Book Reviews

Dynamics of Cell Division. Frontiers in Molecular Biology. Edited by S.A. Endow and D.M. Glover, Oxford University Press; Oxford, 1998. xviii+322 pp. £31.95 (pb). ISBN 0-199-63682-6.

This book, edited by Sharyn A. Endow and David M. Glover, adds another volume to the series 'Frontiers in Molecular Biology' and gives a comprehensive overview of the regulation, dynamics and mechanics of cell division. The nine chapters follow an order analogous to the sequence of key events during cell division, starting with a description of checkpoint mechanisms that monitor the integrity of the replicated genome before entering mitosis, followed by chapters on nuclear envelope breakdown, spindle assembly, behaviour of chromosomes in mitosis and meiosis, function and structure of the centromere and kinetochore, sister chromatid separation, cytokinesis and partitioning of the cytoplasm. Each chapter is logically structured, providing the reader with an introduction, a critical presentation of recent achievements in the field, allowing space also for experimental approaches, a thorough comparison of regulatory mechanisms among different species, and a future outlook which points out the critical questions that remain to be answered. In addition, many chapters are accompanied by a number of useful tables and cartoons. Another very accomplished feature of this book is the fine tuned balance between the presentation of recent discoveries and historical achievements such as the description of chromosomes, centrosomes and the mitotic spindle, findings that date back a hundred years or so, thereby paying tribute to the fact that cell division is one of the most traditional sciences in cell biology.

Acknowledging the significance of cell cycle checkpoints, surveillance mechanisms that monitor the order of events and the integrity of the genome at each transition during the cell cycle, the first chapter, written by Kristina R. Yu, Robert J. Duronio and William Sullivan, summarises the advances made in understanding checkpoint controls activated in response to damaged or unreplicated DNA or to unattached kinetochores at the spindle assembly checkpoint. Interestingly, the authors also point out differences in the role of checkpoints in early embryonic cell cycles of frog and fly. The following chapters then deal with the structural and mechanical changes of a cell entering mitosis, such as nuclear envelope breakdown and reassembly (Brian R. Miller and Douglass J. Forbes), the ultrastructure of spindle pole bodies and centrosomes, and the coordination of their replication and movement with the cell cycle (Ian M. Hagan, Keith Gull and David M. Glover), microtubule dynamics, molecular motors, and chromosome behaviour (Isabelle Vernos and Eric Karsenti). Proceeding further through mitosis towards metaphase, the reader is updated with structural and mechanistic aspects of the centromere-kinetochore complex in a chapter written by Kevin S. Sullivan. As much as the summarised achievements in these disciplines must be appreciated it becomes clear that these fascinating mitotic events keep much of their secrets still, as is pointed out in the future perspectives of each chapter.

Before embarking on the finish of the cell division journey via cytokinesis (Michael L. Goldberg, Kristin C. Gunsalus, Roger E. Karess, and Fred Chang) and inheritance of cytoplasm during cell division (David T. Shima and Graham Warren), the reader is taken on an excursion through special features of meiotic cell division (Gary H. Karpen and Sharyn A. Endow) and properties of telomeres, specialised chromosome ends, their structure, synthesis and cell cycle regulation (Timothy R. Hughes and Victoria Lundblad). Although the enzyme machinery involved in regulating telomere length is not essential for a cell to divide, telomeres appear to represent a clock counting the limited rounds of cell division, since their length is shortened with every round of replication. Included in this chapter is also a brief summary and discussion on the role of telomeres in immortalisation, tumorigenesis and ageing of cells, underlining the significance of very recent findings on telomere biology.

As we currently witness an explosion of new knowledge on the molecular events in mitosis, including the separation of sister chromosomes and mitotic exit driven by the anaphase promoting complex, and as mitotic regulators emerge to be targets of DNA damage checkpoints and are potentially involved in tumorigenesis, this book comes at a very good time to provide scientists with an excellent basis for the understanding of the complex regulation of cell division. Taken together, this book provides a comprehensive summary of the molecular mechanisms and dynamics of cell division. The 'Dynamics of Cell Division' can be recommended to both scientists in the field and interested students of cell biology who wish to extend and deepen their knowledge beyond a level that a textbook can provide.

