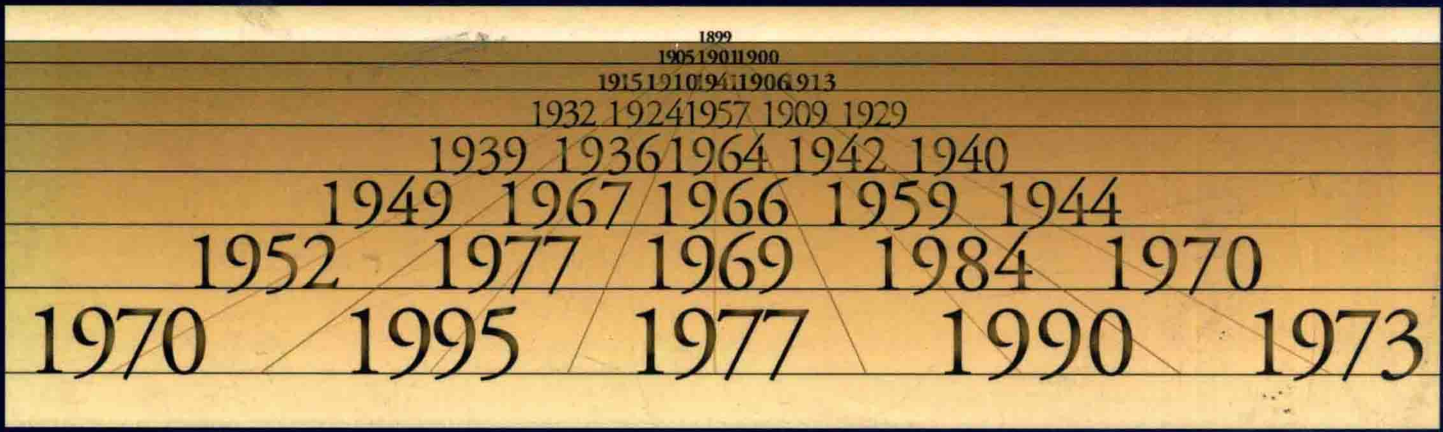
# Microbiology

## A CENTENARY PERSPECTIVE

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WITH A FOREWORD BY

**Joshua Lederberg**

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ASM Press

# *Microbiology Past, Present, and Future*

JOSHUA LEDERBERG

The advisory committees charged with compiling this collection have concluded a yeoman's task despite many potential frustrations, above all the draconian limits of space. What has been distilled is a set of exciting episodes, with each paper ably introduced to provide the local context of discovery. The introductions are necessarily brief, each merely opening a window to a larger vista of historical and personal biographical portrayals and stories from which many more lessons can be learned.

Other works are available to offer further detail on these seminal stories in microbiology, although none as far as I know concentrates on biographies of microbiologists; an annotated bibliography of such works could be valuable in bringing us forward from Paul de Kruif's *Microbe Hunters* and René Dubos' *Louis Pasteur—Free Lance of Science*. Not to be overlooked are less hagiographic studies, like Gerald Geison's *The Private Science of Louis Pasteur*. Sensitive, well-informed autobiographical works such as François Jacob's *The Statue Within* or Arthur Kornberg's *For the Love of Enzymes* are treasures, but few and far between. But the task assigned to the committees was to represent more the work of microbiologists in history than their lives, and this volume presents the opportunity to see the works essentially as they were initially published.

Because students will often exploit any excuse not to read, particularly not to read works more than 5 years old, not to mention those that predate their own lives, the ready reaccessibility of these historic documents will be of some assistance in connecting 21st-century researchers with their 20th-century roots. This may be less a problem in future, as more of the literature becomes available (and, one hopes, is well archived) in electronic media. Today, science libraries are in a state of transition; there is just no longer room for masses of old paper, and the "right stuff" embedded therein becomes harder to find. It is hard to foresee how all the back issues of print journals could be translated into byte-lingo, although without that the ravages of time and acid paper are bound to diminish our heritage. A valuable task for scientific societies and organizations would be to attend to the long-term preservation of this literature, perhaps on CD or via the Internet.

