Book Reviews

Phage Studies

The Bacteriophage Lambda. A. D. HERSHEY, Ed. Cold Spring Harbor Laboratory, Cold Spring Harbor, 1971. xii, 792 pp., illus. $24. Cold Spring Harbor Monograph Series, vol. 2.

Like the first book of the series (*The Lactose Operon*, 1970), *The Bacteriophage Lambda* consists of two parts: the first contains review papers written by specialists in the field, the second represents the proceedings of a meeting held at Cold Spring Harbor a year earlier.

"Lambdology" has long remained an esoteric science. The book attempts to make it accessible to all biologists. This is a very welcome effort, since the results and concepts emanating from the study of phage lambda will undoubtedly find applications in a variety of other fields; they already inspire the thoughts of those who study genetic recombination, DNA replication, cell differentiation, morphogenesis, and the transformation of animal cells by oncogenic viruses. The review papers, in general excellent, vary considerably in style. One of them, tedious but useful, will give you all physical and chemical parameters you may wish to know on phage lambda DNA. In another you will find attractive but debatable ideas on how a temperate phage may buy the privilege of establishing its own genes within the host chromosome. A large fraction of the book is devoted to the different types of recombination which the DNA of phage lambda can undergo: "general," "site-specific," and "illegitimate." General recombination, the basis for classical genetics, occurs between any homologous regions of genetic material. Site-specific recombination, like that which allows the phage chromosome to integrate into the bacterial chromosome, occurs at fixed points on the DNA and requires no extensive base-sequence homology (perhaps no homology at all) between the recombining DNA's. Illegitimate recombination, a rare event involving an exchange between presumably any nonhomologous regions of genetic material, and leading to such aberrations as deletions, duplications, insertions, and transducing phages, must be of profound evolutionary importance. In the light of the new data presented, molecular models of these different types of recombination are discussed.

Emphasis is also put on the regulation of viral functions: regulation allowing the proper temporal sequence of gene expression during the lytic cycle and regulation concerned with the choice between the two pathways offered to the infecting phage, lysis of the cell and production of more phage or lysogenization usually involving a harmless integration of the phage genome into that of the host. For instance, a clear account is given of the evidence that the phage repressor, long known to prevent expression of the lytic genes in lysogenized bacteria, is itself regulated by several other genes.

Two years ago, most "reasonable" molecular biologists agreed that replication of a circular chromosome proceeded in a single direction, and also that the replication of genes was totally independent of their expression. Why the same molecular biologists are no longer so positive about these points you will find out by reading *The Bacteriophage Lambda.*

The review papers, completed by spring 1971, give an up-to-date description of lambda biology, and will be of invaluable help to a very large audience. The research articles, on the other hand, intended for the specialist, come a little late, since they contain results obtained by 1969 or 1970. An improvement in the future monographs of the series could be to publish the two sections in separate volumes and make the research papers available as soon as possible.

Aside from this reservation *The Bacteriophage Lambda* is an excellent book, from which, thanks to the editorial ardor and skill of A. D. Hershey, most of the jargon has been excluded.

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Phylogenetic Mechanism

Evolution by Gene Duplication. SUSUMU OHNO. Springer-Verlag, New York, 1970. xvi, 160 pp., illus. $16.50.

Blue Crossopterygian Man dominates the dust jacket. A forewarning? Ah yes—you are warned: you will be stimulated, cajoled, and, unless you have a more than passing acquaintance with at least one of the subject matters from which the author spins his argument, perhaps misled.

Ohno makes clear from the outset that this is no general treatise on evolution; his focus, as he traces the human germ plasm to the purines and pyrimidines of the primeval soup, is on man. His introduction, unnecessarily expounding an "origin myth" for the genetic apparatus, is the standard chapter on the subject. Then, after a brief discussion of chromosomes, he classifies gene mutations as forbidden or tolerable. Forbidden mutations alter active sites of essential macromolecules. Natural selection is cast as an "extremely efficient policeman" that forbids adoption of significant change. Tolerable mutations, such as those that distinguish the hemoglobin chains of related species, yield diversity and adaptation, but not novelty in evolution at the molecular level. Karyotypes are similarly conservative. The number of chromosome arms and their genic contents remain remarkably stable through the cycle of fusions and inversions common in speciation that diversifies chromosome numbers.

Ohno assails the "Lamarckian illusion" in which the process of evolution is visualized "as members of a successful species advancing shoulder-to-shoulder to a higher and higher state of being." He avoids the Darwinist concept that the favored few reproduce disproportionately to become ancestral to entire later populations, opting instead for an Adam-and-Eve ("founder effect") interpretation: close inbreeding in a tiny isolate is indispensable to speciation. Polymorphism in large populations is not the stuff of which new species are made.

True evolutionary progress requires the liberation of a gene from the "relentless" scrutiny of natural selection so that it is free to accumulate "forbidden" mutations until it becomes preadapted to a new function. Gene duplication is necessary, though not as employed for mass production of stable RNA's.

Ohno presents two of the several

modes of achieving duplicate loci—"unequal exchange" (intrahomolog translocation), generating tandem duplications, and tetraploidy. Tandem duplications are inherently unstable. One duplicated region can be eliminated by a well-placed crossover after asymmetric pairing. On the other hand, tetraploid segregation of a locus is hardly independent. The former homologs must diverge appreciably, "diploidize," before independent transmission emancipates one of the duplicate genes. Any mode of duplication may cause a gene-dosage problem, depending on species and the particular portion of the genome. Polyploidy is lethal in mammals, but tetraploidy and subsequent diploidization have been documented in many plants and, more pertinent here, in several modern fish.

