Book Reviews

A Field of Genetics

Proceedings of the International Conference on Quantitative Genetics. Ames, Iowa, Aug. 1976. EDWARD POLLAK, OSCAR KEMPTHORNE, and THEODORE B. BAILEY, JR., Eds. Iowa State University Press, Ames, 1977. xxiv, 872 pp., illus. $18.50.

The blue-ribbon conference recorded in this volume was convened to consider how well quantitative genetics is fulfilling its great promise. Recognizing substantial concern about the quality and applicability of existing theory, the organizers asked "leading researchers . . . to spell out in some detail [its] strengths and shortcomings . . . and to give their views about what is to be done to remedy the latter." This focus naturally limited the number of papers solicited in population genetics and human genetics.

Evidently the conference succeeded. The book contains both concise essays on specific basic issues and well-developed technical papers. Although floor discussions are not quoted directly, it is clear that they influenced subsequent papers, including four invited discussions. With this sense of dialogue, and in the summary addresses, one gets a historical perspective whose depth stems from the harmony (not unison) of many viewpoints. No important breakthroughs are indicated, but the obstacles seem well defined in most cases, and advances are expected in various sectors of a broad and complex front.

There are three things to be gained from this book. First, it reveals a thoughtful current view of a scientific field by some of its foremost practitioners. In this it is both unpretentious and astute. Second, it brings together some historical components of quantitative genetics that few people previously comprehended. These should be of especial interest to population geneticists, too. And finally, there are detailed contemporary papers, some quite demanding, which abound in equations and matrices. All this makes for a singular introduction to the field.

Kempthorne's two rambles, the introduction to the conference and a general paper entitled "Status of quantitative genetic theory," combine to make an exemplary contribution. The introduction considers both the center ("Can we predict response . . .?") and the vital periphery (population genetics) of the field. The general paper resumes consideration of Fisher's germinal ideas in an area common to population and quantitative genetics. Fisher recognized a simple relationship between selection differential and selection coefficient that somehow all but got lost. Griffing applied it in an impressive series of papers, but several interested parties (including myself) had never found the trail back beyond Haldane. As Kempthorne indicates, Fisher's early approach to selection (expressed almost offhandedly in his 1918 paper on correlation between relatives) embodied a closer relationship between quantitative variation and the segregation of alleles than is common today.

It is difficult to capture the protean spirit of this general address, which includes Kempthorne's " ' Epilogue' view of the conference." History (some conjectural) is interwoven with the analysis of the analysis (sic) of variance and the exposition of elements of selection theory, punctuated by some fairly sharp attacks, mostly well founded. Fisher's 1930 treatment of genetic variance is called "rather incoherent"; the IQ issue is recommended for immediate burial (presumably with dishonor); and the "Birmingham school" (Mather and Jinks) gets both barrels (several direct salvos from Kempthorne and a quotation from Falconer) for the "super-gene" construct and its associated self-obfuscating mechanism of phenogenesis. Kempthorne has an eye for devastating quotations: my hand shakes as I write this. In sum, the paper is good, stimulating reading.

Among the introductory articles is Falconer's "Why are mice the size they are?" The statement of the problem and the call for an explanatory theory are lucid. The concepts Falconer wants reconciled—pleiotropy, overdominance, stabilizing selection, and fitness—are not. Clearly, that's part of the problem.

Three disparate articles follow under the rubric Implications of Population Genetics and Molecular Biology. One is a Lewontin gem, directing quantitative geneticists to look at and use what's being found inside their black box. The structure of the genome, the basic mechanism of gene action, the sites of recombination, and the distribution of allelic variation are all proper grist for the mills of quantitative genetics. Also, the opportunities offered by plasmid technology are noted.

Three sections of the book deal with experimental findings on laboratory species, crop plants, and livestock, respectively. Falconer reviews the Edinburgh mouse experiments: goals, results, conclusions, limitations, rationale. J. W. Dudley reports on 76 generations of selection in maize (starting in 1896!). Nordskog details the successes, failures, and, above all, uncertainties in poultry breeding. In 1976 it was necessary to say, "Little is known about nonadditive variance in chickens." Kempthorne thereupon asked, "What's different about chickens?," and D. L. Harris's subsequent "invited discussion" paper offers some explanation: The high reproductive rate in poultry makes possible small breeding populations. This exacerbates the noise generated by the traditionally unreplicated experiments. Marketing problems have also had an unfavorable influence on research programs.

Although the basic concept of selection is about as simple as they come, evolution has produced systems that tax the process (and those who try to bend it to their use) to the limit. Thus the tuning of the mechanism continues to be of great importance, together with the testing of particular predictions. Gallais describes a series of such tests on tetraploid alfalfa.

Mathematical and Statistical Genetics is one of several divisions of the book where bridges are initiated between quantitative genetics and population genetics. It is noted in various parts of this volume that the two fields are at present distinct to an unfortunate degree, despite their common origin and common goal of defining and relating genotypic variation and phenotypic variation. For most people, the analysis of either requires full attention, and the conceptual vocabulary of any field is limited. So population geneticists begin with alleles and work toward the promised land of total phenotypic definition, while quantitative geneticists begin with phenotypes and yearn for the shining map in the hereafter. Although each group has plenty to do in its own garden, there is hope of clearing some common ground. For example, Felsenstein discusses the use of

normal distributions in a variety of genetic, ecological, and evolutionary contexts. He then extends Russell Lande's description of conditions under which the joint distribution of individually normal allele effects at many loci remains multivariate normal.