Claudia and Jiri L. Bartek

Animal Cell Biotechnology. Methods and Protocols. Methods in Biotechnology. Edited by N. Jenkins, Humana Press; Totowa, 1999. xiv+302 pp. $99.50 (hb). ISBN 0-896-03547-6.

Mammalian cell biotechnology is a rapidly expanding area of research. A number of advanced techniques have been developed to approach the challenge of taking discoveries in fundamental cell biology to the level of clinical application. *Animal Cell Biotechnology* brings together techniques used in both industry and research laboratories that are focused on the expression of recombinant proteins and other commercial uses of animal cells. The book is divided into five parts describing techniques relevant for each step in this process.

Part I, 'Enabling technologies', describes the equipment needed for setting up a new cell culture facility and supporting facilities, and even provides a laboratory floor plan for absolute beginners. Since the goal is to produce recombinant protein biotherapeutics, the following chapter very thorougly described the adaptation of mammalian cells, in casu CHO cells, to serum-free growth. Detailed protocols are provided including recipes for culture media. In the last chapter of Part I, the problem of virus contamination of cell cultures used for the manufacture of therapeutic reagents is addressed and the subject is broadened to encompass viruses in both humans, laboratory animals and livestock. Different testing procedures are described. As for the latter, it would, however, have helped the reader if recipes and discussion were separated, and, although extensive reference to specific literature is given, in the description of in vitro assays of testing, an example of the entire procedure for one of the viruses would have been helpful. Overall, Part I very adequately prepares the reader for the next step, which covers the molecular methods of the biotechnology.

Part II, 'Molecular methods', comprises six excellent chapters on gene expression optimization, immortalization strategies, production of monoclonal antibodies, cell bank preparation and cell type characterization, including cytogenetic characterization and DNA fingerprinting. A method for optimization of gene expression by increasing gene dosage through the choice of appropriate plasmids and use of in vitro amplification of multiple concatemers is described, and the individual steps in the expression procedure are briefly but adequately commented upon. As a method to cytogenetically characterize the recombinant cells, fluorescent in situ hybridization is described and detailed protocols for this elegant technique are provided. The chapter

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on immortalization strategies discusses different methods of gene transfer based mainly on SV40 as immortalizing agent. Several immortalization techniques are currently available and information about other immortalization protocols such as HPV E6/E7 or telomerase would have been appropriate. The last two chapters deal with the very relevant issues of storage and characterization of the established cell lines. It is less obvious why a chapter on the production of monoclonal antibodies is included, and although this chapter is also well written, a reference to contemporary literature might have been sufficient. Overall, however, Part II provides a general background and detailed recipes of the individual procedures, and this part is indeed comprehensive and scholarly.

Once the cells of interest are established one may need to measure their proliferation, viability, metabolism and productivity. Methods available for measuring these parameters are the subject of Part III, 'Cell evaluation protocols'. Some of the methods have of course already been touched upon in the preceding chapters, but cross references are given. The first chapter includes both direct (counting of cells or nuclei) and indirect measurements (protein, glucose or DNA determination) of cell number as well as viability tests based on colony formation, dye exclusion or enzyme activity. Also, a chapter on flow cytometry to perform cell cycle analysis in addition to cell number and viability measurements is included. The last two chapters deal with monitoring of cell death and cell metabolism as assessed by nuclear magnetic resonance, respectively. I suppose the former is included for the scientist who wants to know the reason why his recombinant cells are dying or exhibit a slow net increase(!).

Part IV, 'Specialist techniques', discusses some of the more specialized techniques used for large scale protein production, including culture of cells in microspheres and production of GPI-anchored fusion proteins. The biology of GPI-anchored proteins is thoroughly described, and the techniques used for fusion and harvesting of GPI-anchored proteins are well described. Other specialist techniques include cultivation of hematopoietic cells for transplantation and as gene therapy vectors. The inherent challenge of hematopoietic cell culturing is the heterogeneity of the cell population resulting from the presence of different lineages as well as multiple differentiation levels within each lineage. The reader is given the impression that the authors of these chapters do indeed have hands-on experience in the field.

