

Review of Manuscript "Introduction to Molecular Genetics"
by O. Siddiqi.

It is unfortunate that much of the material in this book is out of date, in some cases by more than a year. Together with the fact that its treatment of the subject is not well suited to the requirements of an introductory textbook I see little justification for its existence.

It is impossible to provide a meaningful introduction to this subject as it stands today with omission of so many new results of importance. To mention just one, the implications of the scheme of degeneracy among RNA coding triplets corresponding to various amino acids comprise a fundamental aspect of this subject beyond the range of this book. While the same criticism can be applied to Hayes' book, the difference is that his treatment really adds something of permanent value to the subject it treats, and furthermore at the time of its publication was not far out of date.

I should state at the outset what my criteria for a desirable book in this area are. Several major new discoveries in molecular genetics, some a matter of weeks old, make this a difficult field in which to attempt any kind of summation, even a review. There is nevertheless a need for a fairly up to date textbook which emphasizes the approaches to molecular genetics and which can retain its value in an expanding subject because of its clarity and insights for the student. Discussion of experiments which are already classical should not state what was done and therefore "X is true," but the more subtle points relating to each experiment should be dealt with, with a detailed exposition of exactly

what is proved and what is implied by each, and with some indication of what the experiment specifically cannot relate to. It is helpful in these discussions to point out why each step was taken, too. For example, in the density gradient experiment of Meselson and Stahl (1958) concerning the semi-conservative replication of DNA many questions can be raised by students which are simply ignored in most texts, the present one included. Why is no material seen which is intermediate in density between the heavy parental DNA and the hybrid band if the cells are not synchronously dividing? To omit discussion of this kind is to provide another review of the material and not an introductory text. I should indicate here also that the only work which to my mind constitutes a satisfactory text in this area is Hayes' book, "The Genetics of Bacteria and their Viruses." Apart from some excellent illustrations, Watson's more recent book is unsatisfactory in terms of the criteria stated above. The difference between these books is that Hayes considers a topic in detail with an analysis, whereas Watson is content to state facts rather dogmatically without adding any insights. This latter procedure involves relatively little effort on the part of anyone working and teaching in molecular genetics and presumably conversant with significant new developments.

Siddiqi's book constitutes a review of the subject and not a text, and not a current or particularly authoritative review at that. A partial list of significant topics omitted in part or in entirety in this work includes:

- 1) new structural data on nucleic acids, particularly the double stranded viral RNA's and especially Holley's complete structure of an alanyl transfer RNA.

2) details of the complete genetic code scheme as it has emerged from the work of Nirenberg and Khorana and their collaborators, as well as the nonsense codon information from Brenner's and Garen's laboratories (this should include mention of the sRNA anticodon schemes too).

Siddiqi has one paragraph on the binding of messenger RNA triplets by ribosomes and sRNA which is inadequate.

3) the mechanism of recombination, including recombination less mutants of *E. coli*, and evidence from transformation experiments.

4) the mechanism of suppressor mutation

5) the recent work on RNA replicative enzymes (Spiegelman's group, and Hayashi).

6) new data on circularity and superstructure in DNA's of certain viruses.

7) the several indications concerning the existence of new replicative forms of DNA (Yoshikawa, Kozinski).

8) discussion of the newer genetic information of Jacob and coworkers on the promoter gene, and mechanics of operator gene function

9) new work on the mechanism of protein biosynthesis, and

10) recent data on the biosynthesis of ribosomes.

Let me now pass to a somewhat more detailed review of the manuscript.

I have few objections to Chapter I, except to note that there is a prerequisite implied here of some familiarity on the reader's part with genetics. The reader with a physical or chemical background will find this introduction incomprehensible in its condensation and brevity (note that Hayes' introductory chapters can stand on their own).

Ch. II is I think the best one in the book, reflecting the author's

familiarity with genetics per se as opposed to his feeling for the structural and physical-chemical aspects of the subject. The account of Benzer's work is concise and detailed.

