BOOK REVIEWS

Decaying Dark Matter

Modern Cosmology and the Dark Matter Problem. D. W. SCIAMA. Cambridge University Press, New York, 1994. xviii, 216 pp., illus. Paper, $29.95 or £17.95. Cambridge Lecture Notes in Physics, 3.

The Renaissance of General Relativity and Cosmology. A Survey to Celebrate the 65th Birthday of Dennis Sciama. GEORGE ELLIS, ANTONIO LANZA, and JOHN MILLER, Eds. Cambridge University Press, New York, 1994. x, 331 pp., illus. $49.95 or £30. From a meeting, Trieste, Italy, April 1992.

What is the universe made of? We know about some of it—the electrons and baryonic quarks that make up ordinary matter—but most of the matter of the universe is detected only by its gravity (the force that holds galaxies together) and could in principle be something else. Indeed, if the big bang picture of the early universe is correct, most of the matter is probably in some "nonbaryonic" form; otherwise the predicted abundances of the light elements would not come out right.

The big bang theory also suggests an idea of what form the nonbaryonic matter might take. The density in the hot cauldron of the early big bang was dominated by radiation, the photon component of which, cooled by the expansion of the universe to the microwave background we see today at 2.78 degrees Kelvin, is now a tiny fraction of even the baryonic density. The relic primordial radiation field left behind, in addition to the microwave background radiation, an invisible component not of radiation but of a form of nonbaryonic matter—a vast sea of elusive neutrinos, filling all of space.

Every nook and cranny of the universe, including the space filled by ordinary matter, is filled with primordial neutrinos; on average a cubic centimeter of space contains hundreds of them, a billion times more than the number of atoms contained. If it turns out that these neutrinos have a mass, even if it is very tiny, there are so many of them that they could dominate the mass density—and it would be fair to say that the universe is made mainly of neutrinos.

How can one test this hypothesis? The primordial neutrinos, though abundant inside all laboratories, interact so weakly and with so little energy that they cannot be detected directly. The distribution of cosmic dark matter offers a few clues, but these are inconclusive, as the gravity from neutrinos acts like the gravity from anything else.

On the other hand, if the neutrinos were to decay into something else, their effects might be seen much more easily. Dennis Sciama has for the past five years pursued a bold idea: not only is the universe made mostly of neutrinos, these neutrinos are slowly decaying into radiation. He has pursued this "decaying dark matter" into a tiny corner of parameter space, publishing precise values for the neutrino mass, the Hubble constant, and even the neutrino lifetime. Images showing the ghostly fluorescence of gas illuminated by a galaxy halo of neutrinos decorate the frontispiece and the cover of the two books under review here, one of them a monograph by Sciama on the DDM hypothesis and the other a festschrift in honor of his 65th birthday.

The hypothesis is particularly fascinating both for its boldness and for the connections it makes. To dominate the universe, the mass of neutrinos must be a few tens of electron volts, so that their decay creates ionizing ultraviolet radiation. If they decay fast enough, they can dominate the ionization of large regions of interstellar space. In Sciama's scheme, the ultraviolet light of neutrinos plays an important role in the astrophysics of many systems, examples including the ionization of pregalactic gas and the ionization of interstellar gas in our galaxy. Various constraints on the ionization of hydrogen and nitrogen in interstellar space then restrict the range of mass to a narrow range—$m_\nu = 29.4 \pm 0.4$ electron volts—and the lifetime to $\tau_\nu = (2 \pm 1) \times 10^{23}$ seconds, almost a million times the present age of the universe. Since the average number per volume is known from big bang theory, the mass also fixes the mean density. With the additional leap of faith that the universe is exactly flat (and why not? it is so close anyway once the mass is fixed at this value), the mean density is then precisely related to the rate of expansion, so that the Hubble constant must have the value $H_0 = 57 \pm 0.5$ km sec^{-1} Mpc^{-1}. This is certainly the most precise value for H_0 ever achieved by a serious scientific argument, all the more surprising since it involves no actual measurement of the Hubble constant or indeed even of a distance, a velocity, or an age.

In spite of its attention to the unusual DDM model, Sciama's monograph is a worthy modern successor to his classic *Modern Cosmology*, organized around "what has become the most important single problem in astronomy and cosmology"—the dark matter problem. Sciama presents lucid explanations of cosmology and the dark matter problem in general, worth reading for their clear distillations of complicated observational facts to the elements with the most essential impact on theory. It contains in particular an excellent survey of the subject of cosmic and galactic ionization, at a level of detail not found in cosmology texts.

