

to detection of nucleic acid on filters many researchers will probably claim that this is at present still more easily done with radioactive probes because resolution is not a major problem and you can benefit from the indisputably high sensitivity of radioactive systems.

It is therefore not surprising that—following a chapter on non-radioactive probe labelling—four of the remaining seven chapters deal with *in situ* applications, namely (1) cytogenetic analysis, (2) *in situ* detection of DNA in tissues, (3) *in situ* detection of RNA in tissue and monolayers cells and (4) the combination of non-radioactive *in situ* hybridization and immunochemistry. Only the last three chapters deal with other applications, namely (5) non-isotope detection of nucleic acids in membranes, (6) non-isotope DNA analysis and (7) PCR analysis of RNA.

The chapter on probe labelling is well written and gives an extensive overview on the many possibilities for nonradioactive labelling together with a number of detailed protocols. The four *in situ* chapters are in the layout used in this series with detailed protocols interspersed with background information and practical hints for choosing between protocols. Especially the very important issue of pretreatment of samples in order to achieve both conservation of structures and penetration of probes are dealt with in detail in these chapters. On the negative side it may be said that a little more attention to troubleshooting would have been nice.

Among the last three chapters the section on detection of nucleic acids in membranes is also very detailed with many hints and an

extensive troubleshooting guide. The chapter is therefore certainly a very useful guide to the beginner in this field but one is still left with a feeling that the full utilization of non-radioactive techniques in this field must await the development of either simpler staining systems or less expensive high sensitivity image acquisition systems.

The last two chapters give detailed protocols on PCR-based methods for the analysis of DNA sequence variations (the amplification refractory mutation system, the artificial restriction fragment length polymorphism analysis and single stranded conformation polymorphism analysis) and on the PCR-based generation of cDNA (RT-PCR). The protocols in both chapters are detailed with many hints, but since all these methods are based on initial PCR there is no very pressing need for specific non-radioactive detection systems, as also illustrated by the fact that most of the illustrations shown are ethidium bromide stained gels. So these two chapters seem somewhat outside the scope of this book.

The general impression of this book is that most chapters are very useful in their wealth of information and also well written. My main problem is to envision the target group for this book. Clearly the *in situ* part of the book is the most important and certainly very useful, but if you are a beginner in this field other and more detailed books could probably be recommended including a recent *in situ* hybridization manual from the same publishers.

S. Kølvrå

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**Kinetics for the Life Sciences: Receptors, Transmitters and Catalysts;** Edited by H. Gutfreund, Cambridge University Press, Cambridge, 1995. xi + 346 pp. \$29.95 (pb). ISBN 0 521 48586 X.

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This is neither a monograph nor a text book -- it is a book with a message, intended for experimental biologists and biochemists concerned with time dependent phenomena, and its message is that the same mathematical framework can be used to describe, and therefore quantitate, widely different processes in biology. Recognition of this fact may, it is hoped, in the words of the author, 'cross fertilize ideas between different kinetic approaches'.

The book as a whole does not provide much new material. Its value lies in giving, in a single volume, a considerable number of examples of sometimes elegant kinetic investigations which in their time were landmarks in quantitative biochemistry, and in showing what kind of information, such as the number and character of intermediates, can be obtained in such investigations. As such, the book should be useful for anyone wanting an overview of the general field of kinetics in biology, and the insight obtainable in biological systems, during the last 40 years. Most of these examples are from the authors extensive work with proteins, and enzymes in particular, and all are concerned with transient kinetics rather than steady state methods.

The book may be thought of as consisting of 3 parts, varying somewhat in sophistication and detail. Part 1, encompassing chapters 1–3 (about 100 pages) establishes the 'ground rules' in kinetics. It describes some kinetic principles, at a level often found in elementary textbooks, as well as some mathematical introduction for use in the following part, consisting of chapters 4–6 (130 pages). This part constitutes the main methodological section of the book, dealing with the methods for treating systems of differential equations. This part contains the majority of the examples. The third part, chapters 7–8 (70 pages), is concerned with factors influencing rates of chemical reactions, such as temperature and viscosity (chapter 7), while chapter 8 reviews the methods involving different kinds of applications of light for initiating or monitoring reactions. The book contains about 400 references.