The American Society for Microbiology maintains extensive and valuable archives at the Albin O. Kuhn Library on the campus of the University of Maryland, Baltimore County. The National Library of Medicine (NLM) also is stepping into the breach with its excellent MEDLINE bibliography. (The delimiters "biography" and "famous persons" tend to point to journal articles of interest; books are harder to find.) In a new program, the NLM is opening a web site for archival material: its prototype collection (which I had the fortune to compile) relates to the same 1944 paper on DNA by O. T. Avery (with Colin, MacLeod, and McCarty) selected for the current volume. Because this paper presents the recognition of the genetic function of DNA, there is little controversy about its seminal role in the dawning of modern biology. See also http://www.profiles.nlm.nih.gov to browse relevant publications, including several books, and personal correspondence pertaining to that discovery. If the NLM archival experiment can be extended—and future barriers are more likely to be institutional and connected with intellectual rather than technical or economic property—there will be a fuller exploitation of the newest media to better understand our historical past.

My own commentary here intentionally minimizes reference to primary sources—several encyclopedic reviews are readily available for detail, and the stories are too complex to be encompassed by single references.

Turning now from process to concept, from trees to forest, can one extract some enduring themes from all the pickaxe work of factual discovery? I believe so, but with some relief that the detail is also beautifully presented in the selections. History is rarely wrapped in tidy, non-orthogonal packages; so my categories admittedly overlap, nor are they all at the same level of abstraction.

## Integration of Microbes with Mainstream Biology

As late as 1925, Edmund B. Wilson's magisterial *The Cell in Development and Heredity*, in all its 1232 pages, indexed just three oblique references to bacteria: p. 84, "nucleus" (described as controversial); p. 209, "division," amitotic; and p. 580, "sex" ("In the Bacteria, Cyanophyceae, and certain other low forms no sexual process has thus far been made known . . ."). For their part, textbooks of bacteriology were no more revealing about the relationship of bacterial cells to the rest of the biological world. With the outstanding exception of Topley and Wilson's *Principles of Bacteriology and Immunity* in its numerous editions since 1929, they tended to be even more obfuscating well into the 1950s.

A major conceptual turning point was the publication of René Dubos' *The Bacterial Cell* in 1945, just in the midst of the wave of discovery of spontaneous mutation, of genetic transformation, of (conjugal) genetic recombination—i.e., sex—in bacteria, and soon after of virus-mediated transduction.

These discoveries bolstered the idea that findings in bacteria could be correlated with genes, linkage maps, chromosomes, mutation, and hence Darwinian evolution, as had been worked out for most of the rest of the plant and animal kingdoms. It was particularly important to dispel the confusion between the bacterial culture (or colony) and the single plant or animal organism, by understanding that the culture had to be regarded as a population of potentially disparate units, each capable of clonal propagation. The concept of the "clone" was all-important in understanding, for example, selection for drug resistance; eventually it fed back into macrobiological thinking, encouraging theories such as the origin of cancer in somatic mutation. These axioms are so thoroughly interwoven in today's cell biology that it is hard to recall how many sermons had to be preached in days of yore.

The biochemists were far in the lead, and the very earliest studies of metabolic pathways and enzymes spoke to the underlying unity of biochemistry, almost to a fault. (As Seymour Cohen has pointed out, we do ultimately rely on biochemical disparity for the effectiveness of chemotherapy.) The realization that the same nutritional building blocks—amino acids, vitamins, purines, and pyrimidines—were found in bacteria and other species spoke strongly for that unity. The initial discovery of the amino acid methionine by J. H. Mueller in 1922 as a bacterial growth factor was a particular triumph.

We should understand, however, that bacteriology was originally founded on the idea of a martial struggle: disinfection—ridding the human environment of parasitic germs, or, failing that, immunization to counter them—took priority over fundamental curiosity. The idea that we could discover more of our own nature by dispassionate study of the microscopic "bugs" was beyond the ken of the hygienic enthusiasts. Never mind that we could hope to match the immense reproductivity of microbes, their germinal potential, only by the use of our own wits—that is a lesson we are only now assimilating while being assaulted by HIV, malaria, and tuberculosis as ongoing scourges. By contrast, the "Delft School" of general microbiologists, represented by Martinus W. Beijerinck, Albert J. Kluyver, C. B. van Niel, and R. Y. Stanier, taught that those who "loved" the microbes would learn better how to deal with them than those who hated them.

These movements led to the displacement of the "medical" with a "biological" perspective in microbiological studies, from about the middle of the 20th century on. Now that we are further along with our fundamental concepts and tools, there is a reconvergence, and studies of pathways of microbial pathogenesis and of the dynamics of evolution of virulence are among the most exciting challenges in molecular physiology. Just this decade, when so many pathogens are being DNA sequenced almost by the month, we have these same challenges as prime motivations for functional genomics.

