The ABCs of genomics

A Primer of Genome Science

By Greg Gibson and Spencer Muse

Sinauer Associates Inc., $44.95, ISBN 0-87893-234-8, 200.

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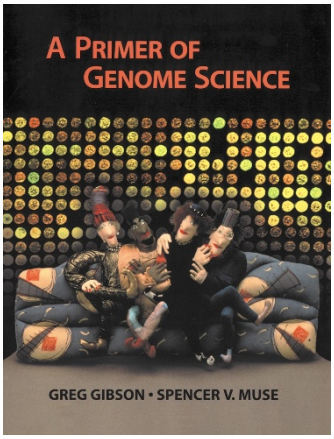
Some observers say that we are now entering the post-genomic age. If so, *A Primer of Genome Science,* billed as "the first introductory genomics textbook," would be missing the wave. More broadly interpreted, however, genome science will be the watchword for the next two decades, and this volume provides a handy introduction and reference.



Gibson and Muse intend their volume as a text for advanced undergraduates and for graduate students entering the field. The book assumes a strong background in college-level genetics and molecular biology. It is firmly grounded in statistical genetics and presents a critical view of most of the latest techniques in the literature. Introductory chapters on the basics of mendelian genetics, linkage, the central dogma of molecular biology, and bioinformatics might have been useful, especially if the book is to help students who may be moving from the information sciences into genomics, as well as traditionally trained biology students who need to better understand informatics. The text may be ambitious for an undergraduate course, but certainly bridges the gap between yesterday's training and today's genomics for graduate students and professionals in need.

A Primer of Genome Science, for all it takes on, is astoundingly accurate. Most definitions, in the text itself or in a thorough glossary, are rigorous, eschewing the *ad hoc* terminology that has come to characterize the field of genomics as it evolved from biochemistry. The authors take an appropriately broad view of genomics. Rather than state, as many have, that genes make proteins, Gibson and Muse recognize the key role of certain RNA molecules that are not translated into proteins. These include *Xist* in mammals, which has a central role in X-chromosome inactivation. The authors state, without documentation, that *Xist* "is disrupted in individuals with fragile-X syndrome," an interesting connection, but probably a typographical error. Nevertheless, the authors seem to understand that the genome has a role beyond the proteins it encodes.

In their coverage of the human genome project, Gibson and Muse steer appropriately clear of the politics, although a little clarification of 'who's who' in the various human genome projects would have been useful, given the ongoing battle between the leaders of the public and private sequencing projects. The lengthy chapter on genome projects really does cover a range of organisms. Gibson and Muse make ample use of comparative data, emphasizing throughout the book the usefulness of various organisms in facilitating our understanding of genomics. Perhaps one day we will no longer have to use the patronizing term 'model organism' to justify studies that are not of direct medical or agricultural relevance.

The book not only presents a wide variety of technical approaches, but carefully analyzes how they are used and when specific methods are most appropriate. For instance, the use of different kinds of microarrays, including the Affymetrix GeneChip, are contrasted and evaluated, as is serial analysis of gene expression (SAGE). The statistical methods required for assessing the information from microarrays are described in detail. Description of the preparation of arrays and probes distinguishes this text from the many purely informatics-oriented books that have appeared over the past year. In addition, the authors include several methods of assessing genetic linkage, including case-based association studies and linkage disequilibrium mapping. They are attuned to some of the pitfalls of human genetics.

Pharmacogenomics receives surprisingly little attention. This is a pity, because a book like this could be very useful to the pharmaceutical community, where genome science is likely to lead the way in drug discovery and 'personalized' medicine.

The text is supported by a website (http://www.sinauer.com/genomics). It features exercises, some of which require that data files be downloaded by the reader (for the enthusiastic student, there are ample exercises at the end of each chapter that do not refer to the website). This is an essential tool, as many of the concepts are not quite clear until one actually carries out the tasks, like alignments and contig assembly, that are described in the text. In addition, links mentioned in the book appear as hypertext on the website. This feature, however, does not seem to include all links, and was organized by chapter rather than as a comprehensive and useful catalog of links. The text itself has a better list of links in the chapter on integrative genomics, with useful descriptions of each entry. This, too, was restricted in coverage, not even including many of the sites mentioned elsewhere on the very same two-page spread.

In an all-too-brief final chapter, Gibson and Muse take on the emerging fields of metabolomics and systems biology. The authors review *in silico* genomics, in which the analysis of genomes and proteomes gives way to the modeling of gene networks and metabolic pathways. Starting from "the predominantly reductionist framework of contemporary genetics…as a means for identifying genes of interest which can then be studied using classical methods," the authors assert that "genome science will emerge as an independent discipline when a novel framework for studying and understanding biological complexity matures."

The problem is an interesting one. Microarrays, for instance, can provide enticing views of 'patterns' of gene expression or genetic polymorphisms. We can digitize, cluster and view them graphically so that our minds can make sense of them. This understanding can then be used to classify disease states and describe stages of development. The systems overview is indeed crucial. But to effect therapy or experimentally perturb developmental processes, we must know about the expression of specific genes, even if there are scores of them with a predominant role. The goal of pharmacogenomics is pharmacogenetics, and the goal of genomics is genetics. Is genomics (or any other –omics we name) really a new discipline, or is it the next incremental step in the quest that Mendel began in the nineteenth century? □