BOOK REVIEWS

The Founder of Genetics

Gregor Mendel. The First Geneticist. VÍTĚZSLAV OREL. Oxford University Press, New York, 1996. xii, 363 pp., illus. $49.95 or £29.50. ISBN 0-19-854774-9. Translated by Stephen Finn.

A new biography of the founder of genetics prompts one to reflect on the contrast between the views of Mendel and Darwin on heredity and variation. Darwin claimed that all variation is ultimately due to changes in the conditions of life—either directly and definitely, as in Lamarckism, or indirectly and indefinitely, as in the random individual differences among sibs. Hybrid progeny displayed the most marked of indefinite variation, he believed, as a result of the commingling in the hybrids of two different constitutions. The constitutional differences resulted from the antecedent exposure of the progenitors to different conditions of life. A powerful engine of variation was thus the act of bringing organisms from the wild into cultivation, acclimatizing them, and enriching their nutrition. The most significant cause of variation was thus the conditions of life, rather than hybridization.

Gregor Mendel. [Corbis-Bettman]

Mendel, in his famous paper of 1865, "Experiments on Plant Hybrids," rebutted this view and reinterpreted the greater variation of cultivated plants in terms of enhanced opportunities for hybridization that cultivation affords. The complete independence of the seven pairs of character differences that he studied convinced him of the tremendous potential for variation that hybridization offers. Whereas Darwin played down the significance of this aspect of hybridization for species transformation, Mendel emphasized it, and, as Orel shows, he fully appreciated its importance for the practical breeder.

As emeritus director of the Museum Mendelianum in Brno, Orel writes from an unrivaled position of authority and knowledge of the documents and discussions—some more, some less scholarly—concerning Mendel's life and work. In his duties for the museum and for the international community he has been tireless. Now the fruit of his long devotion is available for the reader of English. He has drawn chiefly on his own researches and those of a number of Czech authors, but also on the work of such authorities as Franz Weiling (on Mendel) and Onno Meijer (on De Vries). But whereas Darwin scholars have been overwhelmed with the wealth of documents from which rich and intimate biographies have been written, students of Mendel have been underwhelmed and undernourished.

This dearth of biographical data on Mendel has led to two tendencies—unbridled speculation in the interpretation of limited and often minor incidents and the recounting of trifling and anecdotal evidence. Many of the interpretations of Mendel's work are attacked by Orel, especially those unfavorable to the image of Mendel as the hero of genetics. This is not another blow in the culture wars between scientists and their alleged deconstructors, the social historians. Rather, it is the statisticians, led by R. A. Fisher, who are the arch-villains. In 1936 Fisher accused Mendel of reporting too good data. Orel has come to Mendel's defense here, as he has over the attempt to deny Mendel the label "Mendelian." He charts an increasingly baneful trajectory stemming from my own paper "Mendel No Mendelian?" of 1979. Does he realize that the purpose of that paper was to distinguish the claims that Mendel himself made from those made by those who called themselves Mendelians in this century? It was not to deny Mendel his founder status.

The most interesting chapter in this book is the last, given to the changing climate of opinion regarding Mendelian genetics in Brno and Prague during this century. Orel describes the increasing support for the inheritance of acquired characters that emerged in the 1920s and the attention paid to Paul Kammerer's support for the doctrine—even at the 1922 centenary celebration of Mendel's birth. He concludes with an enthusiastic account of the restoration of genetics in Czechoslovakia at the time of the 1965 Mendel centenary celebrations. The book offers an extensive overview of debates in the interpretation of Mendel's life and work and a valuable description of the economic and political climate in which Mendel made his great contribution to science. Unfortunately it has not been possible to add significantly to our knowledge of Mendel himself.

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Drug Discoveries

The Psychopharmacologists. Interviews by DAVID HEALY. Altman (Chapman and Hall), New York, 1996. xxxiv, 633 pp. $82.95 or £45. ISBN 1-86036-608-4.

This entertaining book gives an overview of the development of psychopharmacology through interviews with 25 of its leading practitioners, who give their personal views on how the field grew and relate their own contributions to it. Healy has chosen a good mix of clinical and preclinical scientists from both sides of the Atlantic, and his structured interview style helps to give the book a coherence it might otherwise have lacked.

The development of effective drug treatments for mental illnesses during the past 40 years has had a dramatic impact on the practice of psychiatry, even to the extent of removing the need for large custodial mental asylums. The introduction of these medicines has also fundamentally changed the way in which we think of mental illnesses,

with more emphasis being placed on their biological basis and less on the previously dominant psychoanalytical viewpoint. The history of the science underlying these profound changes reveals a curious mixture of perceptive and often unexpected clinical discoveries and a scientific detective hunt to understand how the powerful new drugs work.

