
Thanks largely to the staggering developments in computer technology and to the decreasing costs of computer hardware the area of flow cytometry has during the 1990s expanded considerably with respect not only to the number of high-output instruments installed, but most importantly – to the diversity of applications developed for this technology. The proceedings from this NATO Advanced Study Institute held in France in May 1995 amply demonstrate the latter point by covering a wide spectrum of methodologies.

Divided into three parts (Membrane dynamics and function, Cell proliferation and gene expression and Data management systems, cell sorting, microscopy), the book takes the reader from well-trodden grounds like ‘Cell cycle and cell proliferation markers’ and ‘Analysis of cell death by flow cytometry’, over more specialised topics like ‘Molecular cytogenetics’ and ‘Myc control of proliferation and apoptosis’ to connoisseur’s choices like ‘Endogenous lectins in circulating cells and their glycosylated ligands: their role in T cell homing’ and ‘Use of different cytometric techniques to study the cytotoxic interactions between natural killer cells and K562 target cells’.

Information about books for review in FEBS Letters should be sent to: Professor J.E. Celis, Department of Medical Biochemistry, Ole Worms Allé, Building 170, University Park, Aarhus University, DK-8000 Aarhus, Denmark.

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I think this is a really good book. The editors have brought together experts who are directly involved with the current science and status of knowledge of these diseases. Furthermore, the range of scientific perspective presented is outstandingly broad. Of the currently published work on these diseases, I could perhaps only fault this book for not including the recent extensions published in 1996 of our own progress with a spinal fluid marker for transmissible spongiform encephalopathy. Just joking! Since our work was published after this book was prepared, I cannot even fault the authors for this omission.

There are 18 chapters, some complementary, some divergent in content, that the editors have orchestrated into a very good sequence, from many different authors (39 are listed as contributors at the beginning, although one author will probably be upset at being omitted from this list). To summarize this overall layout, I really could not imagine a more diverse set of experts brought together with so little confusion and redundancy, or with more success. This result is a very fact-filled, largely error-free, very readable text. It was gratifying and somewhat unusual for this reviewer to find that the contents of each chapter actually related to its title.

In the first chapter, Ridley and Baker present features that make these diseases so intriguing. The second chapter, Human Spongiform Encephalopathy, describes the clinical presentation and diagnostic tests used in the currently defined human forms of these diseases. In the next two chapters, Ironside and Bell present detailed, very informative perspectives on the neuropathology of human prion disease. Since I am currently looking actively at this pathology, I know enough to recognize there was enough detail and I still learned a lot. Stack, Keyes and Scott present detailed methods in the fifth chapter on the diagnosis of bovine spongiform encephalopathy and scrapie by the detection of fibrils and the abnormal protein isoform. Taylor reviews the exposure to, and inactivation of, the transmissible agents in these diseases. Since this is an area of major concern in the management of these diseases, one is more than a little disappointed with the lack of control we have over these agents. However, this review is very comprehensive and useful.

The seventh chapter is a survey of the human diseases by Will, who has contributed substantially to this area himself; not surprisingly, this is both detailed and accurate. In the next chapter Brown reviews the environmental causes of human spongiform encephalopathy. Again we are frustratingly ignorant of these causes, but Brown has discovered much himself and dug up very well what else is known in this area. The ninth and tenth chapters are very tightly connected: Wilesmith first reviews the epidemiological analysis methods used from the beginning of the BSE epidemic in the UK followed by Tyrrell and Taylor who described the 'handling' of the epidemic in Great Britain. I have been watching this area closely and am very impressed with both of these chapters. On one hand, it was surprising to me that there is some apparent defensiveness in a scientific book such as this for what has been accomplished. On the other hand, considering the intense scrutiny and media pressure perhaps it should not be surprising. Whatever criticism one could make in a retrospective analysis, I think outstanding and quite heroic efforts were made to do 'the best' in this situation, as is described in these chapters.

