Book Reviews

Oswald T. Avery

The Professor, the Institute, and DNA. RENÉ J. DUBOS. Rockefeller University Press, New York, 1976. x, 238 pp. $14.50.

During a remarkable career devoted to the study of pneumococcus, the bacterium causing lobar pneumonia, Oswald Theodore Avery made several discoveries of the utmost significance concerning the chemical basis of biological specificity. He was the first to show that substances other than proteins possessed specificity when, with Michael Heidelberger in 1923, he demonstrated the antigenicity of the polysaccharide in the pneumococcal capsule. In fact, in the days before antibiotics, the antiserums Avery helped to manufacture against the several types of capsular polysaccharide were a principal means of combating pneumonia. In 1944, capping an already richly productive career, Avery showed, with Colin MacLeod and Maclyn McCarty, that DNA possessed genetic specificity insofar as it was the substance responsible for hereditary transformation of capsular type. This discovery can truly be said to have opened the race to the double helix.

Yet Avery never received a Nobel Prize, a failure that has often invited speculation. Two recent explanations—that Avery was unaware of the broad significance of his discovery concerning DNA, and that the discovery itself was premature in that Avery's contemporaries did not appreciate its fundamental importance—are effectively scotched in this perceptive book by René Dubos. We are left with the simple but reasonable explanation that the Nobel committee, like all human institutions, is not infallible in its judgments.

Dubos was especially well equipped to write Avery's biography. Not only was he once a member of Avery's department at the Rockefeller Institute for Medical Research (now Rockefeller University), he also helped Avery directly at one stage by finding an enzyme secreted by soil bacteria that was capable of digesting the polysaccharide of type 3 capsules. Dubos is clearly a great admirer of Avery (as indeed seem to be all the persons who worked closely with him), and this biography is written not only with the lucid style we have come to expect in Dubos's books but with a wise and sympathetic understanding of an unusual man.

A bachelor, "Fess" (short for Professor) Avery could be socially charming and gracious, on the one hand, and resentful of intrusion into his privacy, on the other. An articulate and witty speaker, he came to eschew occasions for giving lectures, particularly of the formal variety. He refused honors when they would take him far from his laboratory: on fairly flimsy pretexts he refused to go to Germany to receive the Paul Ehrlich Gold Medal in 1933, to Cambridge University for an honorary degree in 1944, or to the Royal Society of London for the Copley Medal in 1945. When Avery retired in 1948 to Nashville, Tennessee, in the vicinity of his younger brother Roy, he quietly withdrew from the world of scientific affairs he had known to become, as it were, a country gentleman.

Until now we have had precious little information about Oswald Avery, except for his extraordinary scientific creativity. Avery probably preferred it that way. But now, thanks to Dubos, the veil of mystery has been pierced. We have access in Dubos's book to Avery's upbringing as the son of Baptist missionaries to New York's Bowery, to the years of changing interest from religion and humanities to scientific medicine, and finally to the ideas of Avery as he tested them on his colleagues in research and as he expressed them with greater finesse in his reports to the directors of the Rockefeller Institute.

The Institute emerges as a second hero of the book. Dubos draws a wonderful picture of what the Institute was like at its founding and in the exciting years (of Loeb, Van Slyke, Rous, Levene, and Landsteiner) that led up to the present university. The Institute proved a most congenial place for a person with the personality and talents of Oswald Avery: committed to helping the ill but impatient with any but a scientific approach to knowledge, Avery flourished in the medically oriented but scientifically heady atmosphere of the Rockefeller Institute. There he gained the chemical expertise, often through the collaboration of the experts who always seemed to be around, that enabled his subsequent successes with problems of which no one appreciated the profound significance better than he. Perhaps only at the Institute could a medical microbiologist make such a stunning contribution to the rise of molecular biology. A biographical study of Avery was long overdue, and we can be grateful to have this very good one at last.

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Regulation of Cell Growth

Multiplication and Division in Mammalian Cells. RENATO BASERGA. Dekker, New York, 1976. xiv, 240 pp., illus. $22.50. The Biochemistry of Disease, vol. 6.

