is thus very rash to use simplicity and elegance as a guide in biological research. While DNA could be claimed to be both simple and elegant, it must be remembered that DNA almost certainly originated fairly close to the origin of life when things were necessarily simple or they could not have got going.
> Biologists must constantly keep in mind that what they see was not designed, but rather evolved. It might be thought, therefore, that evolutionary arguments would play a large part in guiding biological research, but this is far from the case. It is difficult enough to study what is happening now. To try to figure out exactly what happened in evolution is even more difficult. Thus evolutionary arguments can usefully be used as hints to suggest possible lines of research, but it is highly dangerous to trust them too much. It is all too easy to make mistaken inferences unless the process involved is already very well understood.

This was an astonishing and exemplary memoir filled with anecdotes and guidance all along the way. Crick is modest, candid and brilliant. But what is really amazing and inspiring to see is his passion to know and to find answers. The title itself (which is taken from John Keats' poem, *Ode on a Grecian Urn*) is suggestive of the impossibility of certain endeavours but what he sets out to prove is this: it can be achieved if people keep asking the right questions. And he certainly accomplishes in doing just that, both in his lifetime as well as in this excellent book.

Frank Ryan says

What else could one give but five stars to one of the brilliant two-some who deciphered the stereo-chemical structure of DNA! Crick was a physicist and hadn't yet completed his PhD (he was disinterested in the theme) when he and Watson solved the "mystery of the code of life". It was all the more remarkable since neither Crick nor Watson did much in the way of background research. Instead they put together the findings of others and, in an act of brilliant scientific creativity, assembled the three-dimensional jig-saw puzzle.

Crick was said to be brilliantly witty and entertaining company. He and Watson lived in relative poverty while working on DNA but, together with his second wife and artist, Odile, he managed to throw parties and entertain his friends in the poky apartment over a shop where he lived in Cambridge.

An extraordinary story of an equally extraordinary human being.

Mohamed IBrahim says

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Mirriam Seddiq says

I’m sure this book makes sense to scientists and people who are not as dumb as me. But - it even made some sense to me and I enjoyed it immensely. Who knows why. But I wanted to learn about what make me this living thing and now I have some ideas and I feel better for it. Warning - it’s slow if you don’t have a science background (and I don’t) and the concepts are difficult to grasp so don’t be fooled by it being ‘only’ 170 pages.

Abhilesh Dhawanjewar says

Francis Crick upon encouragement from the Alfred P. Sloan foundation set out to document some of his experiences before and during the classical field of molecular biology: a discipline he himself invented in the 1950s with the discovery of the structure of DNA in this short and exhilarating narrative. A biographical account of the most prolific years of scientific career, *What Mad Pursuit* is also full of helpful advise and musings on the process of scientific investigation itself.

The opening chapters of the book recount Crick’s childhood and the circumstances that landed him at Cavendish a pursue a PhD in biology. Starting his doctoral studies at a relatively ripe age of 33 in post-war Britain, Francis Crick’s dissertation goal was to investigate the three-dimensional structure of proteins through the use of X-ray crystallography. Around this time, inspired by Schrödinger’s *What is Life?*, Crick became immensely interested in solving the mystery of life: the question of how biological information is passed on down the generations. The discovery of the structure of DNA itself forms a rather small part of the book but Crick relates the ideas and insights that led to the discovery in a simple and brilliant fashion. Having solved the structure of DNA, Crick then moved onto the next important problem, how does the information in DNA relate to the rest of the cell and protein synthesis? In the rest of the book, Crick lays down the story about cracking the genetic code and reporting his thoroughly insightful views on the role of a theoretician in biology.

At the age of 56 with a nobel prize in hand, Francis Crick then moved to the Salk Institute in California to work on his main long-term interest: consciousness. The epilogue comprises of Crick’s dabbles into cognitive sciences focusing on the workings of visual systems in animals. What Mad Pursuit is a candid, modest account of one of the finest minds in biology and portrays Crick’s knack of choosing the most pressing and the most important questions to pursue.

I would recommend reading James Watson’s *The Double Helix* prior to picking this up as this would give the

reader enough background to follow the characters and the science mentioned in this book. While Watson’s book relates the story of the road to the double helix in a more “gossipy” fashion, Crick focuses on ideas more than people in his own account. Together, they provide an entertaining and enlightening report of the most important discovery in biological sciences.

Bruce Caithness says

As much as I enjoyed the recap of Francis Crick's and James Watson's unravelling of the structure of DNA I focussed on the wisdom of his musings about the attempted avoidance of error. Excerpts are quoted below:

Page 16 "I've known a lot of people more stupid than you who have made a success of it."

P 24 "Even a cursory look at the world of living things shows its immense variety."
"The second property of almost all living things is their complexity."

