Book Reviews

Molecular Pathologies

DNA Repair and Mutagenesis. ERROL C. FRIEDBERG, GRAHAM C. WALKER, and WOLFRAM SIEDE. ASM Press, Washington, DC, 1995. xviii, 698 pp., illus., + plates. $79. New edition of *DNA Repair*.

Living organisms have multiple ways by which they respond to, and mitigate the effects of, damage to their DNA. This revision of a 1985 book by Errol Friedberg details these mechanisms in a manner accessible to students who wish to understand how the system works. The volume also includes an astounding amount of detail, both textual and bibliographic, for the professional who needs to ascertain the current status of an unfamiliar subspecialty. We are indebted to Friedberg and the coauthors of this edition for their careful assembling and evaluation of a vast amount of information.

The text is written from the viewpoint of comparative biochemistry and celebrates a central belief that what is true of *Escherichia coli* is true of elephants. In fact, and as the authors illustrate, elephants are also more complicated than *E. coli*. An already complex mechanism of excision repair in bacteria is made even more so in eukaryotes by the attachment of essential vital functions to some of the repair proteins. But the basic plans remain homologous, and often so do the proteins involved. Human mismatch repair genes were identified because of their homology to yeast and to bacteria.

A description of the known details of the metabolic process made up the 1985 edition of this volume. The discovery that the genic material did not stand permanently aloof from cellular metabolism was a major surprise of the 1950s and '60s. In 1946, when D. E. Lea published his book *Actions of Radiations on Living Cells*, the most productive paradigm was that the genetic material of cells was a target which when hit by a radiation "bullet" immediately, and irreversibly, suffered damage leading to death (or mutation). Insofar as biologists thought that anything as complicated as the properties of a gene could be ascribed to a single chemical structure, that structure was thought to be protein. In the next decade it gradually became clear that genes could be chemically defined as well as modified by mutagens such as mustard gas. The genic material was identified as deoxyribonucleic acid but at first was considered to be exceptionally stable in contrast to the proteins, which isotope studies showed "turned over" at an extraordinary rate. The observation that it was possible to modify physiologically the genetic effects of treatment of cells, as well as to isolate mutants that gave vastly different responses to the absorption of equal amounts of energy, implied that metabolic events intervened between the absorption of radiation and its end effects. Rather than being stable, the DNA was an active participant in the events of cellular biochemistry! By 1985, the major metabolic pathways of DNA repair had been discovered, first in the bacteria and then in mammalian cells.

This new edition details the major discoveries made since 1985 that repair genes in eukaryotes are involved in transcription and that damage in transcribed genes is repaired more efficiently. Also new is the discovery that organisms can sense when their DNA is damaged and delay replication until repair processes have had time to act. The existence of these "checkpoints" as part of control of the cell cycle is a still-developing aspect of the study of DNA repair, hardly mentioned in the text of a decade ago. Throughout the present work we see the insights gained through our ability to look for sequence homologies by comparison of the DNA of different species. Studies on yeast are remarkable predictors of the human system! The current revision has been expanded to include a detailed discussion of the phenomenon of mutation, which has always been thought of as the reverse side of the phenomenon of repair. As with all aspects of molecular biology, the study of mutation has been vastly altered by the ability of investigators to determine the exact sequence of the changes produced, and large sections of this new work are devoted to an attempt to integrate the new information into an understandable framework.

The authors point out that the new findings challenge one of the most cherished ideas in cancer research: the assumption of a necessary connection between DNA damage, DNA repair, mutation, and carcinogenesis. For years the incidence of skin cancer in excision-repair–deficient xeroderma patients has been used as an example of the importance of excision in preventing the mutation that occurs during replication by cells with damaged DNA, and this in turn has been used to connect mutagenesis and carcinogenesis. Consider the surprise of the repair community in discovering a syndrome in which individuals may have low excision repair activities owing to a defect in the same gene producing xeroderma but without the susceptibility to tumors. We may have been misled. Perhaps it is not the excision repair activities of the xeroderma gene that are important but the transcription regulation—or some other factor. This uncertainty is exacerbated by other recent findings. One of the major discoveries of the past few years has been the identification of a colon-cancer susceptibility gene as controlling one of the mismatch repair genes. But studies too recent to be included in this book (R. Parsons *et al.*, *Science* **268**, 738 [1995]) point up the mysterious finding that individuals with almost no mismatch repair activity, whose cells have high mutation rates, do not have the tremendously high cancer incidence that these findings would predict, a fact noted in a recent letter to *Science* by Bryn Bridges (*Science* **269**, 909 [1995]).

