

Book Review

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The Inside Story: DNA to RNA to protein. Ed. J. Witkowski. Cold Spring Harbor Laboratory Press. 2005. 373 pages. ISBN 087969750 4. Price £16.95 (paperback).

Before the Deluge

The Central Dogma proposed by Watson and Crick a few years after suggesting a structure for DNA conceptualised a unifying theme for those involved in identifying the molecules and mechanisms responsible for the flow of information from DNA into protein.

The Inside Story: DNA to RNA to Protein charts the progress made during this period through a collection of retrospective essays written mainly by the scientists who were directly involved in this groundbreaking research. The essays, originally published in *Trends in Biochemical Sciences*, provide an insight into the process of scientific discovery and vividly reflect the urgency, excitement, surprise and occasional frustration felt by those engaged in the quest. The collection as a whole also identifies the genesis and growth of a research community that established the foundations for much of what we now take for granted.

The main focus of this compilation is the experimental work that made a substantial contribution towards establishing the veracity of the “General Idea” or Central Dogma: the focal areas of DNA replication, the early days of protein synthesis, deciphering the genetic code, discovering tRNA and solving its structure, the surprising journey towards the identification of mRNA, and finally, a return to protein synthesis at the level of the ribosome. These personal recollections are full of fascinating insights into the technologies of the day, often underlining the need to operate in response mode when you are unsure of what you are doing and even more unsure of the outcome. They also clearly underline the value of communication and collaboration with your colleagues and of course, the role of serendipity.

One group of the essays, entitled “DNA Molecules”, brings together four topics not quite so directly focussed upon the Central Dogma. For me,

however, these were the highlight of the book, as they connect closely with my own experience of the period. My research career began at the end of the sixties in Peter Walker’s group at the MRC Mammalian Genome Unit at Edinburgh University, where my task was to compare the satellite DNAs of three closely related species of wood mouse, using as my primary tools DNA denaturation, renaturation and hybridisation. Consequently the pioneering studies of the discoverers of these phenomena, Marmur and Doty, whose work is the focus of the first of the four essays, became very well known to me.

As a postgraduate student, my immediate supervisor was Ed Southern. In the second essay of this section, he recollects the diversity of influences resulting in his inspired development of nucleic acid blotting, a procedure which revolutionised our ability to identify and compare specific DNA sequences. The Southern blotting procedure was only the first of many fundamental protocols that depend upon the capacity of DNA to be denatured and, more importantly, renatured with specificity. Subsequent applications include DNA sequencing, PCR, FISH and microarray technologies which, combined, have led to a deluge in nucleic acid-related information. When I left Edinburgh, a year before the blotting methodology was published, I carried a hand-written copy of the procedure in my rucksack.

My destination was the University of California in San Diego and there I found myself on the same floor of the Biology department as Bruno Zimm. His contribution to this section describes how viscoelastic methods were used to measure the lengths of intact chromosomal DNA molecules. While reading this essay I became excited on learning that to estimate (correctly) the length of a DNA molecule from a *Drosophila* chromosome required an extrapolation from the reference DNA (T2-phage) of more than two decades! On relating this point to a colleague sitting beside me on a bus returning from the Scottish highlands, I was disappointed that he seemed unimpressed but consoled myself with the thought that perhaps for him, an evolutionary geneticist, two decades is but the blink of an eye.

This set of essays ends with Jacob Lebowitz recounting the discovery of supercoiled DNA, a topic which has fascinated me since my days as an undergraduate. I have taught the subject for over 25 years and I am well aware of how tricky it can be to get one's mind around the concept. Contemplating the work of Lebowitz and his colleagues, I can readily imagine how difficult and frustrating the process of discovery must have been and yet how fulfilling the surprise and satisfaction at the outcome.

It is worth highlighting that a crucial step in the realisation that DNA molecules can be supercoiled came from "playing" with lengths of telephone cable. These simple model-building experiments carried out in the hands of the researcher, or student, often provide a perspective that is difficult to attain by any other approach. It was undoubtedly fundamental to the discovery of the structure of DNA.

The collection also contains a number of essays on the contributions of individual scientists, explanations

of the driving philosophies of the period – particularly those concerning the newly established field of molecular biology – and interpretations of the meaning, veracity and implications of the Central Dogma itself. Reading the latter does make one wonder whether those at the forefront of this developing creed could possibly have appreciated its future impact on the ways we now study biological molecules. The confidence we have in the validity of our strategies for determining high-resolution structures and relating these to function, for following the paths of individual molecules in living cells or tracing the interrelationships between the members of the entire proteome of a cell, is based on our unwavering acceptance of the Sequence Hypothesis which, less than fifty years ago, was no more than informed speculation.

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Books Received

Principles of Gene Manipulation and Genomics, 7th Edition. S. B. Primrose & R. M. Twyman. Blackwell Publishing. 2006. 626 pages. ISBN 1 405 13544 1. Price £29.99 (paperback).

The Strongest Boy in the World. P. R. Reilly. Cold Spring Harbor Laboratory Press. 2006.

257 pages. ISBN 087969801 2. Price £29.99 (hardback).

Gene Cloning and DNA Analysis, 5th Edition. T. Brown. Blackwell Publishing. 2006. 408 pages. ISBN 1405111216. Price £29.95 (paperback).