Ohno ignores other modes of duplication involved in speciation in organisms whose chromosomes permit study—for example, Diptera—and herein lies the most serious flaw of the book. One finds duplications in reverse order or well separated on the same or different chromosomes. These are not lost by asymmetric crossing-over and do not require extensive chromosome change (diploidization). They do, however, originate infrequently, as do the inversions and translocations more easily identified in related vertebrate species.

Ohno takes lack of linkage between the mammalian hemoglobin alpha- and beta-chain loci or immunoglobulin light- and heavy-chain loci to signify that "either at the fish stage or at the amphibian stage, the mammalian ancestor went through at least one tetraploid evolution." He attributes the nearly uniform number of isozymic loci for many other enzymes in fish, birds, and mammals to loss of redundant loci during diploidization, though tetraploid fish, such as carp and salmon, have double the number of these isozymes.

Genome size has undoubtedly evolved. Although DNA loss sometimes accompanies specialization and although some "living fossils" have the highest DNA content known, the net tendency must have been for DNA increase in most vertebrate lineages. Tetraploidy can be ruled out in the urodele lineages. Here Ohno attributes the increase in genome size exclusively to tandem duplication, demonstrating that enormous redundancy can stop a lineage "dead at the amphibian stage."

Other lineages must have incurred meaningful, function-changing duplication—tetraploidy. Ohno proposes separate chromosome-doubling events in the lineages leading to birds and to mammals. The grounds for this are threefold: constancy of genome size within these groups though the bird genome is about half the size of the mammalian (living reptiles spanning the gap); presence of microchromosomes among vertebrates only in some of the snakes and lizards, reptiles with small genomes, and birds; and sex-determination in birds, snakes, and mammals by a chromosome confined to one sex—the female in birds and snakes and the male in mammals.

That the separation of bird from mammalian ancestry is ancient is confirmed by paleontology. That it occurred in the most recent ancestral group capable of polyploidization (which Ohno convincingly argues is incompatible with well-defined chromosomal sex determination) seems doubtful. This would imply at the least a biphyletic origin of living reptiles, placing turtles and crocodiles with the mammals, a view of reptile phylogeny not shared by many paleontologists.

The necessity for this phylogenetic artifact disappears with other types of duplication, whose existence is shown most simply by the number of chromosomes in the haploid set that can carry ribosomal RNA cistrons: only 1 in the frog *Xenopus*, at least 5 in man, and possibly all 11 in the Chinese hamster.

Found throughout the book are inconsistencies, misrepresentations, and errors of fact. Trivial errors even on page 1 bespeak careless editing and are counterpersuasive. Some corrections are perhaps worth making. Only about 20 percent of the sense strands in the *Escherichia coli* genome are expressed most of the time, similarly to the nonrepetitive DNA in mouse brain. Some "living fossils"—*Limulus*—are as polymorphic for isozymes as are other species. Actin is considered potentially homologous to the subunit of microfilaments, not of microtubules. Sister-chromatid exchange in ^{3}H-labeled cells is very likely induced by ^{3}H decay.

The errors, aggravating but mostly not crucial, raise the question, To whom is this book addressed? This is fun reading for armchair biologists, or for serious biologists who find sustained conjecture diverting. It may also goad somebody into generating data relevant to the more pivotal conjectures. As Ohno says, "In order to avoid early obsolescence, the author, judging on the basis of the scant evidence available, is obliged to anticipate future developments and paint a picture with broad strokes of his brush." I would demur slightly. It was a palette knife.

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Neuroendocrinology

The Pineal Gland. A Ciba Foundation symposium, London, June 1970. G. E. W. WOLSTENHOLME and JULIE KNIGHT, Eds. Churchill Livingstone, Edinburgh, 1971 (U.S. distributor, Williams and Wilkins, Baltimore). xii, 402 pp., illus. $14.50.

Between the lucid 20-page introduction to this symposium by Kappers and the excellent 10-page summary of it by Wurtman lie some 350 pages of fascinating reading. It reads like a "who dunnit," even though the membership list in the front tells us that all 26 distinguished participants did it. The first half of the book concerns what the pineal is, the second half what it can do. In the end, we learn that the pineal is undoubtedly a classical endocrine organ (Mess), a photo-neuro-endocrine organ (Collin), or a neurotransducer (Antón-Tay), designations that are not mutually exclusive. We learn that, under the influence of neural input (light/dark especially), it synthesizes potent amines and indoles (Axelrod; Shein) and other active principles (Moszkowska) which appear to act selectively upon the midbrain and hypothalamus (Antón-Tay; Fraschini) or pituitary (Moszkowska) to modify the synthesis and release of pituitary gonadotropin (Moszkowska; Mess; Reiter; Fraschini; Herbert) and adrenocorticotrophic hormone (Motta; Singer). We learn also that electrical activity of the brain, and behavior, are modified by the pineal (Nir; Martini) and that melatonin (administered, and presumably also from the pineal) is unique in its ability to increase a brain enzyme (pyridoxal kinase), which catalyzes the formation of pyridoxal phosphate, a cofactor necessary for the formation of such potent compounds as serotonin, dopamine, and gamma amino butyric acid. And we learn much more, not only from the formal presentations but also from the generally extensive discussions. (Either the discussions were carefully planned or many of the par-