ken is one of the fascinating aspects of their proof. The implications for the future of mathematics are daunting, and in this account of the four-color problem Saaty and Kainen explore them at some length:

> One particularly significant thing which has emerged from this approach is that the computer will play an increasingly fundamental role in mathematical thinking. Here it has been an invaluable aid in generating exhaustive analyses of a problem by cases. From now on mathematicians will dare to use the computer more and more in constructing proofs. As this use becomes more prevalent it would gain greater credibility as a method of approach. This says that we may more often look for constructive analytical existence proofs by working out cases instead of nonconstructive synthetic ones. With this, one would expect that vastly larger and more detailed problems of an abstract nature significant to man's logical view of his thought processes and to his role in the universe will be formulated and solved. Man's imagination creates the domain within which the computer will function.

This intrusion of the computer will undoubtedly change the face of mathematics, and the transformation, from an art to a science, will be unwelcome to some.

The book is divided into two parts. The first discusses the early history of the four-color problem, its reformulation in terms of planar graphs, the basic theory of maps and colorings, and the methodology that enabled Appel and Haken to settle the problem. It is probably this part that will be of greatest interest to the general reader. The important concepts of reducibility, discharging, and unavoidability are clearly explained, and the heuristic reasoning that encouraged Appel and Haken to pursue their goal for several years is described in some detail.

The second part of the book is concerned with the many other approaches to the problem that have been developed over the years. As the authors note, "These variations are a testimony to man's tremendous breadth and imagination in his assaults on a difficult problem." Thirty-five equivalent formulations of the conjecture are described, relating the four-color problem to Diophantine equations, Galois fields, sequences, polynomials, trigonometric functions, and finite projective geometries, as well as to a variety of seemingly disparate graph-theoretic notions.

To conclude, there is an appendix in which certain technical results quoted earlier in the text are proved, and several related avenues of graph theory are briefly explored. It should be noted that the "metaconjecture" at the end of the appendix is equivalent to a well-known conjecture of G. Hajós that dates back to 1953 and was recently disproved by P. A. Catlin.

Although the material is quite well organized and is written so as to be accessible to readers with a modicum of mathematical training, it suffers from a number of defects that may well confuse the nonspecialist. It is not uncommon to find terms and symbols used before they are defined, if indeed they are defined at all; a list of symbols would certainly have helped. There are inconsistencies in notation, with different symbols denoting the same concept and different concepts denoted by the same symbol. Several proofs in the second half of the book are incomplete. Facts that have already been noted are inexplicably repeated; for instance, one may find the following three sentences in quick succession (on pp. 12, 13, and 19 respectively): "It is easy to find a graph, some of whose edges always cross at a point that is not a vertex no matter how we draw them," "Note also that not every graph is planar," "Let us observe that not every graph is planar." And once or twice the authors go out of their way to remark that a certain planar graph is four-colorable, having seemingly forgotten that the purpose of their book is to explain why all such graphs are four-colorable.

Despite these imperfections, *The Four-Color Problem* does provide a stimulating and instructive account of the decline and fall of a major mathematical problem. It also serves as a good introduction to the developing field of graph theory, complete with historical motivation.

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Opiatelike Substances

The Endorphins. Papers from a symposium, Brescia, Italy, Aug. 1977. ERMINIO COSTA and MARCO TRABUCCHI, Eds. Raven, New York, 1978. xviii, 380 pp., illus. $28. Advances in Biochemical Psychopharmacology, vol. 18.

When comparing the contents of this volume with the most recent prior review of the subject (*Opiates and Endogenous Opioid Peptides*, H. W. Kosterlitz, Ed., Elsevier/North-Holland, 1976), it is apparent that there is a wealth of new information, especially on the interaction of endorphins with other neuronal systems and the role of endorphin in the regulation of pituitary hormone secretion. Save for an introductory paper by Zetlar that discusses pharmacologically active peptides present in the nervous system and one by Kosterlitz and Hughes that reviews the development of the concepts of opiate receptors and their ligands, the present volume is designed more for those actively working in the field and related fields than for those who want an overview of the state of the art. For the active investigator, as well as for the beginner, it would also have been helpful to have a critique and a more detailed description of the various methodologies employed; in many instances reported results rely heavily on immunochemical characterization, which does not provide sufficient specificity for the substance being measured, or on extraction procedures that may generate artifactual results with regard to compounds that might not have been present in vivo prior to extraction.