P59 "The failure on the part of my colleagues to discover the alpha helix made a deep impression on Jim Watson and me. Because of it I argued that it was important not to place too much reliance on any single piece of experimental evidence. It might turn out to be misleading".

"Jim was a little more brash, stating that no good model ever accounted for all the facts, since some data was bound to be misleading if not plain wrong. A theory that did fit all the data would have been 'carpentered' to do this and would thus be open to suspicion."

p65 "Our first attempt at a model was a fiasco".

P67 "What was important was not the way it was discovered but the object discovered - the structure of DNA itself. You can see this by comparing it with almost any other scientific discovery. Misleading data, false ideas, problems of personal relationships occur in much if not all scientific work."

P70 "In solving scientific problems of this type, it is almost impossible to avoid falling into error."
"Now, to obtain the correct solution to a problem, usually requires a sequence of logical steps. If one of these is a mistake, the answer is often hidden, since the error usually puts one completely on the wrong track. It is therefore extremely important not to be trapped by one's mistaken ideas. The advantage of intellectual cooperation is that it helps jolt one out of false assumptions."

P109 "The best a theorist can hope to do is to point an experimentalist in the right direction, and this is often best done by suggesting what directions to avoid. If one has little hope of arriving, unaided, at the correct theory, then it is more useful to suggest which class of theories are unlikely to be true, using some general argument about what is known of the nature of the system."

P113 "It is all too easy to make some plausible simplifying assumptions, do some elaborate mathematics that appear to give a rough fit with at least some experimental data, and think one has achieved something. The chance of such an approach doing anything useful, apart from soothing the theorist's ego, is rather small, and especially so in biology. Moreover I have found, to my surprise, that most theorists do not appreciate the difference between a model and a demonstration, often mistaking the latter for the former.

In my terminology, a 'demonstration' is a 'don't worry' theory. That is, it does not pretend to approximate to the right answer, but it shows at least a theory of that general type can be constructed."

P115 "I cannot help thinking that so many of the 'models' of the brain that are inflicted on us are mainly produced because their authors love playing with computers and writing computer programs and are simply carried away when a computer produces a pretty result. They hardly seem to care whether the brain actually uses the devices incorporated in their 'model'.

A good model in biology, then, not only should address the problem in hand but if at all possible should serve to unite evidence from several different approaches so that various sorts of tests can be made of it."

P139 "Physics is also different because its results can be expressed in powerful, deep, and often counterintuitive general laws. There is really nothing in biology that corresponds to special and general relativity, or quantum electrodynamics, or even such simple conservation laws as those of Newtonian mechanics: the conservation of energy, of momentum, and of angular momentum. Biology has its "laws," such as those of Mendelian genetics, but they are often only rather broad generalizations, with significant exceptions to them. The laws of physics, it is believed, are the same everywhere in the universe. This is unlikely to be true of biology. We have no idea how similar extra-terrestrial biology (if it exists) is to our own. We may certainly consider it likely that it too will be governed by natural selection, or something rather like it, but even this is only a plausible guess.

What are found in biology are mechanisms, mechanisms built with chemical components and that are often modified by other, later mechanisms added to the earlier ones. While Occam's razor is a useful tool in the physical sciences, it can be a very dangerous implement in biology. It is thus very rash to use simplicity and elegance as a guide in biological research. While DNA could be claimed to be both simple and elegant, it must be remembered that DNA almost certainly originated fairly close to the origin of life when things were necessarily simple or they could not have got going.

Biologists must constantly keep in mind that what they see was not designed, but rather evolved. It might be thought, therefore, that evolutionary arguments would play a large part in guiding biological research, but this is far from the case. It is difficult enough to study what is happening now. To try to figure out what happened in evolution is even more difficult. Thus evolutionary arguments can usefully be used as hints to suggest possible lines of research, but it is highly dangerous to trust them too much."

P141 " The principal error I see in most current theoretical work is that of imagining that a theory is really a good model for a particular natural mechanism rather than being merely a demonstration - a "don't worry" theory. Theorists almost always become too fond of their own ideas, often simply by living with them for so long. It is difficult to believe that one's cherished theory, which really works rather nicely in some respects, may be completely false.

The basic trouble is that nature is so complex that many quite different theories can go some way to explaining the results. lf elegance and simplicity are, in biology, dangerous guides to the correct answer, what constraints can be used as a guide through the jungle of possible theories? It seems to me that the only really useful constraints are contained in the experimental evidence. Even this information is not without its hazards since, as we have seen, experimental facts are often misleading or even plain wrong. It is thus not sufficient to have a rough acquaintance with the experimental evidence. But rather a deep and critical knowledge of many different types of evidence is required, since one never knows what type of fact is likely to give the game away."

