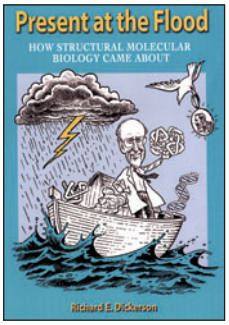
Witnessing the structure revolution



Present at the Flood: How Structural Molecular Biology Came About

by Richard E Dickerson

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Reviewed by David Eisenberg

What was it like to experience the thrill of discovering the first DNA and protein structures? As you read his new book, Richard Dickerson makes you a virtual eyewitness to these discoveries, surely among the most important of the past century. His title, *Present at the Flood*, comes from John Locke's *Essay Concerning Human Understanding*, as Dickerson explains: "To paraphrase Locke, eyewitness testimony is superior to circumstantial evidence. 'Had I myself seen the Ark and Noah's Flood', Locke said, 'as I saw an overflowing of the Thames River last winter, then I should have no more doubt about the reality of the Biblical Flood than about the overflowing of the Thames.'" Dickerson continues, "As you read the papers in this book, you will become eyewitnesses to the structure revolution."

The book grew from a graduate reading and discussion course at UCLA, presented in the final term of his four-and-a-half-decade research and teaching career in structural biology. I was lucky to be one of his two dozen or so listeners. Now his lectures have been packaged with the assigned readings into an attractive large-format paperback book, ready for students in a course on biological macromolecules or structural biology.

Dickerson focuses on the crucial period 1933–1963, when he views two great dilemmas of biochemistry as having been solved. The first was the 'protein dilemma', covering questions such as: Are proteins discrete macromolecular compounds? How are their amino acids linked together? How can proteins function as molecular machines? Are they folded up in some specific manner, and if so, how? The second was the 'DNA dilemma': How are nucleotides linked together in a DNA chain? Is the base sequence specified in some manner?

Dickerson's book is organized with a list of key original research papers on the subject at hand at the beginning of each chapter. The most important of these papers are reprinted at the end of the chapter, after his summary of their findings and significance. He contrasts his approach to that of textbooks that "hand you canned information, with instructions to open the can and swallow the contents whole. Where the contents came from is frequently not specified on the label."

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The brief opening scientific chapter sketches the prestructural view of proteins as colloids. Its title, "Your Cells are Not Micelles!" exposes the author's affinity for puns, which pervade and lighten the narrative. The next chapter charts the false path of the pioneering scholar Dorothy Wrinch, who proposed cyclol rings as the basis of three-dimensional protein structure. The cyclol envisaged by Wrinch was a covalently closed six-atom ring formed by the backbone atoms of two amino acid residues. Such rings were not found in proteins, which turned out to be built from α-helices and β-sheets, as emerged from the work of William Astbury, Linus Pauling, Max Perutz and others, covered in the following chapter. Then comes "The Race for the DNA Double Helix," told through the major research papers themselves, but with fascinating commentary added later by the participants and onlookers: Francis Crick, James Watson, Erwin Chargaff, Perutz, Aaron Klug and Bruce Fraser, who came close to the DNA structure two years before that great discovery but whose paper never saw the light of day until its fiftieth anniversary. Here, as elsewhere in the text, Dickerson presents frontier scientific research as it is really is: a sequence of ideas drawn from data; a few spot-on right, some partially wrong and some, such as cyclols, dead wrong, but even these sometimes stimulating to someone else who moves us closer to the truth.

Next come two chapters on the single-minded determination of Perutz and John Kendrew to develop the tools needed to determine the atomic structures of proteins. Toward the end of this heroic adventure, Dickerson himself was present at the flood, and he offers his eyewitness account of the triumphant endgame. He modestly omits the fact that he wrote the first computer programs to scale together X-ray data from different crystals, to refine heavy-atom positions and to compute the phases needed to see the density of electrons that revealed the structure of the first visualized protein, myoglobin. In these chapters, as well as the one on DNA, Dickerson gives one of the best nonmathematical introductions to X-ray structure determination that I have read.

One unstated subtext of this book is the colossal barriers confronting women scientists throughout the period. Of course there is the well-known case of Rosalind Franklin, which is touched on here. But Dickerson tells us more about Wrinch, who found door after door closed to her as she tried to puzzle out the structures of proteins. Later Dickerson mentions Dorothy Hodgkin, who solved one important structure after another, who was universally admired and who garnered the major awards. Why did Hodgkin become so successful whereas Wrinch did not? To what extent is success the result of mentoring, personality, communication skills, determination or just sheer brilliance? No explicit answers are offered here, but perhaps implicit in Dickerson's historical approach is that one good way to start a scientific career is in the lab of a scientist who defined the field in the previous generation.

Dickerson's writing style is fluid and unpretentious, with a master teacher's knack for appropriate simplification. He can summarize the essence of a paper in a few sentences, making it easy for us to go on to read the original work.

Would I recommend *Present at the Flood*? You bet. I've ordered the book as an auxiliary text for my fall course, so that my students can become eyewitnesses to the structural revolution. ■