Part V, 'Product evaluation protocols', deals with some of the technical problems encountered when working with biologically engineered cells and proteins. The tools to ensure a high yield of recombinant proteins include measures to control proteolytic and glycosidase activity. Also, posttranslational events such as protein folding and glycosylation of the recombinant product are discussed.

Although in some instances the editor has left the reader to wonder why a particular subject is relevant within the context of techniques for large scale production of recombinant proteins, the book is in general well composed and may be a guide both for the beginner and for the more trained scientist in the field of animal cell biotechnology.

L. Rønnov-Jessen

DNA Topoisomerase Protocols. DNA Topology and Enzymes. Methods in Molecular Biology, Vol. 64. Edited by M.-A. Bjornsti and N. Osheroff, Humana Press; Totowa, 1999. xv+327 pp. $79.50 (hb). ISBN 0-896-03444-5

Over the last two decades DNA topoisomerases have evolved from a laboratory curiosity to an important class of enzymes with a pronounced impact on pharmacology, molecular cell biology, and biotechnology. These enzymes are now investigated or used as cloning tools in many laboratories all over the world. However, a comprehensive compilation of methods and background information on DNA topology and DNA topoisomerases was not available until now. This gap is closed by 'DNA Topoisomerase Protocols'. The book addresses itself to the non-specialized reader and puts emphasis on the practicalities of DNA topology work. It comes in two volumes. Volume I, entitled 'DNA Topology and Enzymes', deals with the more basic aspects, i.e., definition and analysis of DNA topology (chapters II–XIII), overproduction and purification of DNA topoisomerases from various sources (chapters XIV–XXIV), and finally some structural aspects of these enzymes (chapters XXV–XXVII). The introductory chapter by the editors gives a beautifully brief and concise overview of the entire family of DNA topoisomerases and related enzymes and can be used as an Ariadne's thread to the key papers of the field. Another useful item is the appended compendium of topoisomerase sequences, which is likely to be helpful in designing expression vectors, deletion mutants, etc. Most of the other chapters contain a lot of useful information and easily followed procedures. However, there are also some highly theoretical elaborates, to which the term protocol hardly applies. By and large the book is a must for anyone who sets out on DNA topology and does not want to go through the methods sections of a multitude of original articles.

Chapters II and III describe the separation and analysis of the more simple topological forms of DNA plasmids by one- and two-dimensional agarose gel electrophoresis. The basic techniques (preparation of gels, electrophoresis conditions, use of intercalators, etc.), and the interpretation of the results are described in great detail so that these two chapters can actually be used as a practical starting point, when setting up analysis of plasmid topology for the first time.

Chapter IV, entitled 'Analysis of altered DNA structures', is more or less about cruciform DNA. The description of the methodology of two-dimensional DNA agarose gel electrophoresis is somewhat redundant to the previous chapter. Moreover, one wonders why the chapter is restricted to the analysis of cruciform DNA and does not include at least some of the other unusual DNA forms (e.g. Z-DNA).

Chapter V describes in great detail the purification of supercoiled DNA by CsCl gradient ultracentrifugation. Undoubtedly, one can purify supercoiled plasmid DNA by this tedious procedure and chapter V will provide a nice guideline for doing so. However, one might be better off using one of the more elegant procedures for plasmid purification which are in use nowadays.

Chapter VI describes the purification of DNA minicircles with different linking number and their use for the analysis of structural transitions and sequence specific deformations of DNA, such as curvature and bending. This very interesting chapter summarizes a lot of useful information from many papers, but it is not easy to read. Moreover, the methods section is not detailed enough to serve as a stand-alone laboratory protocol. More comprehensive information on the subject of DNA bending is to be found in chapter XII, which gives an extensive and at the same time brief and concise overview of various experimental approaches to the problem. It covers all the basic protocols in great detail and reads like a very useful laboratory manual.

