complex, and so eccentrically interpreted, that nobody has ever tried to sort it out.

The Lindegrens did provide some of the first breeding stocks of yeast, started the linkage mapping and, crucially, defined the mating types. The story of the post-Lindegren build-up of yeast formal genetics is well told in articles by Robert Mortimer and Don Hawthorne. Mortimer was responsible for two key advances. In the mid-1950s he made the first extensive collection of auxotrophic mutants, as much an essential basis for yeast genetics as it had been for *Neurospora*. During the same period he, together with his then student Fred Sherman, introduced snail stomach enzyme for the routine softening of yeast asci for much easier dissection of tetrads. Subsequently, Mortimer was involved in two extremely productive partnerships: with Hawthorne, in the 1960s, he greatly extended the yeast genetic maps, and later (in the years around 1970) he joined Seymour Fogel (who contributes his own account) in a massive tetrad analysis of intragenic recombination. The Fogel/Mortimer data still provide the most substantial demonstration of the formal rules, if not the molecular mechanism, of meiotic gene conversion.

The later sections of the book, which take us up to about 1980, deal with the origins of work on mating and mating type, the cell cycle, gene structure and expression, and molecular biology. The 'other yeast', *Schizosaccharomyces pombe*, gets only a minor role, corresponding, I suppose, to its lower profile in the world literature. Urs Leupold contributes a perhaps unduly short article describing how he started *S. pombe* genetics at the suggestion of Winge. Murdoch Mitchison tells us how *S. pombe* came to be adopted as a model organism for the study of the cell cycle.

The final 40 pages deal with departments and institutions. The field was seeded from a rather small number of places: the Carlsberg Laboratory in Copenhagen (Winge), Carbondale in Southern Illinois (Lindegren) and Paris (Ephrussi). The American effort, after Lindegren, came predominantly from Brooklyn College (Hurst and Fogel), Berkeley (Mortimer, later joined by Fogel) and Seattle (Roman and Hawthorne). Rochelle Esposito's lively, even joyful, account of the unique working environments in Brooklyn and Seattle is one of the best things in the book. Here, as well as in several of the other articles, we get a sense of Herschel Roman's beneficial and sustained influence. Another kind of institution, of great importance in the long run, was the Yeast Course, organized for many years at Cold Spring Harbor by Gerry Fink and Fred Sherman. From Fink's account, the course appears to have been part slave camp and part general riot. He credits Sherman with most of the riotous aspect, but we don't get the reciprocal view – Sherman's own contribution is all about cytochrome c. At all events, the course, over the years, had the effect of attracting a good number of extremely accomplished molecular biologists to yeast.

The last essay, 'The International Yeast Community' by R. C. 'Jack' von Borstel (the second of his two contributions), deals with the yeast conferences that have been held, in various countries, every few years since 1961. They seem to have been models of what specialist meetings should be – relaxed, informal and not too large. One hopes that the very evident community spirit has survived the great increase in the numbers of yeast geneticists.

J. R. S. FINCHAM
Division of Biological Sciences,
University of Edinburgh

The Cell Cycle. Cold Spring Harbor Symposia on Quantitative Biology. Volume LVI. Cold Spring Harbor Laboratory Press. 1992. 780 pages. Cloth $210. ISBN 0 87969 061 5. Paperback $95. ISBN 0 87969 062 3.

Following the discovery of cyclins and the universality of the control of entry into mitosis, there was a great flurry of activity into the molecular basis of cell cycle progression in the period 1988–91. Fortunately, the production of this book was timed so as to include the great bulk of this work and for researchers and students of the cell cycle, the vast majority of the important experiments of this time are included here. The year of the 56th Symposium on Quantitative Biology, 1991, probably marked the beginning of the peak of activity of investigations into the occurrence of cyclins and their interaction with the ubiquitous Histone H1 Kinase.

The advantage of a meeting of this nature is the opportunity it affords to meet just about all the people engaged in cell cycle research and a major benefit comes from the informal exchanges of ideas and theories that take place away from the lecture platform. This of course cannot be brought out in any report on the proceedings and consequently one of the most important assets is lost. A flavour of this could be maintained by including a report of the discussions held immediately after the lectures. However, this does not detract from the value of this publication in which the most significant findings of an exciting field of research are described.

The meeting is summed up in the final section of the book where Tim Hunt gives an account of the coming of age of cell cycle research and a synopsis of the current knowledge concerning cdc2 activation and its putative role in the entry into mitosis; the involvement of G-protein in checkpoint controls; the role of START and how long it lasts; and the way that oncogenes fit into the current models of the cell cycle. At the moment most of this involves asking further questions but questions that are likely to be answered in the near future.