The interviewees include some of the key figures in the clinical discovery of the antipsychotic effects of chlorpromazine and other phenothiazines in the 1950s (Pichot, Lehmann, Cole) and the later discovery of clozapine (Angst, Meltzer). One is struck by how easy it was in the early days to test new drugs in patients and how this contributed to the rapid development of the field. The early discovery of the antidepressant effects of imipramine and amitriptyline and the development of these compounds and the second-generation compound clomipramine are portrayed from both the clinical viewpoint (Ayd) and that of one of the companies involved, Ciba-Geigy (Broadhurst, Beaumont). One would have liked to have heard more from scientists who worked in other pharmaceutical companies. Perhaps this can be done in a planned second volume.

Discovering the pharmacological mechanisms that underlie the clinical actions of the new antipsychotic and antidepressant drugs led to the development of a whole new field of basic research. The field has been dominated by the view that the monoamine neurotransmitters, norepinephrine, dopamine, and 5-hydroxytryptamine (serotonin), play key roles in the actions of these drugs. Interviews with Axelrod, Bloom, Carlsson, Delini-Stula, Garattini, Leonard, Steinberg, and Waldmeier describe the development of monoamine research. The discovery of amine reuptake as a mechanism for monoamine inactivation (Axelrod) led to the understanding that the tricyclic antidepressants acted by blocking the reuptake of norepinephrine and serotonin, making more of these substances available to act on receptors in brain. This led in turn to the development of the modern generation of serotonin-selective reuptake inhibitors epitomized by fluoxetine (Prozac), which have had such a large impact in recent years expecially with the *Listening to Prozac* generation of psychiatrists. The discovery of dopamine as a monoamine neurotransmitter in brain (Carlsson) was followed by the key discovery that antipsychotic drugs have a common mechanism of action as dopamine antagonists. These insights into how the new treatments worked led in turn to the development of "monoamine hypotheses" of depression and psychosis, well described by their proponents Coppen, van Praag, Sandler, and Carlsson.

Regrettably, although they have much heuristic value, such hypotheses have proved difficult to prove or disprove. The monoamine era has also not opened really new avenues for the discovery of medicines affecting the central nervous system. The basic mechanism underlying Prozac, inhibition of monoamine reuptake, is not different from that of the original tricyclic antidepressants imipramine and amitriptyline. Although more than a hundred drugs have been introduced for the treatment of schizophrenia, they all resemble the original chlopromazine in their mode of action.

Not all central-nervous-system drugs involve monoaminergic mechanisms. The benzodiazepine tranquilizers (such as Valium) and anti-panic agents act by enhancing the inhibitory actions of the amino acid neurotransmitter GABA (gamma aminobutyric acid). These drugs were enormously popular in the 1960s, and their application to the treatment of panic disorders and the clinical definition of such disorders was another important advance (Klein). The popularity of the benzodiazepines has waned, however, since the understanding that their chronic use could lead to dependence (Lader).

The interviews are fascinating not least for the personal insights they give of the scientists themselves. Overall this book gives a fresh insight into the history of developments of far-reaching impact on medicine and society, and it provides much that should interest readers from many branches of science.

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Vignettes: Weighing Words

I was tired—bone tired—of having to speak in a tentative voice, using the usual mealymouthed academic circumlocutions that allowed me and my friends to say exactly what we thought without having to commit ourselves to its correctness. Our lectures and published reports were riddled with the same waffling words: "implicate," "suggest," "is consistent with." We trembled at the prospect of stating anything with total certainty, fearful that years down the road some enterprising graduate student would find a flaw in what we said and then, God forbid, reveal us as fools. So we built escape hatches into all our prose, and made the wordcrafting of equivocation into a higher form of art.

—*Robert A. Weinberg*, in *Racing to the Beginning of the Road: The Search for the Origin of Cancer* (Harmony)

When Mrs. Horace Busby invited me to speak . . . she wrote that I should talk "about the year 2000 and the changes that will have been *wrought* by then in the lives of women. . . ." As soon as I heard the word "wrought" in her letter of invitation, I realized that in preparing my talk . . . I would have to take greater cognizance of the feminine point of view. For, as you know, the word "wrought"—to a woman—means fashioned, as in the case of jewelry, or elaborately ornamented, as in the case of tapestry. But to a man and a chemist like myself "wrought" means hammered or beaten into shape by tools, or "wrought iron," which contains less than three percent carbon and has one or two percent of slag mixed with it.

—*Glenn T. Seaborg*, in a 1967 talk reprinted in *A Scientist Speaks Out: A Personal Perspective on Science, Society and Change* (World Scientific)

Browsings

The Archaeology of Ancient Arizona. Jefferson Reid and Stephanie Whittlesey. University of Arizona Press, Tucson, 1997. xii, 299 pp., illus. $40, ISBN 0-8165-1380-5; paper, $17.95, ISBN 0-8165-1709-6.

Two archaeologists expound for general readers "Arizona's prehistoric past and the archaeologists who have made it come alive."

Visual Explanations. Images and Quantities, Evidence and Narrative. Edward R. Tufte. Graphics Press, Cheshire, CT, 1997. 158 pp., illus. $45. ISBN 0-961-3921-2-6.

The author of *The Visual Display of Quantitative Information* and *Envisioning Information* presents a new work "about *pictures of verbs*, the representation of mechanism and motion, of process and dynamics, of causes and effects, of explanation and narrative."