Chapters VII and VIII give excellent descriptions of how one should go about making kinetoplast DNA from the protozoan parasite *Crithidia fasciculata* or knotted plasmid DNA from coliphage P4. Both chapters are brief and concise and read like highly refined laboratory protocols. They can easily be followed without additional literature reading. Since kDNA decatenation and P4 DNA unknotting are by now the most widely used procedures for determining type II topoisomerase activity, these two chapters are a must for everyone who wants to measure topoisomerase II activity and cannot obtain such complex DNA substrates from commercial sources or generous colleagues.

Chapter IX deals with DNA catenanes, knots, and related higher order structures of circular DNA resulting from topoisomerization and/or recombination reactions. The introductory section is nicely illustrated and elucidates the highly academic subject of knot topology in a beautiful manner, whereas the methods section is straightforward and easy to follow. Moreover, examples of typical results are provided, which can be used as a guideline for data interpretation. An interesting extension to the subject of knots is provided in chapter XI, which describes the visualization of knotted DNA plasmids by electron microscopy after coating with RecA protein. The procedure is described in great detail and can probably also be applied to other DNA structures.

Chapter X describes the sedimentation analysis of bacterial nucleolid structure, which can be used as a measure of the overall topology of the bacterial genome and, thus, as a descriptive parameter of the in vivo activity of bacterial topoisomerases, such as gyrase and topoisomerase IV. Unfortunately, the subject of bacterial nucleolids is not sufficiently clarified in the introduction. Moreover, examples of typical raw data are not provided, whereas the mathematics of data analysis are described in great detail. As a whole, the chapter is difficult to understand and seems not suited as a laboratory protocol for readers, such as myself, who are not familiar with the subject of nucleolid structure.

Chapter XIII, dealing with the formation of extrachromosomal DNA rings in *Saccharomyces cerevisiae* using site-specific recombination, is very interesting and easy to read. The protocols provided are straightforward and easily followed. However, it did not become quite clear to me how the subject is actually related to the main theme of the book and why one should like to do this.

Chapters XV–XXIV describe overexpression and/or purification of various types of DNA topoisomerases from various organisms. By and large, what is presented is the recipes as used in the laboratories of the authors. In some cases one wonders why so many chromatographic steps are required, while the same degree of purity can apparently be achieved by much simpler procedures in other laboratories. In some other cases these protocols do not really add much to the recipes provided by the manufacturers of the respective expression vectors. However that may be, taken as a whole, these chapters provide the most complete and comprehensive guide currently available for the production of pure DNA topoisomerases.

Chapter XXV gives a comprehensive introduction to the analysis of covalent posttranslational modifications of topoisomerase II. The protocol section summarizes the methodology of metabolic labeling in cell cultures and the analytical protein biochemistry (immunoprecipitation, tryptic digestion, and 2-D protein electrophoresis). These protocols are easy to follow and can probably be readily adapted to the analysis of other DNA topoisomerases as well.

Chapter XXVI deals with immunoblotting of DNA topoisomerases and also covers the subject of immuno band depletion, which is a way of determining the in vivo effect of drugs that stabilize covalent DNA intermediates of topoisomerases. What is described is basically the methods developed by the authors, which seem to work, as they have been the basis of quite a few publications. However, other groups have published simpler procedures, which also seem to work and take less time. One would also have expected in such a chapter an overview and evaluation of the topoisomerase antibodies currently in use.

Chapter XXVII finally provides a detailed description of the protocols and procedures used for the visualization of DNA topoisomerase II by electron microscopy. The methodology has only a few elements specific for topoisomerases that will not be found in electron microscopy textbooks. The chapter is also somewhat redundant to chapter XI. Finally, one wonders who will use these protocols, now that the structure of topoisomerase II has been resolved at much higher resolution by X-ray crystallography.

Despite my criticism about some details I find this book as a whole a very valuable addition to the topoisomerase literature. It summarizes a lot of useful information for those engaged or getting engaged in research on DNA topology or topoisomerases. Those just wanting to carry out some of the analytical procedures will in most cases find what they need, i.e. a concise delineation of the analytical background, some detailed and easy to follow protocols, and a comprehensive guideline for the interpretation of the results. As such, the book definitely deserves a place on many a laboratory shelf.