Hunter and Bruce in chapters 12 and 13 respectively describe genetic typing and susceptibility of sheep to scrapie and strain typing studies of scrapie and BSE. This is a crucial part of the story because of the extent of biological studies performed on the sheep form of this disease and these chapters described the genetics, biology and molecular studies in context with our current knowledge very well. Mansen extends this with a chapter on PrP deficient mice in an area that is clearly providing great insight into the role of the PrP gene. It is about this time in the book that one is yet again reminded of how ignorant we are of the normal role of this prion protein, let alone its conversion to the deadly misfolded form in these diseases. The 15th chapter describes the transgenic approaches to study the prion 'species-barrier effect'. This is well written and very useful and I commend both the author and the editors for including a most relevant topic. The next three chapters, methods to study prion protein amyloid, metabolism and immunohistochemistry, are just excellent descriptions of these approaches to prion disease research by absolute experts in the field. They provide a detailed review of what has been done and the methods to interpret or even pursue this research oneself.

It is obvious I think this is a very good book, but who would benefit from reading it? I would say this has to be the most clearly written and broad text on these very interesting and topical diseases. Thus readers from the lay to the scientific public wishing to learn all of these aspects of this disease would benefit from reading this. I think therefore this demands attention in the libraries across the world as well as in the hands of personal readers who I think, from student to senior scientist, will want to refer to and re-read parts of this book often enough to want their own copy.

Michael G. Harrington


This book contains detailed laboratory protocols for a number of PCR-based methods whose primary purpose is NOT to amplify a specific piece of genomic DNA or cDNA by using highly specific primers. On the contrary, the fingerprinting methods aim at the simultaneous amplification of a number of DNA fragments with unknown sequence and function. A comparison of the gel electrophoretic pattern of amplicons obtained using the same procedure on two or more different targets will then reveal differences in the genetic constitution (if the target was genomic DNA) or gene expression (if the target was cDNA), and these differences can be investigated further by standard methods in the field of molecular biology such as cloning, sequencing, database searches, Southern blotting, Northern blotting, etc. Methods based on arbitrarily primed PCR are gaining increased usage and are becoming valuable and unexpensive tools in many fields of biology and medicine. It is therefore a very laudable effort of the editors to present a collection of these methods.
The book is divided into two parts covering DNA fingerprinting (25 chapters) and RNA fingerprinting (14 chapters). The DNA part is further divided into the five subjects: DNA extraction, fingerprint production, further protocols for ampiclon visualization, marker isolation and characterization, and research applications. The RNA part is divided into four subjects: fingerprint production and ampiclon retrieval, confirmation of differential expression, characterization of differentially expressed cDNAs, and research applications. Each chapter is written by one or more of the 59 contributors and there is no doubt that the fulfilled intention of the editors was to create a collection of protocols that are complete, similar in structure, and easy to follow even for the inexperienced molecular biologist. However, these procedures are tricky to work with because our understanding of specific or arbitrary priming and PCR still is very limited and I doubt seriously that an 'experienced molecular biologist' would be able to adopt the procedures in this manual. For the 'experienced molecular biologist' there is a wealth of information, but it may be very hard to find due to the principle used for editing the book. All the contributors emphasize that it is imperative to have a high quality of starting material. It is therefore obvious to devote six chapters to procedures for DNA extraction. It is less obvious that no chapters deal explicitly with RNA isolation, but this is probably because the commonly used acid guanidinium thiocyanate-phenol: chloroform extraction procedure of Chomczynski and Sacchi is described in detail in each of two different chapters, a manual for a guanidinium thiocyanate-cesium chloride procedure is given in another chapter, and two new and interesting procedures for isolating RNA for differential display from minute quantities of cell material are hidden in a chapter dealing with research applications of RNA fingerprinting!