The first section of the book deals, logically, with START. Cross describes the *CLN* family of redundant

genes, positive factors in the regulation of START, that are regulated in abundance during the cell cycle and the loss of all three prevent transition of the START event. After discussion of the regulation of the G_1 form of Cdc28 protein kinase in budding yeast and the role that cyclins play in cells undergoing START, Kim Nasmyth poses a provocative answer to the question of why cell cycle regulation is very different in different organisms; avoid G_1 if haploid. A number of papers deal with the negative role of cyclins in entry into the conjugation pathway in *S. cerevisiae*. In this case the gene *FAR1* has been suggested as regulating CLN2 negatively during mating and FUS3 plays the same role in post-transcriptional regulation of CLN3 (Elion *et al.*). Steve Reed and his colleagues have extended many of these findings to animal cells in which G_1 control, though more complicated, is also mediated via Cdc28 and its association with cyclins. Further evidence of this is provided by Matsushime *et al.* who demonstrate that growth factors in blood cell development stimulate production of cyclin-like proteins (CLYs) during G_1. How all of this is brought about is suggested by Sutton *et al.* who propose the involvement of a *S. cerevisiae* phosphatase, *SIT4*, in G_1 regulation which regulates the activity of the Cdc28/cyclin complex. An exciting homology between cyclins and the *ras* oncogene is described by O'Farrel and Leopold, suggesting that cyclins are involved as switching proteins by changes in conformation, the most likely mode of action being through phosphorylation. Another piece of evidence linking cyclins with oncogenes comes from the work of Arnold *et al.* who have shown that a putative oncogene *PRAD1*, which is strongly implicated in the pathogenesis of a number of tumours, is a cyclin, but one whose cell cycle function is as yet unclear.

A number of papers are collected under the heading 'Transcription and Mitogenesis' which largely deal with cell transformations and the formation of tumours. The common theme is that G_1 is the period in the cell cycle when those molecules are thought to be regulators of cell division (Retinoblastoma susceptibility gene, *MYB*, *MYC*, *MAX* etc.) break off from their respective associations thus permitting entry into S-phase. The RB gene in particular is shown to complex with a number of proteins including CDC2 and this has led Lee *et al.* to propose a model in which binding of RB to cell cycle regulators, including $P34^{CDC2}$, would halt cell cycle progress. At an appropriate time, cyclins would enter and activate the CDC2 complex which in turn would phosphorylate the RB protein (to the inactive state) and cause release of growth-promoting factors. Another important tumour suppressor protein that has received attention is p53 which limits cell proliferation at least in part, by binding to cyclin-dependent kinases (Zambetti *et al.*; Prives *et al.*). The regulation of the *ras* protein by GTPase activating proteins is discussed by McCormick *et al.* and the role played by tyrosine phosphatases, an essential feature of many signal transduction events, is clearly outlined by Tonks and co-workers.

A sign of the times is the relatively short section of the book that is devoted to DNA synthesis. This is prefaced by a philosophical discussion by Kornberg on the initiation of chromosome replication in *E. coli* and his thoughts on the processes that are involved in replication. This is a short but highly readable treatise, devoid of data but rich in clear and clever thinking. The role of initiation factor, acting only once during the cell cycle, is ascribed by Hennessy and Botstein to one of four genes that are involved in the initiation of DNA synthesis in *S. cerevisiae*, namely *CDC46*. This gene is synthesized periodically then transported into the nucleus at mitosis where it remains until cells are committed to another round of DNA replication. Transcription factors that act through specific sequences to coordinate the transcription of histone genes with S-phase in the mammalian cell cycle are described by Segil *et al.* Ferguson *et al.* have looked at the early and late replication domains of *S. cerevisiae* chromosomes and suggest that what distinguishes the two are regions that have the capacity to be activated at different times during S-phase according to particular cis-acting sequences. The use of SV 40 and human papillomavirus as model systems to study the initiation of DNA synthesis are the subjects of several papers which state that phosphorylation of protein initiators provides the stimulus for DNA replication, a state brought about by the action of CDC2-like kinases. Trun and his colleagues have shown that *E. coli* mutants with larger amounts of DNA than wild-type cells are also larger in size resulting in a more or less constant DNA concentration per cell.

Checkpoints have become very important in cell cycle research and a number of papers deal with this subject. Seino *et al.* show that the protein RCCI (regulator of chromosome condensation) is responsible for coupling the activation of $p34^{cdc2}$ kinase with DNA synthesis in mammalian cells. Matsumoto and Beach, in discussing the mutations *pim* (premature entry into mitosis) and *spi* (suppressor of *pim*) point out the importance of genes such as these that maintain cell cycle dependency relationships, particularly in the growth of tumour cells. Murray has reviewed the information on those events that determine order and sequence during the cell cycle and discusses how cells monitor completeness of DNA synthesis, possibly by detecting single-stranded DNA or replication forks, and spindle assembly, by detecting chromosomes that are not attached to spindles. Enoch *et al.* discuss the roles of *cdc2* and *cdc25* genes in mitotic checkpoint control and Schimke and his colleagues illustrate the differences in coupling cell cycle progression in different cell types.