Deb says

It has been a while since I read this, but I loved it. If you have any interest in genetics or the process of scientific discovery, this book is definitely worth a read. What I remember is that the discovery of the genetic code was something that Crick and Watson were doing in their "free" time while they were working on other "have to do" projects. So as much as it as a story of discovery, it is also a story of passion and friendship.

Robert says

Francis Crick is no Jim Watson...and that's a good thing! This little book, an intellectual biography of one of the greatest scientists of the 20th century, is a revealing look at the "road to the double helix" as well as an update on what Crick did professionally after moving out of molecular biology. Whereas Watson's book ("The Double Helix: A Personal Account of the Discovery of the Structure of DNA") is all about personalities, scientific rivalries, and competition for the ultimate (Nobel) prize, Crick provides, as his subtitle states, "A Personal View of Scientific Discovery" that is short on drama but long on the details of the doing of science. As such, this book provides a long overdue tonic to Watson's telling of the most important biological work of the 20th century.

What I find one of the amazing things about Crick is well described in the "Epilogue: My Later Years". At the age of 60, with a Nobel Prize in hand, he left molecular biology and the study of DNA and the genetic code to study neurobiology, the nature of consciousness, and the workings of the brain at the Salk Institute in La Jolla. Not surprisingly he made some fundamental contributions to that field too. According to his long-time colleague at the Salk Institute, Christof Koch, Crick was "editing a manuscript on his deathbed, a scientist to the bitter end".

What comes through most clearly in this wonderful book is Crick's life-long dedication to scientific understanding and the power of his intellect. Perhaps what set him apart was his ability to clearly see what the big scientific problems were and how best to move forward, sometimes incrementally and sometimes in brilliant flashes, but always as a result of dedication, focus and clarity of thought.

Courtney Johnston says

I guess the risk of reading autobiographies is that you might come out not enjoying the book because you don't like the person.

In James Watson's 'The Double Helix' Francis Crick is painted as brilliant, impatient, prone to irritate others with his bumptious nature and unwelcome knowledge-sharing. Watson portrays himself as the shyer, more uncertain half of the duo - out of place both culturally (as an American) and scientifically (he's blagging time away when he's meant to be working on - phages, I think).

Crick's 'What Mad Pursuit' is, like 'The Double Helix', a story about scientific research. He is however a more self-conscious story-teller than Watson, possibly because he is writing after several attempts have been made to tell the story of the discovery of the structure of DNA in different media.

As he writes at the beginning of the chapter 'Books and movies about DNA':

"I recall when Jim was writing his book he read a chapter to me while we were dining together at a small restaurant near Harvard Square. I found it difficult to take his account seriously. "Who," I asked myself, "could possibly what to read stuff like this?" Little did I know!"

Crick shows some impatience with the general reader:

"The average adult can usually enjoy something only if it relates to what he knows already, and what he knows about science is in many cases pitifully inadequate. What almost everybody is familiar with is the vagaries of personal behaviour. People find it much easier to appreciate stories of competition, frustration, and animosity, against a background of parties, foreign girls, and punting on the river, than the details of the science involved."

This cut me to my reading quick. It's shit like this that I get off on - and it's stuff like this that has taken me from someone who gave up on chemistry in 5th form (because I, with typical teenage disdain, despised my teacher) and suffered through physics in 6th form without learning a damn thing, to someone who now actually understand what the LHC is.

Crick often comes across as quite abrasive. His demeaning adjective of choice is 'sloppy' - sloppy thinking, sloppy model-making, sloppy maths. My favourite write-off, when describing a mathematician he clearly felt to be lack-lustre: "Either he had not read our paper carefully enough or, if he had read it, he had not understood it. But then in my experience most mathematicians are intellectually lazy and especially dislike reading experimental papers."

So, the tone of the book was not one I admired. I did come to appreciate Crick's sheer mental avidity: in his sixties he moved to the Salk Institute and took up serious research on the brain, applying the same vigour and challenging attitude to this that he did back in Cambridge in the 1950s.

And one small paragraph just blew my mind:

"The laws of physics, it is believed, are the same everywhere in the universe. This is unlikely to to be true of biology. We have no idea how similar extraterrestrial biology (if it exists) is to our own. We may consider it likely that it too will be governed by natural selection, or something rather like it, but even this is only a plausible guess."

The closest I've ever come to a religious feeling was when I read about cosmic rays - muons that come from outerspace, pass through the earth's atmosphere, and down into the Earth. I suddenly felt like something much bigger than myself. Particles that had come from the sun could be passing through me right now. Light, sound, rainbows - none have had this almost physical sense of coming to an understanding and connection that this did.

The three sentences above had a similar thrill. I've never been interested in aliens. But the idea that they might not be subject to the same evolutionary mechanism that we are - I imagine I felt the same way that some Christian astronomer did once, laying eyes on a distant galaxy and suddenly wondering - can my God be there too?