Ch. III I think unsatisfactory in most respects. The discussion of X-ray diffraction is just silly and would be better omitted, see e.g. the second sentence of the second paragraph on P. 6. He omits to mention that these effects are important when the wavelength of the radiation approaches that of the distance between scattering centers.

The discussion of the Watson-Crick model and its implications is pretty routine, certainly since 1957, while the section on RNA structure is very out-dated and poorly written. For example, at the top of P. 13, the existence of 20 common amino acids is taken to necessitate the existence of at least 20 species of transfer RNA, a logical fallacy in the absence of other information. The work of Spencer et al (1962) was retracted a year later, and its citation here is perpetuation of a mistake. The sequence information on transfer RNA is about five years out of date, since one has been completely mapped and several others are nearing completion, with no indication of any such overall complementary structures. (Items 1, 5, 6 and 7 in the list above render this and the remaining material in the chapter incomplete, where it is not actually harmful to a student).

Ch. IV again is poor, both in content and in exposition, as mentioned previously, giving accounts of papers in the literature, and no more. The section on replication is particularly uninspired. The discussion of Sueoka's work on B. subtilis implies that a gradient of marker frequency

between exponential and stationary cultures exists under any circumstances, which is not the case. There are strains of B. subtilis the chromosomes of which appear to be in states of incomplete replication even in stationary cultures.

The discussion of the DNA dependent RNA polymerase enzyme is too brief and has no mention of several experiments on strand selective transcription, both in vivo and in vitro. As noted before, none of the recent work on RNA replicative enzymes is included. It is surprising that no mention is made of the replicon model for regulation of DNA synthesis which appeared in 1963, and which bears directly on the question posed on P. 23. Nothing is said about the system of highly specific nucleases in the cell, which are presumably involved in these processes.

In Ch. V, on P. 5, is the misleading implication that all biologically active proteins contain α helical regions. On P. 9 mention is made of "finger printing" proteins, a process which it seems to me should be included in the discussion on P. 4 of methods for primary structure determination, especially since the species differences among various proteins were found by similar techniques (P. 8).

The discussion of the genetic code as has been noted above suffers from omission of a body of recent results and is dated. The same applies to Ch. VI on protein synthesis. Where the material is not out-dated, it suffers from being presented dogmatically, with no discussion of the experimental evidence apart from citing references. See for example the bottom of P. 13 of this chapter -- the basis for these statements is all in the literature, but not even a hint of the methods used can be found in the text. The discussion of the stepwise addition of amino acids to the

nascent polypeptide chain is typical of the superficial treatment accorded those experiments he considers sufficiently important to discuss in detail. No mention is made of whether or not the genes for the α and β hemoglobin chains occur consecutively on one chromosome or not, or how the two chains are brought together. Even if complete information is not available, these points are important.

The chapter on regulation, Ch. VII, is adequate, although again it is out of date (nothing on the promoter segment in the β -galactosidase operon) and it does not provide anything not available in the original literature. Allosteric interactions rate a sentence on P. 15 and are inadequately defined. Similarly Ch. VIII is fairly routine, lacking certain fundamental results on the involvement of seryl sRNA in the mechanism of suppression. The catalogue of chemical mutagens and their probable consequences is available in many sources.

I think that the idea of "division dependence" of the mutation induced by 5-BU and 2-amino purine for example is particularly difficult for the student to grasp. The account in this book unhappily fails to explain or clarify these events in any way, representing exactly what is available in the literature, and no more.

The illustrations lack any novelty or originality, including about a dozen detailed genetic maps of various loci presumably for the reader to meditate upon, or consult in the event that he has new data of his own.

To conclude, I feel that this book has little to recommend it, either to the teacher or student of molecular genetics. In no case is there any indication that the author has devoted thought to the problems confronting

a newcomer to this subject, or tried to develop a new point of view. It constitutes a sketchy, out of date summary of the literature, constantly noting the ingenuity and brilliance of work in the field but failing to convey this to the reader. Its utility as a guide to the experimental literature is mostly vitiated because it is out of date.