

evidently existed among participants at this symposium regarding interpretation of these and other properties of NGF, it would have been useful to emphasize some of these issues by including the discussions, or a summary of them, in the volume.

The dramatic selective growth-stimulating effects of NGF on sensory and sympathetic nerve cells of chick and mouse embryos (as well as on mature sympathetic neurons) are well reviewed by Levi-Montalcini and P. U. Angeletti; recent studies of ultrastructure and metabolic effects of NGF on these target cells are included. Zaimis's demonstration of similar selective hypertrophy of sympathetic ganglia (and adrenal medulla) in kittens and rats after one to two weeks of daily NGF injections in the neonatal period should provide valuable biological preparations for analyses of "the role of the sympathetic nervous system and the way in which structures innervated by it can be affected by drugs." L. Papadaki provides a detailed electron micrographic study of the NGF-hypertrophied sympathetic ganglion cells in Zaimis's kitten and rat experiments, and E. Nicolescu *et al.* demonstrate increased fluorescence attributed to catecholamines in heart, spleen, and other organs in these same NGF-treated kittens and rats. M. G. Larrabee reviews a series of interesting metabolic studies (carried out with L. M. Partlow) on NGF-stimulated chick embryo sensory and sympathetic ganglia, *in vitro* and *in vivo*.

N. R. Saunders provides a critical review of earlier claims by Scott and Liu (1963, 1964) that NGF promoted regeneration of spinal cord neurons in kittens, and concludes that "these experiments do not appear to provide convincing evidence that NGF can effect the outgrowth of spinal neurons after damage." He also describes his own attempts to detect NGF effects on regeneration of peripheral sensory nerves after crush lesions in rats and rabbits. The results were negative (although the superior cervical ganglia of the NGF-treated animals did show expected enlargement). Levi-Montalcini had already reported that although "sensory ganglia . . . dissected out from a large number of mammalian fetuses respond to NGF *in vitro*, . . . during postnatal life, mammalian spinal ganglia show no growth response when treated either *in vivo* or *in vitro* with NGF." The experiments by Scott and Saunders were based on the hope that introduction of high concentrations of

NGF might nevertheless produce physiologically significant enhancement of adult sensory neuron regeneration. Although these attempts have been discouraging, recent studies by Björklund and Stenevi (*Science* **175**, 1251 [1972]) demonstrate that "a single intraventricular injection of NGF . . . has a potent stimulatory effect on the regenerative sprouting and growth of severed central noradrenaline axons." No growth-stimulating effects had been detected, however, on *intact* central nervous system neurons during Levi-Montalcini's studies in chick embryos and neonatal mice. It will therefore be of great interest to determine whether NGF may indeed, as proposed by Björklund and Stenevi, "play a role in . . . the normal development, maturation, and growth of certain central [catecholamine] neuron systems, . . . similar to that in peripheral, sympathetic neurons." Perhaps these questions will soon be clarified by further applications of sensitive fluorescence histochemistry techniques as well as by systematic analyses with CNS tissue cultures.

The chapters on NGF-antiserum cover a wide range of biochemical, physiological, and behavioral alterations which occur in animals during and after experimental immunosympathectomy. Larrabee describes metabolic and electrophysiologic deficits which develop in sympathetic ganglia during the first few days after a single injection of NGF-antiserum in 7- to 10-day-old mice. Zaimis provides a valuable review of the usefulness of immunosympathectomized animals in cardiovascular research, but limitations in this experimental method have been noted by L. Iverson in his recent review of a related book, *Immunosympathectomy*, edited by G. Steiner and E. Schönbaum (*Science*, 12 Jan. 1973, p. 171). The latter book provides an excellent extension of the Zaimis and Knight volume, especially in regard to NGF-antiserum.

The chapters on technical problems in the assay of NGF and its antiserum include valuable data and advice by D. C. Edwards, F. L. Pearce, and I. A. Hendry. Serious pitfalls in the bioassay of NGF by standard serial dilution are emphasized by Pearce, who shows that reversible adsorption of NGF on glass pipettes can easily lead to absurd errors in estimation of potency (and may account for some of the conflicting data already in the literature, for example Shenkein *et al.*, *Science* **159**, 640 [1968]). A new radioimmunoassay

procedure developed by Hendry *et al.* avoids these dilution problems as well as the subjective errors involved in the usual bioassay, where the magnitude of nerve fiber outgrowth is estimated by microscopic observation. The new immunoassay is also 20-fold more sensitive than the bioassay. Angeletti *et al.* also utilize a microcomplement fixation assay to demonstrate the presence of significant amounts of NGF in membrane-bound particles isolated from a microsomal fraction of heart, kidney, and spleen tissues. This new technique should facilitate "recognition and characterization of the receptor sites at which this unique [NGF] molecule binds . . . [which] would be of the utmost importance in clarifying its mechanism of action."

In general, then, the book provides a useful review of current trends in NGF research. The references cited at the ends of chapters are adequate for those seeking further details in technique or data. An author index would have been helpful in this regard. No serious attempt has been made to integrate the diverse chapters, but most readers will probably find chapter 5, by Levi-Montalcini and Angeletti, an excellent introduction from which to proceed to more specific topics in this exciting area of developmental neurobiology.

STANLEY M. CRAIN
Department of Physiology and
Rose F. Kennedy
Center for Research in Mental
Retardation and Human Development,
Albert Einstein College of Medicine,
Bronx, New York

Developmental System

The Biology of Imaginal Disks. H. URSprung and R. NÖTHIGER, Eds. Springer-Verlag, New York, 1972. xviii, 172 pp., illus. \$14.60. Results and Problems in Cell Differentiation, vol. 5.