The production of fingerprints can be divided into two parts: arbitrarily primed PCR and gel electrophoresis of amplicons. These are the key issues of a manual like this. How do you get a robust procedure that reproducibly produces many (though not too many) amplicons, and how do you visualize these quickly and easily in a gel with high resolution? The descriptions of PCR reactions are breathtaking. Almost every chapter introduces a new list of stock solutions and recipes for premixes to be distributed in an overwhelming number of trays or tubes in various arrays. Taste is naturally always a matter of debate, but since arbitrarily primed PCR is even more sensitive to variations in nucleotide concentrations and buffer compositions than 'ordinary' PCR, I at least would have found it easier to compare the various procedures if I knew the final concentrations in the reaction tubes rather than the cookbook recipes. Apparently any kind of gel electrophoresis and staining or labelling/autoradiography can be used for some kind of arbitrarily primed PCR. The book would have been much thinner if ordinary agarose gels or standard denaturing polyacrylamide sequencing gels were described only once, but many interesting alternative gel systems can be found scattered in the many chapters (some are even documented with figures).

Once an interesting amplicon has been visualized as a band in a gel it must be shown that it is indeed an interesting amplicon and not an artefact. This was a main problem for the first users of RNA differential display, but many elegant solutions have been found and are described in this book. In most cases one would also like to clone the amplicons, know their sequence, and use them as probes in hybridization assays and so on. Methods for all of these analyses are presented in this manual though naturally only very inauspiciously. Most of these chapters (or parts of chapters) seem superficial to me. The choice of methods for these kinds of analysis depends in my view much more on the equipment and tradition in your lab than on the procedure used for obtaining a sequence tag. However, it should be mentioned that the manual includes a description of a very complete and coherent system for RNA differential display and characterization of differentially expressed mRNAs developed by the groups of Michael Strauss and Henrik Leffers. Unfortunately, due to the way this book is edited, the procedures have been split into three independent chapters, but the elegance of the system is still visible.

In conclusion, this book contains a very broad collection of methods for characterization of DNA and RNA samples by arbitrarily primed PCR. All the methods are described as detailed ready-to-go laboratory protocols. The exact methods you are looking for may be hard to find but they are probably there — and your technicians and graduate students will be delighted when you hand them a photocopy.

Per Hove Andreasen


For many years the significance of the discovery that there is a specific mechanism by which cells die (now called apoptosis) went unrecognized. It is now known that cells in most tissues contain a death programme and that the role of cell death in tissue maintenance and development is crucial. In the last few years there has been an explosion in the number of publications on apoptosis. The complex biochemistry of the apoptotic cascade is being rapidly unravelled.

As the number of laboratories working on apoptosis increases, so has the need for books describing the key laboratory methods. This volume attempts to meet this demand in the field of neurosciences. It contains several chapters describing biochemical methods for detecting apoptotic cells, a chapter on gene tools, one on PCR amplification of reverse-transcribed RNA (RT-PCR), one on p53, one on the expression of the protein, statin, and a chapter on the use of the nematode, _Caenorhabditis elegans_, as model for studying neuronal cell death.

We should ask whether neuroscience requires special treatment when the apoptotic process appears to be common to cells from all tissues and, if so, whether this book does indeed meet the need for a methods book on this topic. Does it also fulfill the claim on the book cover that "It is certain to serve as an illuminating introduction to the basic ideas behind the phenomena of apoptosis and necrosis"?

Unfortunately, for me, this book did not meet the need or fulfill its claim. It is a multi-authored volume which appears to have been assembled without a clear overall plan or any coordination between the different chapters. I would have liked to have seen an opening chapter which gave an authoritative overview of the apoptotic process and linked that to studies on cell death in the CNS. The techniques needed to study the different aspects of cell death could then have followed in context. This approach would have imposed a structure on the other chapters. Such a review and any structure was lacking. There are several well documented methods for detecting apoptosis. Apart from straight morphology (still an important tool), many of these rely on the observation that the DNA in apoptotic cells is degraded into oligomers of about 200 base pairs. Two of these methods (DNA gel electrophoresis and end-labelling of DNA strand breaks - TUNEL) have been used widely. Inevitably there are small variations in the way the method is applied between laboratories. A worker new to the field needs some guidance as to the significance of these variations and their importance.