Fritz Boege

Bioinformatics. A Practical Guide to the Analysis of Genes and Proteins. Edited by A.D. Baxevanis and B.F.F. Ouellette, Wiley; Chichester, 1998. xiii+370 pp. £38.95 (pb). ISBN 0-471-19196-5

The increasing importance of computation within biology has taken many by surprise, including biologists, computer scientists and most certainly publishers. There are precious few books available for bioinformatics training, and there is a need for a range of books that is somewhat unusual for a new field. For some, bioinformatics is narrowly defined as the computational support for storage, retrieval and analysis of genomic sequence data. Others prefer a broader definition in which most of computation applied to biology falls under an umbrella. The authors clearly lean more towards the narrow definition, although the Preface outlines their vision of a more expansive academic and research-oriented discipline.

There are at least three dimensions to consider in the creation of a bioinformatics text. First, the authors must decide whether to target their books to biologists or computer scientists (a class of biocomputation professionals is emerging, but is still quite small). Second, authors must decide whether to focus their books on the creation of tools or the use of tools. Finally, they must decide whether to create a general introduction to the field, or something more specialized. *Bioinformatics. A Practical Guide to the Analysis of Genes and Proteins* is targetted to biologists as tool users and attempts a general introduction to the field.

The National Center for Biotechnology Information (NCBI) at the National Institutes of Health has been a major resource for the storage, delivery and retrieval of bioinformatics data over the last decade. About half of the authors of the chapters within this text have affiliations with NCBI or NIH, and as such, this book serves as a useful manifesto of the approach to bioinformatics taken by NCBI. In particular, the discussions of the NCBI Data Model, the information retrieval philosophy, GenBank, the structure databases and creation of phylogenies come principally from NCBI scientists who offer a useful glimpse at the underlying logic and philosophy behind the services provided by the center. The remainder of the chapters offer useful introductions to the internet (although already somewhat dated), GCG, sequence alignment (pairwise and multiple), predictive methods, physical mapping, the popular ACEDB database environment, and nuts and bolts instructions for data submission.

This book is not for people who want to know how sequence alignment algorithms work. It does not discuss implementation details for any system, and is more a guide to the use of some common resources. It does not cover hidden Markov models in any significant way (see texts by Durbin et al. [1] and Baldi et al. [2] for excellent coverage of these). There is no significant discussion of the issues of protein structure prediction (as defined by the CASP series of meetings, for example [3]). There is no discussion of RNA folding algorithms. I was disappointed that the book does not cover data integration technologies other than the NCBI Entrez system. The creators of SRS [4] and DBGET [5] have made contributions and have approaches that ought to be mentioned even in an introductory guide. Consistent with its mission, it does not cover the technical details of data structures, programming languages, CORBA for distributed computation, BioPERL, or the other tools of the bioinformatics trade.

The most interesting chapter for a bioinformatics professional may be the overview of the NCBI data model which is critical to understand how data are organized and delivered at this scale (in fact, the chapter could usefully provide greater detail). The chapter on phylogenetic analysis is a very well done tutorial on the topic. I found the discussion of genefinding to be disappointing, however, and only cursory. The coverage of the NCBI-served databases is generally quite good, although the book does not cover in a substantial manner some of the newer features to support genomics, such as the clusters of orthologous groups, the LocusLink resource or the Unigene resource. Similarly, the emerging fields of gene expression array analysis and whole genome analysis are not really addressed.

On the whole, this is a worthwhile addition to the library as a reference guide for biologists using computational resources, and desiring an introduction to the use of some important tools. Even though it was published in 1998, it may need revision soon because of the tremendous pace of progress in this field. I think that bioinformatics professionals should also have this book because of its ex-

cellent treatment of some areas, and because I frankly suspect that it may become of historical interest as a snapshot of the bioinformatics capabilities provided on the web in the late 1990s. This book is not a textbook for bioinformatics trainees, and I fear we still await the perfect book (or book series) for training biocomputational professionals in all areas required.