Within a maggot or a caterpillar there are sacs of presumptive adult cells, called imaginal disks, that depend on the larva for nutrition, waste disposal, and gas exchange. During metamorphosis larval cells die, but these embryonic adult cells are transformed into a fly or a moth.

This volume, consisting of six reviews of imaginal disk biology, is dedicated to the distinguished Swiss developmental geneticist Ernst Hadorn. In most of the book, emphasis is placed on data

obtained from *Drosophila*, because of the utility of genetic techniques in the study of development.

The imaginal disks are an ideal system in which to investigate a number of questions in developmental biology. A selection of interesting themes approached by this book might include the following four problems. One is the chemical nature of substances incorporated into an egg during oogenesis which appear to specify the developmental fate of embryonic nuclei. Papers by R. Nöthiger and W. Gehring discuss the initiation of developmental commitments in embryonic cells. The analysis of maternally influenced mutants which alter developmental fates and techniques of nuclear and cytoplasmic transplantation into eggs promise to shed light on the molecular constituents of the egg which initiate specific developmental pathways in particular cells.

A second problem discussed in this volume is the mechanism by which precise spatial patterns are generated during development. A. Garcia-Bellido's analysis "has revealed an extreme cell autonomy in the organization of the final pattern." But recent results are cited involving disks regenerating in situ, disks duplicating during culture, and disks reaggregating after cell dissociation, which might be explained on the basis of interacting groups of cells cooperating in the formation of spatial patterns. Which of these explanations is more generally applicable awaits further study.

A third developmental problem profitably investigated through the use of imaginal disks is the stability of the determined state. Gehring tells how cells committed to a particular developmental pathway can be cultured indefinitely in the abdomens of adult females. Changes in determination—transdeterminations—occasionally occur during culture. For example, prospective antennal cells will change sometimes to leg cells. Transdetermination occurs in repeatable sequences from one disk to another in specific frequencies. Furthermore, there is a class of mutants which cause the same transformations in situ, so that a fly may have legs growing out of its head which replace its antennae. An adequate and testable model to account for these intriguing alterations in genetic control functions has yet to be presented.

A fourth problem in developmental regulation is the hormonal control of

differentiation. Ursprung reviews the ultrastructural changes occurring in disks during metamorphosis. J. W. Fristrom and H. Oberlander show that imaginal disks cultured in vitro with ecdysones can be caused to undergo morphogenetic and biochemical changes like those occurring during normal development. Disk metamorphosis in vitro presents an opportunity for the analysis of the molecular mode of action of the steroid ecdysone. The collection of mutants which develop abnormally only at metamorphosis may permit a genetic dissection of differentiation similar to that used by the bacterial geneticists in working out biochemical pathways in procaryotes.

Hadorn and his European colleagues published in German many of the important original findings cited in this volume. The editors thus provide not only a comprehensive compilation on the biology of imaginal disks but also convenient access to this information for the non-German-speaking scientist. The reviews are well written and illustrated, and will be useful not only to professional developmental biologists but to students as well.

The quantity of interesting experiments on the imaginal disks indicates that the system is ripe for solution of several fundamental questions. But the lack of any unifying hypotheses in this volume indicates that a lot of basic investigation and analysis remain to be done.

JOHN H. POSTLETHWAIT

*Department of Biology,
University of Oregon, Eugene*

Exposition for Biologists

Biological Applications of Electron Spin Resonance. HAROLD M. SWARTZ, JAMES R. BOLTON, and DONALD C. BORG, Eds. Wiley-Interscience, New York, 1972. xii, 570 pp., illus. \$27.50.

Electron spin resonance (ESR) is a form of microwave spectroscopy applied to the electron spin or magnetic dipole transitions of paramagnetic compounds, that is, compounds containing one or more unpaired electrons. Numerous excellent books on the theory of ESR exist, as do review papers and symposium volumes on its applications in biological research. This work, however, is a thoughtful and rather comprehensive presentation of both the theory and the applications.

The editors believe that the ESR method of detecting and characterizing paramagnetic species is underused, at least partly because its theoretical basis is not familiar to most biologists. Many are thus poorly prepared to use ESR in research or even to follow much of the literature on its use. It is for this group of able but uninitiated persons that the book is intended.

The book first introduces the theory, instrumentation, and methodology of ESR in a way which is concise, clear, and yet detailed. The level is quite appropriate for the uninitiated student and provides both a qualitative and a quantitative description of ESR. This section as a whole is one of the best practical introductions to ESR available. There are, however, a number of omissions. For example, the discussion of the quantitation of spin counts dwells almost entirely on instrument parameters (modulation field, microwave power, and so on) and does not include certain factors intrinsic to the sample (spin population factors in states of multiplicity above doublet, and *g* values) that are of vital importance in the case of transition metal ions.

The remainder of the book consists of a set of chapters, each by a different author, which describe the application of ESR to a wide range of biological systems and summarize the state of research as of 1971. Covered are studies of cells and tissues, photosynthesis, compounds of pharmacological interest, radiation biology, spin labels, and those enzymes that contain flavin, iron-sulfur complexes, molybdenum, and copper as functional redox groups. Research on heme proteins is omitted because, as the editors explain, the chapter on it was incomplete at the time of printing. This omission seriously detracts from the overall value of the work, and it is to be hoped that a second edition will cover the heme proteins.

Aside from this one major omission, the coverage is essentially complete and includes all the areas in which ESR so far has made major contributions in understanding the occurrence of paramagnetic species in biology. The book can be highly recommended for the research worker and for graduate study.

THOMAS C. HOLLOCHER

*Department of Biochemistry,
Brandeis University,
Waltham, Massachusetts*