The remainder of the book deals with mitotic control and mitosis itself in two large sections. Most

of the papers in the first section deal with the activation of $p34^{cdc2}$ kinase and its cell cycle coupling with cyclin B. Other genes involved in this interaction are *cdc25*, *wee1* and *stf1*. Of interest is the paper by Pines and Hunter who examined cyclin A and cyclin B in HeLa cells. Although both have been shown to induce mitosis in frog oocytes, they are likely to have different cellular functions because, although they are obviously related, they are only 43% identical in the most highly conserved regions. Cyclin A can associate with two different cdc2-related protein kinases, $p34^{cdc2}$ and p33, and is active throughout S and G_2 phases; cyclin B only associates with $p34^{cdc2}$ and is tightly negatively regulated until the start of M-phase. The role of Cyclin A in *Drosophila* is discussed by Lehner *et al.* and although it is possible that the role may be a redundant one, curiously there is a lack of closely related cyclin genes. The localization of the $p34^{cdc2}$/$p63^{cdc13}$ complex is discussed by Alfa *et al.* and they show that there are two populations in cultures of *S. pombe*, one associated with the mitotic spindle pole and the other residing in the nucleolar matrix. This is an important observation since it suggests a role for the p34 kinase in fission yeast which does not have histone H1. Several papers then deal with the complicated question of the roles of cyclin in maturation of frog oocytes, in particular the role of Cyclin A. Maller *et al.* conclude that this cyclin alone can complex with $p34^{cdc2}$ and allow cells to enter mitosis and then, on being degraded, permit cells to exit from mitosis. The section on the control of mitosis ends with papers on the roles of *wee* and *cdc25* genes which are involved respectively in inactivating and activation of $p34^{cdc2}$. Hudson *et al.* describe a gene, *stf1*, that bypasses the requirement for *cdc25* in *S. pombe* and is postulated as being a new regulatory element of the mitotic initiation pathway acting on *cdc2* by a pathway independent of *cdc25* and *wee1*. Fantes *et al.* give an account of those genes that interact to control the entry into mitosis, paying particular attention to the response to the nutritional state of the cell.

Mitosis is the final section of the book and in this section papers deal with the organization of the mitotic machinery and progression through the process of mitosis. The section starts with a useful overview by McIntosh of the structural changes that accompany preparation for division. Kinoshita *et al.* describe the role of protein dephosphorylation in sister chromatid separation in fission yeast and have isolated five genes involved in serine/threonine phosphorylation. Goldman *et al.* discuss intermediate filaments whose subunits are substrates for a variety of kinases and which may have a role to play in signal transduction. A detailed description of the work of Kellog *et al.* into the centrosome is highly enlightening, particularly as this is an obscure organelle; they have identified MAP proteins (microtubule associated proteins) that associate with the centrosome as a multiprotein complex and whose locations vary dramatically during the cell cycle possibly as a result of their association with cyclins. Sikorski *et al.* describe their isolation of a new protein family, TRP proteins, that are characterized by a repeating amino acid motif and which play a role in mitotic segregation. Further papers in this section explore the roles of the centromere and the spindle pole body in dividing nuclei. Glover *et al.* suggest distinct roles for Cyclins A and B during development of the *Drosophila* embryo, Cyclin A being largely cytoplasmic in its location and increasing in amount at a time corresponding to cellularization; Cyclin B on the other hand is associated with the centrosome and its microtubules, suggesting that it has a role in targeting $p34^{cdc2}$ kinase to the astral microtubules. Meiosis is the subject of only one paper in this volume and the subject is dealt with at length and very clearly by Kleckener *et al.* An elegant study of chromosome movement is given by Hyman and Mitchison who show that there are two different proteins that can move in opposite directions and whose activities are regulated by phosphorylation.

Since the 1991 Symposium and the publishing of this book, there has been continued progress in the unravelling of the elements of mitotic control. Much more has been learned about the structure of the different cyclins and how their destruction is brought about and indeed, a variety of new cyclins have been discovered. However, this book is invaluable as a statement of more or less current knowledge of the control of cell division and related events and, although it will fairly rapidly represent where the field has been, it should still prove a useful addition to the bookshelf of the serious cell cycle researcher.

JIM CREANOR
Institute of Cell, Animal and Population Biology, University of Edinburgh

Regional Physical Mapping: Genome Analysis, vol. 5. Edited by K. E. DAVIES and S. M. TILGHMAN. Cold Spring Harbor Laboratory Press. 1993. 140 pages. Cloth. $49.00. ISBN 0 87969 413 0.

The mention of physical mapping usually sends some of my colleagues into a state of apoplexy – 'boring, only a means to an end, not biological' I hear them say. If they could be persuaded to peruse this volume I hope that it might cause them to modulate their views. Regional physical mapping is volume 5 of the Genome Analysis series edited by Kay Davies and Shirley Tilghman. Other volumes in this series have covered physical mapping strategies, gene expression and genotypes and phenotypes. This volume concentrates on the detailed physical restriction maps of four regions of the human genome and, on a rather different level, the long-range sequence analysis of 100 kb of DNA from the T cell receptor loci. Each of