[1] Durbin, R. (Ed.), Eddy, S., Krogh, A. and Mitchison, G. (Contributor) (1 July 1999) Biological Sequence Analysis: Probabilistic Models of Proteins and Nucleic Acids, Cambridge University Press Cambridge (Pap Txt); ISBN: 0521629713.
[2] Baldi, P. and Brunak, S. (January 1999) Bioinformatics: The Machine Learning Approach (Adaptive Computation and Machine Learning), MIT Press, Cambridge, MA; ISBN: 026202442X.
[3] http://PredictionCenter.llnl.gov/
[4] http://srs.ebi.ac.uk:5000/
[5] http://www.genome.ad.jp/dbget/dbget.links.html

Russ B. Altman

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1. Varki, A. et al. (eds) Essentials of Glycobiology. Cold Spring Harbor Laboratory Press; New York, 1999. xvii+653 pp. $95.00 (hc).
2. Scheffler, I.E. (ed.) Mitochondria. Wiley; Chichester, 1999. xiv+367 pp. £64.50 (hc).
3. Henderson, D.S. (ed.) DNA Repair Protocols. Eukaryotic Systems. Humana Press; Totowa, 1999. xix+641 pp. $79.50 (pb).
4. Sharpe, P.T. and Mason, I. (eds.) Molecular Embryology. Methods and Protocols. Humana Press; Totowa, 1999. xvi+756 pp. $135.00 (hc).
5. Brakhage, A.A. et al. (eds.) Aspergillus fumigatus. Biology, Clinical Aspects and Molecular Approaches to Pathogenicity. Karger; Basel, 1999. xii+221 pp. DM 237.00 (hc).
6. Chapman, S.K. and Reid, G.A. (eds.) Flavoprotein Protocols. Methods in Molecular Biology, Vol. 131. Humana Press; Totowa, 1999. xii+256 pp. $79.50 (pb).
7. Chadwick, D.J. and Cardew, G. (eds.) Bacterial Responses to pH. Wiley; Chichester, 1999. ix+265 pp. £75.00 (hc).
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9. Chadwick D.J and Cardew, G. (eds.) Gramicidin and Related Ion Channel-Forming Peptides. Wiley; Chichester, 1999. ix+273 pp. £75.00 (hc).
10. Schena, M. (ed.) DNA Microarrays. A Practical Approach. Oxford University Press; Oxford, 1999. xx+210 pp. £31.95 (pb).
11. Perry, D.J. and Pasi, K.J. (eds.) Hemostasis and Thrombosis Protocols. Humana Press; Totowa, 1999. xiii+368 pp. $89.50 (hc).
12. Salem, H. and Katz, S.A. (eds.) Toxicity Assessment Alternatives. Humana Press; Totowa, 1999. xiii+262 pp. $99.50 (hc).
13. Epplen, J. and Lubjuhn, T. (eds.) DNA Profiling and DNA Fingerprinting. Birkhäuser; Basel, 1999. x+252 pp. ChF 128.00 (sb).
14. Harris, E.A. (ed.) Low-Cost Approach to PCR. Appropriate Transfer of Biomolecular Techniques. Oxford University Press; Oxford, 1998. xxi+304 pp. £27.95 (pb).
15. Lowrie, D.B. and Whalen R.G. (eds.) DNA Vaccines. Methods and Protocols. Humana Press; Totowa, 2000. xix+529 pp. $99.50 (hc).
16. Kmiec, E.B. (ed.) Gene Targeting Protocols. Humana Press; Totowa, 2000. xv+244 pp. $89.50 (hc).
17. Winkler, J.D. (ed.) Apoptosis and Inflammation. Birkhäuser; Basel, 1999. ix+244 pp. ChF 188.00 (hc).
18. Bucke, C. (ed.) Carbohydrate Biotechnology Protocols. Methods in Biotechnology 10. Humana Press; Totowa, 1999. xii+337 pp. $79.50 (hc).
19. Darby, I.A. (ed.) In Situ Hybridization Protocols. Methods in Molecular Biology Vol. 123. Humana Press; Totowa, 1999. xiii+343 pp. $79.50 (hc).
20. Wang, J.T.L. et al. (eds.) Pattern Discovery in Biomolecular Data. Tools, Techniques, and Applications. Oxford University Press; Oxford, 1999. xix+251 pp. £45.00 (hc).