The next section, Theory of Response and Limits to Selection, is similar in spirit. Alan Robertson contributes to both sections: a theoretical attempt to explain the common observation of selection asymmetry and a simulation study on selection with a large number of linked loci. Griffing describes a method for minimizing adverse effects of genotypic interaction, and Sved considers the opposition to artificial selection by natural selection at linked loci.

Three papers on mixed model theory relate to the use of performance records in the choice of breeding stock.

The three general papers will be of especially broad interest. Kempthorne's has already been mentioned. Comstock writes on the design of breeding programs for "*maximum* exploitation of . . . allele resources . . . in *minimum time*." Feldman and Cavalli-Sforza present one of the few attempts to break new ground, rather than to wrest the promised rewards from existing methodology. In "Quantitative inheritance, stabilizing selection, and cultural evolution," they describe an approach to the transmission of phenotypes that may apply to cultural—nongenetic—evolution as well. They begin with the original Fisher model of quantitative variation (two alleles; three genotypes with respective phenotypic contributions of $-a$, d, and a) and develop the consequences of an additional genotype-environment interaction, where the important environmental factor is the parental phenotypes.

In a special invited paper, Sewall Wright gives his views, after some 60 years as a major figure in the field, on evolutionary changes in phenotypic characters. He is challenged by a creationist (Paul Cornelius) and replies incisively.

The conference was seasoned with, among others, papers by Thoday on polygenes, Rendel on canalization, and Hartl on meiotic drive. Other major contributors include Karlin, Weir and Cockerham, and W. G. Hill, to name just a few. The book was promptly produced and is well composed and attractive. The editors did an admirable job.

Quantitative genetics is at once quantitative and inexact, successful in some of its applications and uncomfortable with some of its theory, full of inexorable arithmetic and modest conjecture. The present volume by design does not include human quantitative genetics and behavior genetics. Nevertheless it is a splendid portrait of a scientific reunion at a fitting homestead, Ames, Iowa.

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Neuroendocrinology

Hypothalamic Peptide Hormones and Pituitary Regulation. Proceedings of a workshop, Bethesda, Md., Nov. 1976. JOHN C. PORTER, Ed. Plenum, New York, 1977. viii, 366 pp., illus. $32.50. Advances in Experimental Medicine and Biology, vol. 87.

Three celebrations of progress in neuroendocrinology have been organized under the aegis of the National Institutes of Health, long the largest single sponsor of neuroendocrine research; this volume is a report of the most recent of these.

The first symposium, in 1962, was devoted to anatomical and physiological validation of the evidence that the brain controls the pituitary gland and that hormones influence brain function. Though based on sound principles, the conference had overtones of what Roger Guillemin has called the "prophetic era" of neuroendocrinology, an era characterized by clinical anecdotes and by insensitive bioassays of pituitary function.

The second symposium, in 1969, was the product of a frustrated NIH and its study sections; despite the continuing accumulation of physiological evidence of neural control of the adenohypophysis and the demonstration of biological activities in hypothalamic extracts corresponding to releasing activities for all the known anterior pituitary hormones, the crucial evidence, the identification of the structure of even one hypothalamic hormone, had still not been provided. The chemistry of the hypophysiotropic factors remained "prophetic."

But by 1969 the laboratories of A. V. Schally and of Guillemin were very close to identifying the chemical nature of thyrotropin-releasing hormone (TRH). Its structure was announced between the time of the conference and the production of galley proofs of the proceedings. This demonstration can be said to be the crucial validation of the portal-vessel chemotransmitter hypothesis of anterior pituitary control. It is the step that converted neuroendocrinology into a branch of neurobiology. All that was needed to legitimize the field was a genuine molecule. It is at this point that the era covered by the present volume begins. The field is so extensive now that no one volume can cover all the important issues. This volume contains a representative selection of some of the best work in neuroendocrinology and includes summaries of recent studies, many unpublished new data, valuable generalizing concepts, and comprehensive bibliographies of recent work.

The years since the last conference have seen the introduction and widespread use of radioimmunoassay, proper emphasis on the general phenomenon of neurosecretion, better understanding of the molecular biology of cell secretion and protein synthesis, and the elucidation of the chemical structure of two more hypothalamic hormones (luteinizing-hormone–releasing hormone, LHRH, and somatostatin) and the use of these substances by clinicians. The present volume describes these advances. Guillemin contributes an essay emphasizing that at least two of the classical hypothalamic hormones, TRH and somatostatin, are widely distributed outside the hypothalamus and that they may be derived from neuroectoderm. In fact, such cells may be part of the diffuse neuroectoderm system described by A. G. E. Pearse as part of the APUD (amine precursor uptake and decarboxylation) system. This view, reinforced by the recent dramatic discoveries of the endorphins, enkephalins, neurotensin, substance P, and the remarkable distribution of many peptides in specialized cells of both brain and gut (for example vasoactive intestinal peptide, cholecystokinin-pancreazymin, bombesin), permits a broad reconsideration of the nature of control of neuron function, which now must include a variety of specialized, pharmacologically (as well as structurally) coded connections.

There are other primarily neurobiological papers. S. Ochs reports on his work on axoplasmic transport in peripheral nerves, a phenomenon that now appears to occur in specific peptidergic neurons, which have been commonly considered to be neurosecretory. The broad distribution and variety of peptides in brain are briefly described by M. J. Brownstein. A. Barnea and colleagues describe the subcellular compartmentalization of the hypothalamic peptides, presumably a reflection of their concentration in presynaptic terminals. J. F. McKelvy summarizes the relatively modest knowledge of the biosynthesis of hypothalamic peptides, the study of which is made difficult because of the relatively small amount of secretion products made by only a small