The festschrift celebrates not only a long and productive career but a broad perspective and a generous spirit. Sciama's collaborators, students, and "grandstudents" provide interesting reviews and original essays—20 in all—on subjects ranging from galactic astronomy to quasars, from quantum measurement theory to superconducting strings. Sciama's own contribution contains a concise summary of the DDM theory. We are reminded of another remarkably compelling theory—the steady state model—that also merited considerable attention because of its eminent falsifiability. Both of these volumes are snapshots of an interesting moment in the development of theoretical cosmology; it seems unlikely that it will be possible much longer to put forward such a radically unique view of such a central subject and still be consistent with the framework of what is known.

Craig J. Hogan
Department of Astronomy, University of Washington, Seattle, WA 98195, USA

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Advanced PCR

The Polymerase Chain Reaction. KARY B. MULLIS, FRANÇOIS FERRÉ, and RICHARD A. GIBBS, Eds. Birkhäuser, Cambridge, MA, 1994. xxii, 458 pp., illus. $79, SFr148, or DM168; paper, $45, SFr84, or DM98.

In his preface to this volume Kary Mullis confesses that books are no fun. "You can never finish your part on schedule and you feel guilty for a long time until you finally do; and then you feel like you could have done a lot better job if you hadn't been rushed." It appears that few of these contributing authors have been rushed, as they have turned out an admirable collection of chapters.

Vignettes: De Revolutionibus

I know of two kinds of revolution in molecular biology. There is the kind where a band of angry, young, well-armed molecular biologists, having formented [*sic*] their plans in the chill, rarefied air of the UCLA winter symposia, meeting clandestinely on the slopes during the morning talks, and later in the darker corners of the bar while the poster sessions wind down, converge in the Spring on Bethesda, assault rifles and ugly unpatriotic slides on hand, to settle once and for all the issue of NIH post-doc stipends.

Then there is the other kind, referred to as a paradigm shift, or a retreat to the drawing board, when disappointing data can no longer be hidden or explained by old notions. New concepts become fashionable and new paragraphs have to be written for introductions to papers and grants. Usually there are a number of powerful elders in important places that have to retire or die before things get rolling. Like for instance, Maddox, who is aging at the same rate as everybody else, or Dan, who may take a little longer. It could happen here.

—*Kary B. Mullis*, in *The Polymerase Chain Reaction*

When the polymerase chain reaction (PCR) made its way into the scientific consciousness in 1986, the simplicity of the procedure prompted some to wonder what use it would be and many to wonder why it had not been proposed before. It is useful. The ability to select a segment of nucleic acid within a complex mixture and to multiply that segment to such an extent that the fraction of untargeted molecules is reduced to insignificance has allowed the study of nucleic acids previously considered too rare to afford examination and often obviates cloning of a sequence of interest in preparation for further characterization. In the ensuing years, the uses of the PCR have come a long way from the simple reproduction of a nucleic acid segment, with researchers adapting this method for diverse applications, including random mutagenesis, genetic recombination, reconstruction of degraded DNA, and in vitro molecular evolution. A cursory search of the literature since 1990 turns up more than 20,000 PCR citations, indicating the degree to which the method has been incorporated into both clinical and basic research. The impossibility of maintaining currency with such an overwhelming amount of literature is a frustration for many, and to alleviate the burden is the stated motivation for the assembly of this book. The question whether the PCR had been proposed earlier is discussed in the final chapter.

Several monographs have been produced to serve as at-the-bench manuals for the PCR. This volume is more a second-generation reference on the theory and application of the technique. An understanding of the mechanism of amplification by PCR is assumed, and the familiar schematic depicting the process is not presented. The editors have tapped many of the leaders in PCR innovation to explore their particular twists on the technique and to discuss its impact on their fields. The resulting chapters provide thorough examinations of basic and advanced PCR techniques, with a satisfying balance between theoretical analyses and observed results, and often include the type of anecdotal advice not found in journal articles.

In the foreword, James Watson traces the lineage of this branch of molecular biology, from his realization in 1953, with Francis Crick, that the base-paired structure of the double helix suggested a model for replication that would double the number of identical DNA molecules with each round to the current in vitro extension of this concept, the polymerase chain reaction, made possible by the advent in the interim of synthetic oligonucleotides and purified DNA polymerase. Mullis's preface has the stream-of-consciousness style of a newsy letter, and he introduces many of the authors with colorful, good-natured similes and personal anecdotes that amuse and add depth to the following chapters.