Caveat emptor. This book is apt to charm the reader into believing that all is well in the study of mammalian cell multiplication, in that the major outlines for explaining the control of that multiplication are established. The book opens by noting that modern biology began with the discovery that deoxyribonucleic acid is the stuff of which bacterial transforming principle is made. Few would argue with the thesis that the molecular biology of the gene has been the most prominent theme of biological investigation in the past two decades. There are, however, phenomena to which it has little immediate relevance: quick metabolic responses to hormones, transmission of the nerve impulse, the mechanism of enzyme action, the control of transport. In other areas, where the lines are less clearly drawn, there is a great temptation to borrow explanations (and explainers) from that dominant big brother, molecular biology. The regulation of cell growth is an example. It seems natural to think of cell multiplication in terms of DNA and to think of other aspects of cell growth in terms of RNA and protein. The author makes his position clear when he states that the book "deals only with cellular processes strictly connected with the flow of cells through the cell cycle" and that "metabolic activities

which occur in cycling as well as in noncycling cells will not be considered unless they relate specifically to the cell cycle traverse or the prereplicative phase of stimulated G_0 cells." This leaves it to him to define what processes are strictly connected to the cell cycle. It also reveals one of the major themes of the book, that cell populations in an active state of multiplication differ qualitatively from those in which only a few cells are detectably multiplying. These provisos have the virtue of preventing large digressions from the main theme, but they have the defect of isolating cell replication from the integrated functioning of the cell.

The author occasionally uses models from bacteria and draws only selectively from studies on chicken embryo cells. The restriction of the book to mammalian cells is unfortunate. The chicken embryo cell has been studied more extensively than any other normal vertebrate cell, and the results are not compatible with several of the major theses of the book.

The strength of the book lies in its detailed presentation of data, many of them from the author's laboratory, pertaining to the molecular events associated with transit through the cell cycle. There is extensive treatment of the biochemistry of DNA synthesis during the S phase, although most of the information bearing on the mechanism of DNA replication necessarily is derived from bacteria. Only cursory attention is given to the conventional G_1 phase. The so-called G_0 period is more generously treated. Indeed, one of the main themes of the book is that cell populations that are growing very slowly or not at all are in a state, termed G_0, that is qualitatively different from the conventional G_1 phase of rapidly growing cells. While the author argues strenuously for such a distinction, he presents none of the data that have raised questions about it. For example, he ignores the increasingly accepted model of Smith and Martin which accepts a G_0 (or indeterminate) period but assumes that it occurs in both slow-growing ("resting") and fast-growing populations, albeit with different duration in the two cases. The author quotes extensively evidence that the length of the prereplicative period (time from application of the stimulus to the onset of DNA synthesis) varies with the method used to bring the cells into the "resting" state in the first place. But when the variables are strictly controlled, it has been shown that the length of the prereplicative period in stimulated cultures is independent of the growth rate of cells prior to stimulation. Again, one of the original reasons for inferring a special G_0 period in "resting" cultures was the apparent existence after stimulation of a considerable period of time *before* the onset of DNA synthesis, during which the cell was firmly committed to proceed into the S period even if the stimulus was withdrawn. More recent experiments have shown that such a committed period is an artifact of the method of stimulation, namely the use of serum.

The author is at his best when he questions claims that have been, at one time or another, widely accepted. He puts to rest any lingering belief that the size of the nucleotide pool determines the onset of DNA synthesis, and he does the same for cell size. He is properly skeptical about the use as models for normal cells of lines of cells that have been adapted to grow in culture and that have abnormalities in chromosome number and in other characteristics. He lays to rest the widely publicized notion that cyclic nucleotides are major regulators of cell growth and adds a spadeful of earth to the burial of the chalone theory. He has a mildly sarcastic style which, when coupled with the liberal use of Latin quotations, is ideal for demolishing bandwagon pretensions. Unfortunately, he uses the same style to put down some claims and findings that deserve more generous treatment but conflict with some of his major arguments. Thus, he dismisses with mild contempt the idea that *p*H is a growth factor. It has not been claimed that *p*H is a growth factor in the sense in which hormones and serum are, only that intracellular *p*H might transduce the effect from without to a response within the cell.