In this book, DNA gel electrophoresis is described in four chapters (written by Gschwind and Huber; Linnik; Mosey and Michel; and Bonfoco et al.). Similarly, the TUNEL method has its own chapter by Kerrigan and Zuck but is also described in chapters by Mahalik et al., Mosey and Michel, LaFerla and Jay, Geiger et al. and Bonfoco et al. While the initial preparation may differ depending on the source of material, the main methods are the same. It is irritating to read several versions of the same procedures without any critical assessment.

On the other hand, there are omissions. A method for preparing cells for electron microscopy is given without showing an example of an electron micrograph of an apoptotic cell. We must be shown that it is indeed an interesting amplicon and not an artefact. This was a main problem for the first users of RNA differential display, but many elegant solutions have been found and are described in this book. In most cases one would also like to clone the amplicons, know their sequence, and use them as probes in hybridization assays and so on. Methods for all of these analyses are presented in this manual though naturally only very inauspiciously. Most of these chapters (or parts of chapters) seem superficial to me. The choice of methods for these kinds of analysis depends in my view much more on the equipment and tradition in your lab than on the procedure used for obtaining a sequence tag. However, it should be mentioned that the manual includes a description of a very complete and coherent system for RNA differential display and characterization of differentially expressed mRNAs developed by the groups of Michael Strauss and Henrik Leffers. Unfortunately, due to the way this book is edited, the procedures have been split into three independent chapters, but the elegance of the system is still visible.

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Per Hove Andreasen
Suppose you are a biologist not familiar with computer tools for DNA or protein sequence data analyses, and suppose you have a personal computer. Then, *Sequence Data Analysis Guidebook* may be useful. This book is not for reading through, but for reference by topic.

Let’s say, you have a DNA (or a protein) sequence that you or someone else sequenced, and perhaps what you want to do first is to find sequences similar to yours. Then, you may look in chapter 14 of this book, in which Eugene Shapiro presents database similarity searches, putting emphasis on a revised version of the Smith-Waterman method. He wrote this chapter in a way that protein sequence searches come first and DNA sequence searches follow. I think, however, that the other way around would be better, because what you usually have first are DNA sequences rather than protein sequences. By using the method in this chapter you have obtained sequences similar to yours. Next, you may need to compare for similarity more closely between a pair of the sequences. If this is the case, you would open to chapter 10, where Phil Taylor writes about methods of pairwise sequence comparison. He introduces four methods for this purpose, the simple, gapped, homology alignment and homology matrix methods. The first method involves aligning the two sequences in question without introducing gaps just like with BLAST, and the second one allows gaps like FASTA. If somehow you know that the sequences to be compared are similar to each other in both size and content, you might use the third method for better performance and results. The fourth method will give you all possible alignments at a glance.

After making sure that all the sequences are mutually similar to each other by executing one of the methods just mentioned, you may be interested in aligning all the sequences simultaneously. Then, you go to chapter 9, in which Jonathan Clewley and Catherine Arnold introduce two multiple alignment methods, CLUSTAL V and MALIGN. CLUSTAL V, which is the first version, however, is obsolete now. Its third version, CLUSTAL X, is already available.

After multiple alignment, you might want to know how your sequence is phylogenetically related to the others. For this purpose, chapter 2 is helpful. This chapter was written by Jonathan Eisen, who explains PHYLIP among others. PHYLIP is a well-known package for phylogenetic analysis of DNA and protein sequences which contains several tree-making methods such as the maximum likelihood, maximum parsimony, neighbor-joining methods, and others. For the first two methods, what you need are sequences aligned as the input data (you have to eliminate beforehand those aligned sites where at least one sequence has gaps). For the third method, you need a distance matrix which may be obtained by computing a distance between every pair of sequences. There is, however, no chapter for computing distances in this book. Since this distance method is widely used, there should have been such a chapter. Finally, you have obtained a phylogenetic tree on which your sequence is clearly located. I think, however, that this is not the end but the beginning. You are now ready to carry out biological discussion on the basis of the phylogenetic tree thus obtained.