The body of the book is divided into three parts: Methodology, Applications, and PCR and the World of Business, comprising 35 chapters. Thirty-three of the chapters fall into the first two parts, between which there is considerable overlap, as many of the methods are presented in the context of specific applications. The methodology part is further divided into sections, each comprising four or five chapters, covering basic methodology, quantitation, non-isotopic detection, instrumentation, and sequencing. The first chapter in each of these sections provides something of an overview, though each individual chapter also provides background and context for the particular technique discussed. The chapters in the applications sections are less interconnected. The section on general applications alone covers in vitro evolution, forensic applications, and PCR from ancient DNAs and offers an intriguing chapter on the use of DNA segments as submicroscopic labels for commercial products. Other sections cover genetic analysis, assessment of therapy effectiveness, and diagnostics with equally diverse collections of chapters.

There is a remarkable continuity of high quality throughout both parts. Each chapter provides background on the particular scientific problems addressed and the rationale for the approach presented. Though there may appear to be some overlap among the contributions (for example, single-strand conformation polymorphism analysis is discussed in three chapters), the effect is more one of breadth than of redundancy. It is worthy of note that the authors have, at least in the chapter titles, avoided over-reliance on burdensome PCR-variant acronyms, the list of which now reads like a directory of government agencies. The lists of references provided at the end of each chapter include the full titles, and the index seems to be thorough and well cross-referenced.

The discussion of PCR and the business world is noteworthy because it presents topics not usually addressed in a technical work. That more than half of this section is devoted to the story of a patent trial provides editorial comment, perhaps unintended, on the business of biotechnology. Though the business and legal discussions in these chapters are particular to the story of PCR, there are general lessons to be learned about the ownership and marketing of ideas.

How does an inventor or company secure a financial return on the often substantial investment in the invention, development, and patent processes? In "PCR in the marketplace," Ellen Daniell tells the story of how Cetus Corporation, an aspiring pharmaceutical firm, approached the problem of marketing a technological innovation in the face of stiff competition and limited resources for in-house development. She describes the combination of strategic partnering and licensing used to support the commercialization of PCR, culminating in the acquisition of the technology by Hoffmann–La Roche in 1991.

In the final chapter, Mullis offers his account of the patent trial in which DuPont attempted, unsuccessfully, to prove that prior art made the Cetus patent covering PCR invalid. As he notes, on the verdict

hung "a serious fraction of a billion dollars." Mullis tells a good story as he recounts his invention of PCR in 1983 and the subsequent patent travails. He describes the science that was at the heart of the dispute, reprints the passages of text cited by the DuPont group as prior art, and explains the arguments made in response by the Cetus team. His breezy prose is enjoyable to read but belies the intensity of his antipathy toward the opposition, as personified by Arthur Kornberg. Clearly, bygones are not yet bygones. Though it is unlikely that this account will sway those who have strong opinions, one way or the other, on the justice of the verdict, the chapter does illustrate the subtlety of patent claims drafting and provides a window on the courtroom drama of a high-stakes dispute.

Mary Ann D. Brow
Third Wave Technologies, Inc., Madison, WI 53711–5368, USA

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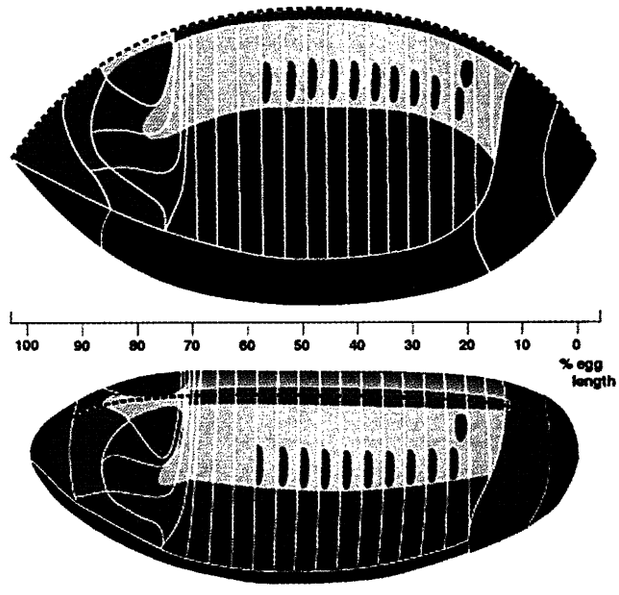
Fly Assembly

The Development of *Drosophila melanogaster*. MICHAEL BATE and ALFONSO MARTINEZ ARIAS, Eds. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1993. In two volumes. xxii, 1558 pp., illus., + atlas + poster. $350.