Similarly, the author scoffs at the reports of a prompt increase in transport of low-molecular-weight compounds into the cell after stimulation because the observations were made in aneuploid cells and such an increase is not found in the diploid human fibroblasts he studies. He simply ignores the multiple reports that uptake of at least four low-molecular-weight compounds is accelerated by growth stimulants in primary diploid cultures of chick embryo fibroblasts. This easy dismissal of the diverse elements of the coordinate response of cells to stimuli is in keeping with the goal of not straying far from the subject of cell cycle traverse. As a result, however, the author overlooks the central fact that in cultured normal cells intermediary metabolism, differentiated function, and growth respond similarly to external signals. This prevents him from applying the mountains of hard biochemical data available from studies of metabolic regulation to the phenomena of growth regulation.

The author does recognize that transport changes occur in stimulated cells and is careful to point out that these are more likely to be concomitants or effects of the growth response than causes of it. But when he gets to membranes and transport changes he is on foreign ground, and the text is replete with errors, for example, that the K_m of glucose transport is altered by growth stimulants rather than, as many papers since 1973 have shown, the V_{max}. He repeatedly cites experiments that have proved impossible to replicate or are notoriously unreliable, for example, reports of restoration of normal growth to transformed cells by monovalent concanavalin A and of protease stimulation of 3T3 (in contrast to the reported stimulation of chick embryo cells, which has been reproduced in many laboratories). He embraces single reports that purportedly rule out contact inhibition but ignores weightier data that support it.

One thesis of the author's is that chromatin template activity is the major determinant of DNA synthesis in mammalian cells and that gene activation plays a central role in the response of cells to stimulants. To support his thesis, the author relies heavily on evidence that chromatin template activity, that is, the ability of isolated chromatin to synthesize RNA, is increased in stimulated cells. On the whole this evidence is fairly convincing to a nonspecialist in this area. There seems to be no a priori reason to doubt that different parts of the genome are expressed as a cell traverses G_1 on its way to the S period, or that more genes are being actively transcribed in a fast-growing population of cells than in a slow-growing population. The question is whether gene activation sets the clock or is merely part of a preprogrammed sequence of events that inevitably occurs at a faster rate once the clock has been accelerated. A basic presupposition for accepting the criticalness of the gene activation step in control is the highly questionable existence of a distinctive G_0 period characteristic only of "quiescent" cells. A more convincing case can be made for the proposition that growth control is part of and dependent on a more general control of cellular activity. This shifts the focus to what is controlling the integrated functioning of the entire cell. Gene activation then becomes just an incident predetermined by the cellular phenotype and hardly a critical control.

Upon reading this book, however, one gets the impression that there is no plausible alternative to the gene activation model of growth control.

The criticisms notwithstanding, the book is an extremely worthwhile source of data on many important aspects of mammalian cell growth, particularly those having to do with macromolecular synthesis. It neatly disposes of some (but not all) of the most popular myths about the control of growth. It is, therefore, recommended, with the proviso that it be taken along with a healthy dose of skepticism and a subscription to a current journal of cell physiology.

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Myrmecology

Ant Larvae. Review and Synthesis. GEORGE C. WHEELER and JEANETTE WHEELER. Entomological Society of Washington, Washington, D.C., 1976. vi, 108 pp., illus. Paper, $11. Memoirs of the Entomological Society of Washington, No. 7.

Ant larvae, glimpsed when a nest is exposed by the turning of a stone, appear to be little more than helpless white lumps. A closer examination will reveal that they are anatomically complex and capable of no small amount of behavior. Recent research has shown that those belonging to at least some species provide secretions important to the welfare of the adults.

For nearly 50 years George C. Wheeler, later assisted by Jeanette Wheeler, conducted close studies of the external anatomy of ant larvae. In all, the Wheelers were able to examine 182 genera, representing all of the 10 living subfamilies and 47 of the 60 tribes. In this summary of a life's work they have integrated numerous previously published articles into an account that places the study of ant larvae on a solid foundation. Many species are beautifully illustrated with line drawings, and keys are provided to the level of genus.

