

BOOK REVIEWS

Genetic Paradigms

The *lac* Operon. A Short History of a Genetic Paradigm. BENNO MÜLLER-HILL. De Gruyter, Hawthorne, NY, 1996. x, 207 pp., illus. Paper, \$35.95, DM 54, öS 400, or sFr 54. ISBN 3-11-014830-7.

This book was motivated by the inability of a Ph.D. student during an oral exam to tell the author what Max Delbrück did, even though they worked in the eponymous laboratory. Müller-Hill laments, "Molecular Biology has no history for the young scientist." The result is a book that begins with Noah and ends with Goethe. In between is a terse but complete narrative of the genetic vehicle that allowed the working out of the Central Dogma and the regulation of gene expression. Müller-Hill's scientific career spans the entire development of the *lac* operon from theory through repressor isolation, DNA sequencing, and protein three-dimensional structures. It began with his β -galactosidase mechanistic studies as a thesis project and the isolation of Lac repressor as a postdoc with Walter Gilbert. His productive laboratory in Cologne sequenced the repressor protein and has unfolded much of the complexity of *lac* operon regulation in the past two decades. Although Müller-Hill started life as a chemist, this book is the perspective of a geneticist. It is one part chronicle, one part memoir, and one part scientific review. The time is right for this retrospective, since molecular structures of β -galactosidase and the repressor with DNA have just been worked out.

Part 1 begins with the background to the Cartesian publications of François Jacob and Jacques Monod. It ends in 1976, when Monod died and Gilbert, distracted by DNA sequence determination, failed to attend the second Cold Spring Harbor *lac* operon reunion. What most students see in today's biology and genetics textbooks as the paradigm of gene regulation is the picture of 1976.

Part 2, Misinterpretations, is in the spirit of the *au courant* memoir, stopping short of revealing alcoholism or mental illness. In addition to describing several *faux pas* from his own laboratory, the author names names, pointing out, with literature citations, the gaffes of noted geneticists, biochemists, crystallographers, and genome

lexicographers, some dead, most living. The list is not all-inclusive but reflects the centrality of the *lac* operon in the epistemology of gene regulation.

Part 3 is an excellent scientific review of the current knowledge of transcriptional regulation in the *lac* operon and its uses as vector and indicator in eukaryotic systems. Today's molecular biology was presaged in the study of the *lac* operon. A genetic vector with overproduction was first constructed for the isolation of Lac repressor (and amber suppressor Su III⁺ RNA) in order to do biochemistry. Analysis of the *lac* operator DNA by Gilbert led to the sequence of the *lacI* gene by Philip Farabaugh. Combined with the Herculean genetics of Jeffrey H. Miller, this sequence foreshadowed p53 hot spots and malleability of DNA with tandem repeats.

Absent from Müller-Hill's account is the introduction of allostery by Monod, J.-P. Changeux, and Jacob in 1963—an essential feature of macromolecular control through small-molecule interaction. Also missing are the von Hippel school's attempts to understand Lac repressor specificity and thermodynamics in the context of the other 4.7 million base pairs of genomic DNA and the ions of the intracellular milieu.

Müller-Hill declares the *lac* operon a paradigm because of the biological principle that "what works survives; what does not work becomes extinct. Elegant solutions are used again and again. Paradigmatic systems have thus revealed their beauty earlier than others." Actually, there are three practical reasons for the *lac* operon's paradigmatic position: (i) β -galactosidase activity has a 1000-fold dynamic range upon induction; (ii) isopropyl-thio- β -galactoside is a gratuitous inducer, not affected by β -galactosidase; (iii) when hydrolysed by β -galactosidase, X-gal gives the familiar blue color to bacterial colonies on plates or to tissues.

Müller-Hill's real lament is not lack of interest in history but a paradigm shift in biological research foreseen by Gilbert in 1991 (*Nature* 349, 99): to the high school student biological research is now surfing the Internet; to undergraduates it is PCR amplification of c-DNA libraries; to graduate students it is genetics experiments by sequence homology searches through a genome database; and to the rest of us old

geezers it is word-processing rearrangement of manuscripts, proposals, and unread photocopied publications. There is still a lot to do. For a structural biologist, the RNA polymerase entry at the *lac* promoter is a vast void. The recent publication by Inada *et al.* (*Genes to Cells* 1, 293 [1996]) on interplay between glucose and lactose and the *lac* operon will require major textbook revision.

Who should read the present book? All textbook authors and teachers must read parts 1 and 3. Students should read part 2 to see that some giants, including their thesis advisers, have clay feet.

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A Physical Atelier

The Quantum Theory of Fields. Vol. 2, Modern Applications. STEVEN WEINBERG. Cambridge University Press, New York, 1996. xxii, 489 pp., illus. \$47.95 or £32.50. ISBN 0-521-55002-5.

Some time ago I visited a harpsichord-maker in his workshop. The artisan showed me his materials, explained the various stages in the construction of harpsichords, then treated me to a recording of Igor Kipnis playing a fandango on one of his instruments. But the object he took the greatest pleasure in showing me was not a finished harpsichord but a block plane—clean, precise, and utterly apt—that he had built in order to sculpt soundboards of surpassing beauty and eloquence. This maker of wonderful instruments was also a maker of wonderful tools.

Reading volume 2 of *The Quantum Theory of Fields* took me back to the harpsichord-maker's workshop, because Steven Weinberg is one of our most gifted makers of theoretical tools as well as a virtuoso in their use. His new book conveys both the satisfaction of understanding nature and the feel of the atelier, for the "modern applications" of its subtitle include both the derivation of physical consequences and the development of new tools for understanding and applying field theory itself.

Quantum field theory is the theory of matter and its interactions that grew out of efforts begun in the late 1920s to join quantum mechanics and relativity. Thanks in considerable measure to its successes over the past quarter-century, quantum field theory has become the preferred conceptual