As indicated above, the main part of the book is really part 2, the part in which the mathematical procedures necessary for treating kinetic experiments and for extracting quantitative information from the data are described. The basic mathematical methods are specially marked in the text, and although it is specifically stated that these marked sections of the book should be considered 'advanced' and not necessary reading, it is probably unavoidable that the eager reader, trying to enlarge his or her kinetic expertise, would study these sections, at least as an introduction to the methods. It is therefore unfortunate that these sections are marred by a number of errors which will, in some

cases, prevent the reader from being able to use the methods described. Four examples are mentioned below.

The author is aware of the fact that some biologists have a considerable 'energy barrier' when it comes to learning or applying mathematics. He therefore attempts to provide short cuts by devising 'black box math'. This is not to be recommended.

1. On p. 112–116 the so called matrix method for solving coupled first order differential equations is discussed. But it is confusing to the uninitiated reader to state that we can set  $dc/dt = \lambda c$ , where  $c$  is the basic dependent variable, and  $\lambda$  is an eigenvalue of the coefficient matrix. It simply does not make sense when comparing this equation with that of the kinetic model in question. This equation is true for the *transformed* variables, and the original variables are then obtained as linear combinations of these. The author persists in using this confusing notation, e.g. on p. 212 in the discussion of relaxation methods.

2. The solution to the numerical example pp. 116–118 is not quite correct. The correct values for the amplitudes are more easily obtained from the boundary conditions, including those for the rates at  $t = 0$ , as an alternative to the introduction of the not very useful, and perhaps somewhat confusing, eigenvectors.

3. The method of Laplace transforms for solving coupled differential equations is discussed on pp. 148–151. It is introduced as a 'black box' method as follows: (i) The original differential equations are rewritten by replacing the derivative  $dc/dt$  by  $s c(t) - s c(0)$ , where 's' is considered an 'operator'. (ii) The new equations are solved for the variables  $c_i(t)$ , which now appear to be expressible as functions of s only! (iii) A table of Laplace transforms is consulted and the real solution is obtained. This procedure is, however, wrong. First of all, the derivatives  $dc/dt$  should be replaced by  $s \cdot c_i - c_i(0)$  — note the absence of the factor s in the second term. Secondly, the author overlooks the fact that when transforming the original equation, a constant b becomes b/s in the transformed equation (this can in fact be seen in the extract of the table on p. 150). Thirdly, the transforms are not functions of t, i.e. one can not, as in the book, write the  $c_i(t)$  as functions of the variable (or 'operator') s. The procedure described in the book leads to erroneous equations. When it is further noted that, out of 11 entries in the table of Laplace transforms on p. 150, five are wrong, it is a complete mystery that actually the correct solutions are obtained.

4. On p. 119 the author attempts to explain data from experiments with calcium activation of aequorin by pointing out that the intermediate concentration reaches a maximum with a rate constant which is the sum of individual rate constants. However, looking at the

kinetic equation, Eq. 4.2.22, it is clear that (i) the solution is a single exponential, a monotone, increasing function of time, and therefore can not have a maximum, and (ii) the stated maximal value is not an extremum, but is the limiting value obtained at infinite time! This is easily derived from the actual solution of the differential equation 4.2.22. It thus seems that the kinetic model is not describing the data in Fig. 4.5.

Throughout the book the author strives to define experimental conditions such that the solutions to the kinetic problems will appear as sums of exponential functions, i.e. to find conditions such that the underlying differential equations are of the first order. Although this is conceptually simple it does have the disadvantage that fitting sums of exponentials to data is notoriously difficult, particularly if the corresponding eigenvalues are not too different. The author warns against this problem by providing an example of two functions, both sums of exponentials, that will be a real challenge to unsophisticated

fitting programs. Furthermore, even for relatively simple kinetic schemes the solutions to the differential equations will be too complex for a complete extraction of rate constants from the data, and these are, after all, the quantities of real interest. Only a few pages are devoted to a discussion of the main principles of fitting equations to data, but the book does not mention the possibility of fitting rate constants directly to differential equations without solving them. User friendly programs for this purpose are now available also for the PC.