As in the past, the authors are modest and cautious in their conclusions. They have redefined the limits of some genera and shifted the phylogenetic assignments of a few others. They make no attempt, however, to draw broader evolutionary conclusions. It is their view that the data of larval anatomy are only part of the total evidence needed for stable taxonomic conclusions, and they have left the final synthesis to others. In fact, William L. Brown has already made extensive use of the larval data in his important continuing revision of the ant genera of the world.

The Wheelers' synthesis has set the stage for another kind of study. The larvae of many ant species bristle with strangely shaped tubercles and hairs; those of the Leptanillinae have a remarkably complex, wedge-shaped organ that extends from the prothoracic venter toward the lower surface of the head. There also exists extreme variation among species in body form, flexibility of the thoracic region, and shape of the mouthparts. The significance of almost none of this is known, because research has been directed almost entirely toward anatomy, to the neglect of ecology and behavior. When studies are concentrated on these topics, taking advantage of the excellent anatomical information now available, we can expect to gain considerably in our understanding of the evolution of the ants.

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Atomic Physics

The Physics of Electronic and Atomic Collisions. Papers from a conference, Seattle, July 1975. JOHN S. RISLEY and R. GEBALLE, Eds. University of Washington Press, Seattle, 1976. xiv, 902 pp., illus. $40.

Electron and Photon Interactions with Atoms. Festschrift for Professor Ugo Fano. Papers from a symposium, Stirling, Scotland, July 1974. H. KLEINPOPPEN and M. R. C. MCDOWELL, Eds. Plenum, New York, 1976. xviii, 682 pp., illus. $45. Physics of Atoms and Molecules.

Every two years an International Conference on the Physics of Electronic and Atomic Collisions (ICPEAC) is held. The conferences usually include a number of invited lectures reviewing progress that has been made in the field. There were 58 such lectures at the most recent (ninth) ICPEAC, and they are published in *The Physics of Electronic and Atomic Collisions*. (Abstracts of the 566 contribued papers are published in two other volumes under the title *Electronic and Atomic Collisions*; University of Washington Press, $40.) The lectures are generally authoritative and are well written, but at a level that demands a considerable familiarity with the subject matter.

The volume begins with five reviews of special topics. Harrie Massey writes about negative ions and positrons (mostly positrons), Ugo Fano discusses his recent work on electron correlations, and Rudolf Peierls gives a short theoretical description of decaying states. Ernest Henley surveys possible experiments to detect the coherent parity-violating effects in atoms that would result from the existence of neutral weak currents. Eric Herbst and William Klemperer describe ion-molecule reaction schemes for the formation of interstellar molecules. The remaining articles are collected into 13 sections, each dealing with a particular area of research.

The experimental progress reported in the book has generally been in the development of higher energy and angular resolutions of incident and scattered electron and atomic beams, in the use of coincidence techniques for simultaneous detection of electrons and photons, in the production of polarized electrons, and in the use of lasers, both as sources of intense coherent radiation for use in photoabsorption studies and for the production of excited atoms for use in collision experiments.

Measurements of elastic and inelastic scattering of electrons by neutral atoms, which have traditionally occupied the central role in these conferences, continue to be important, and with the increasing sophistication in experimental techniques, they now provide deeper insight into the detailed nature of the interactions between electrons and atoms. Photon interactions were also discussed at the conference, and reports were presented on absorption of synchrotron radiation, photodetachment of negative ions, photodissociation of positive molecular ions, and multiphoton processes.

Electron and photon interactions with atoms were also the topic of a symposium held in honor of Ugo Fano, whose theoretical studies during the past 40 years have had a major, enduring impact on theoretical and experimental research in atomic and molecular physics. *Electron and Photon Interactions with Atoms*, the proceedings of that conference, contains 57 contributions, both theoretical and experimental. The papers are mostly straightforward reports of current work on electron and photon interactions, emphasizing research on angular distributions, correlations, and orientation and alignment effects. The collection is a testimony to the versatility of Fano's research; almost every paper makes reference to his work. There is considerable overlap, both in subject