Understanding of repair mechanisms comes as a result of studies with different organisms. This truism presents a problem for these authors (or any authors). Is the discussion to be organized by organism or by type of phenomenon? Friedberg *et al.* separate the discussion of prokaryotes and eukaryotes, but properly decide to introduce the best model for double strand break repair when the phenomena that require it are first encountered in a discussion of damage responses in prokaryotes, even though this particular model was developed in yeast. Repair diseases are interesting subjects by themselves, but the analysis of these diseases reflects on the normal condition. The authors seem not quite sure how to deal with this problem. They compromise in a final chapter discussing diseases with defective repair. Much of the material of this chapter is alluded to earlier: for example, data on xeroderma are necessarily included in the discussion of mammalian excision repair genes and proteins in chapter 8. Data on ataxia are included in the section on checkpoints and cell cycle arrest. Most likely this material will be better integrated in the next edition as the molecular biology of the pathology is clarified.

At the end of the book, the authors ignore their own prefatory statement that "in very recent times, progress in the DNA repair and mutagenesis fields has been particularly rapid" and in discussing ataxia telangiectasia imprudently suggest that "progress toward the cloning of the AT gene(s) has been slow and holds no promise for immediate reward at the time of this writing." It may be that this statement alone guaranteed the successful cloning of the AT gene which occurred just a few months after the publication of the book (K. Savitsky *et al.*, *Science* **268**, 1749 [1995]). Studies on DNA repair and mutation are indeed proceeding rapidly. What is impressive is how well Friedberg, Walker, and Siede have done in presenting an overall point of view that will remain useful even as new details are added.

Bernard S. Strauss
Department of Molecular Genetics and Cell Biology,
University of Chicago,
Chicago, IL 60637, USA

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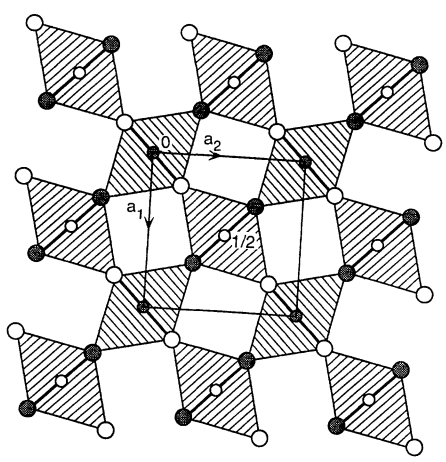
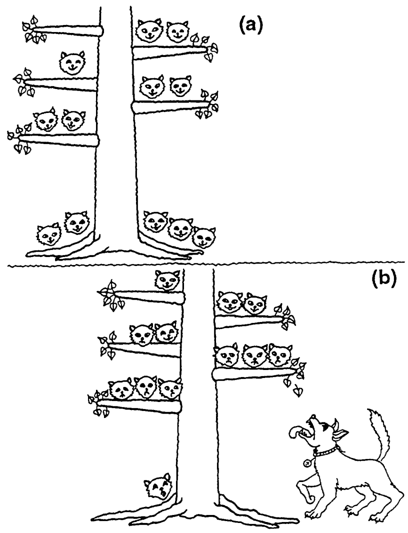
Geocrystallography

Physics and Chemistry of Earth Materials. ALEXANDRA NAVROTSKY. Cambridge University Press, New York, 1994. xiv, 417 pp., illus. \$79.95 or £55; paper, \$34.95 or £22.95. Cambridge Topics in Mineral Physics and Chemistry, 6.

As new technological materials become increasingly complex in structure and bonding, they are beginning to resemble the materials that make up our planet. Perovskite-type crystals are a case in point, defining the structures of both the high-temperature superconductors and the predominant mineral of the Earth. Such novel materials as fullerenes and chemical-vapor-deposition diamond have even been found in rocks



"The structure of rutile, TiO_2. The tetragonal structure consists of edge-sharing chains of TiO_6 octahedra running parallel to the *c*-axis. Octahedra in adjacent chains are joined at their corners. This polyhedral representation is a projection down the *c*-axis, parallel to the chains. The shaded symbols are atoms at a *z*-coordinate of 0, and the open circles are at $z = 1/2$. The unit cell is outlined." [From *Physics and Chemistry of Earth Materials*]



"Schematic of a population inversion. (a) Without an external driving force, the particles (cats) are distributed in the lower-lying energy levels (branches) according to the Boltzmann distributions. (b) With external pumping of energy (dog), the particles populate higher energy states (higher branches) more than lower ones. Lasing action may be likened to an upper branch breaking, returning its occupants to their ground state in a coherent pulse." [*From Physics and Chemistry of Earth Materials*]

and meteorites millions of years old. Thus materials scientists have more in common with geologists than ever before.