There is general agreement that the anatomical distribution of enkephalinergic neuron systems is more diffuse than that of endorphin, as determined by both immunocytochemistry and radioimmunoassay. The enkephalin neurons are present in brain areas assumed to be related to pain and analgesia (periaqueductal gray, medullary raphe nuclei, spinal trigeminal nucleus, and spinal cord), behavior (globus pallidus, stria terminalis), and neuroendocrine effects (median eminence). Little (Bloom *et al.*) or no (Johansson *et al.* and Cox *et al.*) enkephalin is present in the pituitary. Immunological methods alone are not precise enough to fully distinguish between leucine- and methionine-enkephalin, although this has been accomplished by the use of radioimmunoassay after the separation of the two enkephalins under high pressure liquid chromatography (Meek and Bohan). The distribution of enkephalin follows but is not completely parallel to that of opiate receptors. In contrast, the distribution of endorphin cell bodies, fibers, or both appears to be restricted to the hypothalamus, midbrain, and pituitary, chiefly the intermediate lobe. Endorphin (and enkephalin) content in the hypothalamus is unaffected by hypophysectomy, raising questions about the source of such endorphin and the physiological significance of pituitary endorphin. Although the amino acid sequences of endorphin and Met-enkephalin are found within the β-lipotropin molecule (and β-lipotropin has been shown to be present in the central nervous system), there is no evidence that Met-enkephalin is derived via lipotropin degradation. The source of the Leu-enkephalin in the brain is even less clear, for only the sequence

for Met-enkephalin is found in β-lipotropin. The physiological significance of the different distribution of these two types of opiatelike peptides is also unclear. Chronic morphine treatment alone or together with naloxone does not appear to affect regional or whole brain levels of enkephalin or total opioid activity or pituitary opioid activity. Stress is reported to increase (Santagostino *et al.*) or to decrease (Cox *et al.*) pituitary opioid activity.

It is of interest that neuroanatomical, neurophysiological, and neuropharmacological studies provide evidence that opioid peptides interact with other neural systems; that is, endorphin interacts with dopamine and enkephalin interacts with dopamine, gamma-aminobutyric acid, substance P, neurotensin, and acetylcholine. Some of these interactions may be involved in mediating the behavioral and neuroendocrine effects noted for endorphin and enkephalin. Guidotti and Grandison report evidence that the effect of endorphin in eliciting prolactin release is mediated by an inhibitory effect on the arcuate-nucleus–median-eminence dopaminergic tract; Schwartz *et al.* present evidence that inhibitory effects of opiates on dopamine release are mediated by a presynaptic contact of enkephalinergic neurons on dopaminergic nerve terminals, leading initially to decreased dopamine release.

The discovery of endorphins, their behavioral effects, and their relationship to exogenous opiates has led to much speculation concerning their role in normal mental function, response to pain, psychiatric disease, and addictive states. Research in this area has in part been hampered because of the lack of valid assays for measuring endorphin-like material (in peripheral tissue, blood, urine, cerebrospinal fluid) and determining the exact nature of the substance being measured (for example, a substance active in radioreceptor assays is not necessarily endorphin or enkephalin; additionally, at present there is no antibody that reacts with endorphin that does not cross react with lipotropin, necessitating some form of separation prior to final assay). This has made it difficult to correlate the presence of certain forms of behavioral symptomatology with levels of a specific opiatelike compound (assuming that such a compound circulates normally, which has by no means been proven). Moreover, level is a very imprecise measure of turnover, correlation with which would be far more significant. Several papers comment on the difficulty of assigning endorphins a role in normal behavior, for naloxone itself has no behavioral effect in animals or humans. Naloxone, however, has been reported to be effective to a greater or lesser degree in reversing acupuncture analgesia (Pomeranz), in acupuncture treatment of alcohol- and tobacco-dependent states (Malizia *et al.*), and in treatment of psychotic hallucinations (Herz *et al.*). The last finding has not been confirmed by several other studies, which are not reported in this volume. Terenius reports very limited correlation of efficacy of acupuncture treatment in human chronic pain with increases in the content of a nonendorphin opioidlike material in cerebrospinal fluid.

It is apparent that there are many questions, both basic and clinical, that require further methodological advances before they can be answered. It is also apparent that great strides have been made in the short period of time that active investigation has proceeded in this field, so that a compilation of research reports a year hence may clarify some of the questions noted in this review.

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