And for that moment, I will forgive much else.

Derek Davis says

Crick caught me off-guard in the first few pages: Why is he so abstracted when describing his personal background and the wondrous discoveries that made his life an enduring exemplar of scientific discovery during the explosive intellectual aftermath of World War II? And why did I find his sideways verbal constructions so absurd that I'd giggle at them?

Because the man was one of the driest wits that dry-wit England ever produced. After I latched on to this (obvious) truth, his gentle yet needle-sharp jabs at his contemporaries, both friend and too-uninformed-to-be-foe, left me howling with glee through to the last page.
So that's the style, but it's not what the book is or is about. It's perhaps the closest, most caring look at how both experimental and theoretical science is done in the real world. He set out to provide illumination and education, rather than glittering hyperbole, and he succeeded, with a personal yet, as much as possible, objective account of the mechanisms of discovery. My only quibble is his failure now and then to explain a term that must seem obvious to him but sent me online to clarify.
Crick spares neither his cohorts nor himself the careful delineation of the failures and blunders he and they stumbled over on the road to greater success. Or the help received from dumb luck and gratuitous timing.
You meet the giants of modern biology and chemistry, some well-know (Linus Pauling, George Gamow and, of course, James Watson), some familiar only within or around their own disciplines (Rosalind Franklin, Sydney Brenner); you greet them in their personal lairs as well as the lab.
Crick comes across as a firm believer in all areas of scholarly pursuit, but without blinders when kicking the shams and misdirections that litter the intellectual highway.
Damn, I wish I could have met this man.

Ooi Ghee Leng says

We all ponder about the mysteries of life, and the discovery of DNA paves the way to a new level of understanding human can build on. And like human, Crick made all the mistakes he could make before getting there. More often than not, scientists write carefully about their paths to important discoveries, but Crick hides not this. Instead, he exposes all the little and big blunders that deviate him from the right thoughts, and how he manages them in order to maintain a clear mind. I would call this his seminal work that seeks to not just inspire, but to guide aspiring scientists who wish to fulfill their callings. However, I urge you, read this book, no matter you are a scientist or an artist, and listen to the stories of failures that finally led Crick to his successes. You will collect pieces of wisdom and useful techniques that might someday help you to achieve the breakthrough you've been seeking for in your field.

Sambasivan says

Astoundingly intelligent thinker Francis Crick the Nobel laureate who solved the puzzle of the DNA has written an outstandingly illuminating book. Even for a complete novice like me, the perceptive observations and persistent findings the author brings out are fascinating to read. The field of microbiology is so fertile that the author has completely immersed himself into the various experiments in pursuit of the truth behind some of the key questions that determine the life of a human being. Must read.

Yifan Gu says

The best book I have read in years. I wish I had a mentor like him.

Nemo says

An Extraordinary Journey

Dr. Crick shares with the readers his personal journey of scientific discovery. Starting with how he chose molecular biology as his pursuit, the "gossip test -- what you are really interested in is what you gossip about", leading up to the discovery of structure of DNA and the genetic code, and eventually the study of neurobiology when he passed 60, "at my time of life I had a right to do things for my own amusement". Dr. Crick's intelligence and great sense of humor shines throughout.

It's a rare, insightful book that is both entertaining and intellectually stimulating, with many amusing anecdotes and characters. For example, at one point he had to extract enzymes from his own tears and even thought of testing his two-year-old daughter's tears, but "was sternly forbidden to attempt it" by his wife. Mad pursuit indeed.

The Eureka Moment

"It is not easy to convey, unless one has experienced it, the dramatic feeling of sudden enlightenment that floods the mind when the right idea finally clicks into place. One immediately sees how many previously puzzling facts are neatly explained by the new hypothesis. One could kick oneself for not having the idea earlier, it now seems so obvious. Yet before, everything was in a fog."

(Read full review at Nemo's Library)

Colleen Coffin says

One of my favorites. I recommend reading at least one of James D. Watson's books in addition to this book because then you will get a better idea of what their individual personalities are like and how they may have interacted during their time together. His skills as a writer are good in that they convey a sense of what his environment must have felt like, how he comes across personality-wise, and how others come across personality-wise. These points comprise the main things I am in search of when I pick up a scientific discovery memoir (in addition to the educatioal tidbits, which are certain to be there if authored by a prize-winning scientist). One other reason I particularly enjoy memoirs such as this is because the author is writing to a general audience, as such the educational aspects reflect a more relaxed, joyous presentation--sort of like a children's program in spirit. While I don't limit myself to these sources for scientific facts, they compliment any educated or non-educated person's body of knowledge. That's the utter beauty in these books and Crick definitely seems to write with that in mind.