The book has a pleasing format, and the layout is very good. The main goal of the book, that of demonstrating the similarity of models from somewhat different fields of biological research, would seem to have been achieved. But for the reasons described above, anyone who really wants to learn the trade in kinetics should look elsewhere for guidance.

Igor W. Plesner

**T Cell Receptors;** Edited by J.I. Bell, M.J. Owen and E. Simpson, Oxford University Press, New York, 1995. xx + 482 pp. £29.50 (pb). ISBN 0-19-262419-9.

This is an excellent and comprehensive book that deals with one of the most exciting field of immunology. Since the discovery of the T cell receptors, a little over ten years ago, there has been an explosion of activity in this area and the achievements have been very impressive. In this period immunologist and molecular biologists have acquired such an extensive amount of information on the many different aspects of the structure and physiology of the T cell receptors that it is becoming increasingly difficult, even for the experts, to have an updated clear vision of this field. Thus a comprehensive treatise on this subject was very much needed. The editors have to be congratulated for this excellent work.

In general, and with rare exceptions, all the chapters present brief and concise background information and an extensive list of references which provide key articles to support the presented information.

The book starts with a highly readable introduction by J.A.A.P. Miller that presents a historical overview of the subject based on personal experience. The main body of the book subdivided in four parts, each one containing several specialized articles.

Part one deals with T cell populations and the first four articles provide a complete description of the specificity and functions of the different T cell subsets. The next two articles deal with the human and murine T cell repertoires. Here the readers will find all the information on the state of the art of this complex subject. I have particularly appreciated that, in one article, the authors have also dedicated particular attention in describing the distortions of the T cell receptor repertoire that occur in several human diseases. In this part of the book the reader will also find an appreciable description of the methods currently used to quantitate levels of TCR RNA. The last chapter of part one deals with the role of peptides in positive and negative selection. This chapter is essential for those who want to approach the problems connected with the basic paradox of a single TCR inducing positive or negative selection.

The second part highlights T cell functions. All aspects of activation and tolerance are described in four contributions. The first two articles deal with the biochemical pathways of TCR signal transduction, including  $\text{Ca}^{2+}$  influx, inositol lipid turnover and the activation of protein kinase C. The third review describes the importance of transgenesis for studying thymocyte development and selection, as well as the role of T cells in a wide range of immunological phenomena. This article provides an interesting and critical overview of the advantages and the limits of using TCR transgenic mice. The last chapter of this

section deals with superantigens, a group of molecules with particularly intriguing biological activities. Here Acha-Orbea provides a detailed description on the current knowledge about superantigens and describes his personal view on how these substances have been used as tools to learn several aspects of immune response and tolerance.

The third section is devoted to T cell genes. The five articles provide a complete description of our current knowledge of the structural TCR genes as well as on the mechanisms of recombination, developmental regulation and allelic exclusion. Particularly useful is the tabulation and nomenclature of the human and murine TCR  $\alpha$  and  $\beta$  variable regions and the inclusion of a plate section showing the alignment of these sequences and how they are related to each other. These chapters, written by the most outstanding scientist in the field, are valuable references that should be present in the library of every immunologist.

The last section covers most of the aspects of T cell proteins. The apparent plasticity of the TCR-CD3 complex is discussed in great details by Terhorst and his collaborators. Hilyard and Strominger, on the other hand, provide an extensive review on the existing structural information for the TCR based on molecular models generated from protein sequences and the detailed information provided by the crystal structures of MHC-peptide complexes. Models of structural interactions between bacterial superantigens and MHC class II and TCR are discussed in a more general context of physiological TCR-ligand interactions by Fraser and Huston. Finally H. Ploeg describes the different steps involved in the biosynthesis of MHC and their relevance for antigen presentation.

Given the different aspects of T cell receptors, this book is certainly a great, timely and welcome effort to integrate the different facets of TCR biology and function in one comprehensive reference. It is the strength of the editors not only to have chosen some of the best experts in the field but also to have combined their contribution in such a way that the reader is never left with a discontinuous mixture of unrelated entities, rather the reader will discover how the structural and functional aspects of TCR biology are interrelated and cannot be separated from each other.

Thus *T Cell Receptors* is of great interest not only for newcomers, but also it represents an indispensable reference to those already actively engaged in studying these fascinating molecules.

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