Physics and Chemistry of Earth Materials is a unique monograph at the interface between the disciplines. Written by one of the leaders in combining mineralogical and materials research, it illustrates how basic approaches of materials science, solid-state chemistry, and condensed-matter physics can be used to understand what makes up our planet, and maybe even how it works on the inside. One might characterize the book as "elementary" in that it contains few equations, derivations, or details of the underlying physics. Yet it touches on many of the key concepts, as well as the experimental and theoretical methods used in current materials research.

One of the high points of the book is the extensive chapter on crystal chemistry, which contains a superb discussion of how complex crystal structures are related. The rich diversity of both earthly and superconducting perovskite-like crystals is described, as are defect, modulated, and biopyribole-type structures. Insights attained through years of research are incorporated into these pages, and it is vintage Navrotsky to use spinel as a recurring theme throughout the book: this deceptively simple (cubic) crystal structure accommodates a great variety of complexity, including crystallographic disorder, nonstoichiometry, and variable valences.

The overview of chemical bonding is pleasing in the comparisons made between the "chemist's" (molecular, real space) and "physicist's" (infinite crystal, reciprocal space) traditional approaches, but the discussion of theoretical methods now available is less satisfying; though it is useful to have short definitions of the numerous acronyms plaguing theorists, the underlying approximations are not really clarified. Still, the point is well made that simple geometrical models of crystals, such as ionic radii and Pauling rules, remain useful, even in this day of sophisticated "first-principles" calculations.

I have found that the book can work well with two very different audiences: geology or materials students being introduced to modern methods and concepts of materials science, and the more experienced materials researchers, who can enjoy seeing revealed the close analogies between their work and current studies of our planet.

Raymond Jeanloz
Department of Geology and Geophysics,
University of California,
Berkeley, CA 94720–4767, USA

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Books Received

Advanced Engineering Dynamics. Jerry H. Ginsberg. 2nd ed. Cambridge University Press, New York, 1995. xvi, 462 pp., illus. \$74.95.

Advanced Methods of Pharmacokinetic and Pharmacodynamic Systems Analysis. Vol. 2. David Z. D'Argenio, Ed. Plenum, New York, 1995. x, 217 pp., illus. \$75. From a workshop, Los Angeles, May 1993.

Beyond Prejudice. The Moral Significance of Human and Nonhuman Animals. Evelyn B. Pluhar. Duke University Press, Durham, NC, 1995. xxi, 371 pp. \$49.95; paper, \$19.95.

Biochemistry and Molecular Biology of Fishes. Vol. 4, Metabolic Biochemistry. P. W. Hochachka and T. P. Mommsen, Eds. Elsevier, New York, 1995. xiv, 515 pp., illus. \$232.25 or Dfl. 395.

Chemists' Views of Imaging Centers. Ali M. Emran, Ed. Plenum, New York, 1995. xiv, 537 pp., illus. \$129.50. From a symposium, Chicago, Aug. 1993.

Chernobyl. The Forbidden Truth. Alla Yaroshinskaya. University of Nebraska Press, Lincoln, 1995. xxii, 136 pp., illus. \$25; paper, \$10. Translated from the Russian by Michèle Kahn and Julia Sallabank. Reprint, 1994 ed.

The Day Before America. William H. MacLeish. Houghton Mifflin, Boston, MA, 1995. x, 277 pp., illus. Paper, \$11.95. Reprint, 1994 ed.

Democracy, Dialogue, and Environmental Disputes. The Contested Languages of Social Regulation. Bruce A. Williams and Albert R. Matheny. Yale University Press, New Haven, CT, 1995. xii, 256 pp., illus. \$32.50.

The Ecology of the Chernobyl Catastrophe. Scientific Outlines of an International Programme of Collaborative Research. V. K. Savchenko. UNESCO, Paris, and Parthenon, New York, 1995. xx, 200 pp., illus. \$85 or £48. Man and the Biosphere, vol. 16.

The Ecology of Tropical Food Crops. M. J. T. Norman, C. J. Pearson, and P. G. E. Searle. 2nd ed. Cambridge University Press, New York, 1995. x, 430 pp., illus. \$69.95; paper, \$29.95.

Field Penetration and Magnetization of High Temperature Superconductors. Anant Narlikar, Ed. Nova, Commack, NY, 1995. xviii, 445 pp., illus. \$97. Studies in High Temperature Superconductors, vol. 14.

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