Classical embryological and molecular genetics are brought together in this collective summary of fruit fly development. The work is an ambitious venture dogged by a persistent dilemma—exclude reams of detail to make a readable book, or produce the comprehensive descriptions needed by active workers in the field. Almost inevitably the burgeoning field demanded an expansive text, and the editors opted for the latter course. The book is clearly a work of reference for people in the field and not night-time reading for those only casually interested in the subject.

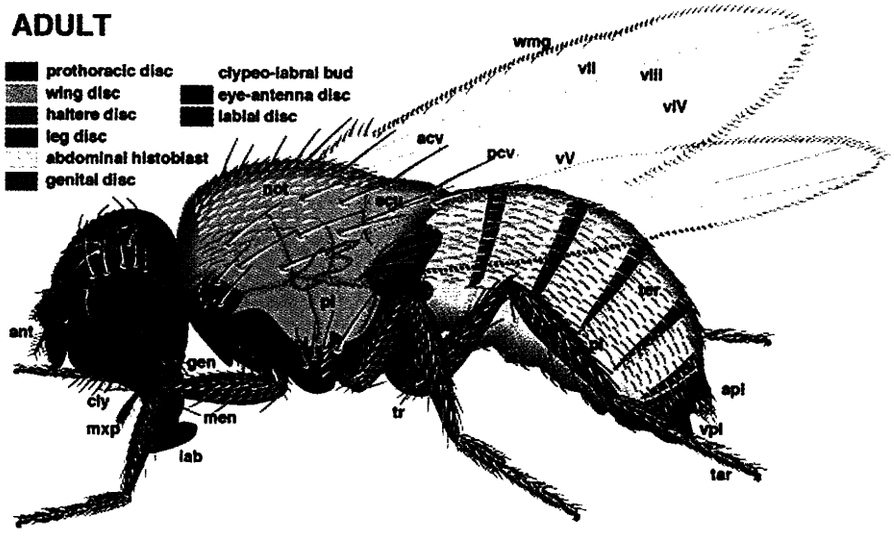
The 24 chapters give an almost comprehensive view of development in the fruit fly, from gametogenesis to the formation of the adult nervous system. The individual chapters are largely autonomous and range greatly in quality. Some are scholarly, objective, and comprehensive accounts of their subjects to date, and others are "cut and pastes" from previous reviews. Although one or two chapters have a quality of "own trumpet-blowing," subjective opinion is mostly held in check.

There are impressive chapters that may eventually garner for this book the reputation and respect afforded to Demerec's long-out-of-print *The Biology of Drosophila*, but to me the chapter by Meinertzhagen and Hanson on the development of the optic lobes stands out. It is an erudite and comprehensive description containing information not to be found elsewhere. The topology of the cellular arrangements in the optic lobes is grueling and the chapter is not for the faint-hearted, but the attention to detail inspires the confidence needed in such a work of reference.



Composite fate maps of the *Drosophila melanogaster* blastoderm. *Top*, "The fate map is projected onto a planimetric reconstruction of the blastoderm. In this type of reconstruction, one half of the curved blastoderm is flattened in order to depict true distances between blastodermal positions. The upper margin of the drawing (*dashed line*) represents the dorsal midline and the lower margin represents the ventral midline." *Bottom*, "The fate map is projected onto a blastoderm shown in the standard dorsal-lateral view used for all drawings in this Atlas. (*Thick dashed line*) Dorsal midline. The anlagen of different tissues are illustrated in different colors used throughout the figures in the Atlas." [From the Atlas accompanying *The Development of Drosophila melanogaster*]

Some subjects are dealt with in two (or more) chapters when one would have been better. This occurs in the cases of the imaginal disks and the adult epidermis, but the striking example is the two chapters devoted to eye development, one a description of the cell biology of the system and the other a molecular perspective of genes and proteins. The molecular and cellular data can be smoothly interwoven in descriptions of eye development, and I wonder why the editors did not coerce somebody to do this. On the other hand, there is no chapter devoted to how the diversity of segment identity is achieved, though there exists a huge body of detailed work that explains how a particular segment is determined as thoracic or abdominal or head, whether it should develop with wings or legs or mouth parts. The subject is given cursory treatment in the chapter on larval epidermis, but even here it appears as an afterthought.



"The epidermis of an adult fly (female)." [From the Atlas accompanying *The Development of Drosophila melanogaster*]