There are more chapters in this book, 26 in total. If you are only interested in your own sequence, you may open to chapters 17 and 18, where Phil Taylor describes methods for finding restriction sites, translating a DNA sequence into an amino acid sequence, and locating open reading frames. You may also read chapter 20, in which Thomas Plasterer writes about restriction analysis in more detail. If you have a protein sequence, you may go to chapter 19, in which T. Plasterer also presents protein sequence analysis tools for finding the α-helix, β-sheet, turn, and coil regions. Also included are methods for estimating secondary structures, carrying out gel simulations for proteins digested by proteases, and others. For editing and presenting your sequence, chapters 1 and 21 will be useful; P. Taylor wrote the former and Bruce Troen the latter.

As you may know, DNA sequences you retrieve daily for your research work are collected, processed and released by the International Nucleotide Sequence Databases. The databases are operated by the European Bioinformatics Institute (EBI) in the UK, the National Center for Biotechnology Information (NCBI) in the USA, and the DNA Data Bank of Japan (DDBJ). Authors in this book, however, incorrectly referred to the databases as GenBank/EMBL (the correct expression being DDBJ/GenBank/EMBL), except for Thomas Flores, Robert Harper and Benny Shomer, who introduce the database activities at EBI in chapters 13 and 26. These two chapters are helpful in outlining the databases, though the authors focus their presentations mainly on EBI activities.

There are four chapters, 22 (P. Taylor), 23 (Juan Estruch), 24 (J. Estruch), 25 (T. Plasterer), on primer/probe design and selection, and three chapters for dealing with the ABI sequencer.

Perhaps, you may have realized now that this book is not well organized. I do not understand what organizational strategy the editor chose as a framework. In addition, there are quite a few duplications among the 26 chapters; for example, chapters 2, 9, 11, 12 all deal with multiple alignment, though to different extents. All the tools presented in this book are in the public domain and available free of charge. One drawback in computer tool books in general is some of those tools introduced and explained will soon become obsolete, and this book is no exception. Thus, I would recommend that the authors of this book update the tools they introduced whenever new versions are made available.

Yoshio Tateno

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Genetic instability caused by somatic mutations in the mismatch repair genes and perturbations in the cell cycle control is believed to be an important factor in the development of some human cancers. Furthermore, genetic instability can be acquired from inherited mutations in some of these genes and the mutations may give rise to a number of familial cancer syndromes.

This book reviews in an excellent way the recent research in the area of genetic instability and tumorigenesis and elucidates some of the molecular mechanisms causing the development of cancer.

The basic topics of the book include a general discussion of the role of increased mutation rates in tumorigenesis. Cell cycle control and genetic instability are exemplified by genetically manipulated yeast. Genomic instability and its role in the development of neoplasia are
reviewed, as are DNA excision repair gene defects and their importance in xeroderma pigmentosum. Furthermore, a more general review on genetic instability syndromes and carcinogenesis with a focus on ataxia telangiectasia is given. Finally, the different genes which are actually found altered in tumors are considered, including the defects in the DNA mismatch repair genes, thought to be responsible for the HNPCC syndrome (hereditary non-polyposis colorectal carcinomas). The reviews are generally well referenced for readers who would like to go deeper into the topics. Furthermore, there is a minimum of redundancy between reviews.

In conclusion, this book is full of useful information, and it gives an up-to-date review of the molecular and genetic basis of cancer. It is recommendable reading for individuals in cancer/oncology research.

Mariann Christensen and Torben F. Ørntoft

Booklist No. 140


September 1997

The most recently published Booklists are the following:

Histochemistry is a somewhat related technique, where various chromogen markers (frequently diaminobenzidene dihydrochloride, DAB) are deposited as the end product of an enzymatic reaction, and thus reveal cells and/or processes positive for certain substances. From: International Encyclopedia of the Social & Behavioral Sciences, 2001.

Histochemistry using GBPs has been an effective means of defining the regions in tissue sections and cell types that express various glycan motifs. The studies of cancer tissue have provided fundamental information about the involvement of glycans in disease. An important class of glycans in epithelial cancers is the Lewis blood group structures and their sialylated and sulfated derivatives.