Nevertheless, paradoxes abound. It was a chemist, Louis Pasteur, who taught the doctors about infectious germs. It was a physician, O. T. Avery, immersed in the immunology of pneumonia, who taught the geneticists what genes were made of.

## Applied Microbiology and New Models

The iron curtain between micro- and macro-biology having been breached about 50 years ago, many of the most exciting methodological and conceptual breakthroughs in *biology* have used bacteria (and their viruses) for basic tools. Much of the DNA revolution—high points including the Avery work, then the findings of Kornberg and his associates on DNA polymerases and ligases, the initial demonstrations of DNA splicing, and hundreds of other items—falls in this category, many of the seminal papers being represented in this volume.

Lysogenic viruses and their integration into chromosomes were first shown in bacteria; analogous phenomena are paramount in our understanding of retroviruses, of oncogenesis, and of gene therapy in somatic cells of higher organisms right up to humans.

The basic principles having been worked out, including methodological and conceptual analogies between bacterial cultures and animal cell cultures, it has become feasible to move from model microbial systems to targets closer to the animal in development and disease. Of course, eucaryotic life differs from that of the bacteria in many important details. Nevertheless, we can regard the past half-century as a triumph of unified studies. The ASM journal *Molecular and Cellular Biology*, and the renaming of ASM's *Microbiology and Molecular Biology Reviews*, are representative of this exciting trend.

## Taxonomy

Meanwhile, we have seen drastic revision in our phylogenetic taxonomy of the little creatures, starting with R. Stanier and C. B. van Niel's separation of procaryotes from eucaryotes and followed by the iconoclastic split off of the Archaea. We have a long way to go in organizing a system that now relegates all multicellular organisms, with humans somewhere between corn and mushrooms, to a smudge on the wall map. And of the cellular organelles, the provenance at least of mitochondria and of chloroplasts from primeval bacteria has strong evidentiary support. In addition, hundreds of retroviral genomes are integrated into our own. We are indeed an evolutionary melting pot.

## Viruses and Smaller?

The ultimate origins of viruses remain enigmatic. All viruses are presumably fragments of DNA (or RNA) escaped from some host genome and reshaped by extensive further evolution to invade and proliferate in cells of the same or vastly different species. In their current incarnations, many viruses are episomes capable of cyclical entry and exit from chromosomal havens. Some are conceptually unified with other plasmids and a menagerie of transposable elements in their mutualistic versus parasitic role in the economy of the host cell. With the recent recognition of prions, we have to cope with the prospect of new kinds of self-propagating units, perhaps dependent on shape (versus sequence)-oriented nucleation of protein conformers.

## The Future: Evolving Boundaries

In sum, as biological science becomes ever more molecularized, we face a joyous riot of confusion about the definition of "microbiology," with its roles and missions in biomedical research, education, and services. The common denominator of experimental biology is functional genomics; this is elegantly applied to core questions of microbial identity and phylogeny and equally to the flanking fields of metabolism, infectious disease, virology, parasitology, immunology, ecology, and burgeoning applications in biotechnology and pharmaceutics.

The dilemma is in educational design: given that time is finite, what is the core curriculum to produce a "microbiologist"; besides cell biology and genomics, what should be required by way of familiarity with lifestyles of diverse microbes, with their natural history? Will the "general microbiologist" survive? We still have much to learn from comparative insights about ideal experimental laboratory objects, overlooked possibilities of disease etiology, or challenges to our generally accepted physiological and evolutionary models. Most of 20th century biology focused on a few standardized models, such as fruit flies and sea urchin eggs, for diverse and often conflicting purposes. It was strenuous labor to work out the care, feeding, and intangible lore of a novel biological system like *Arabidopsis* or *Caenorhabditis*. But if we had stuck simply with *Escherichia coli* B, of wondrous T-even phage fame, our eyes would have been closed to the marvels of conjugation and lysogeny. Now, genomics offers an easily replicable approach to any new organism, and sequence reports are tumbling out of the chute. Even uncultivable species are succumbing to that sophisticated attack—which, nevertheless, must still be informed by a McClintockian "feeling for the organism."

These tensions have riven other parts of academic biology, creating a universal trend toward the dissolution of phyletic boundaries; botany and zoology have merged into biology, then refissured into molecular, cell, developmental, organismic, ecological, and evolutionary compartments. Will microbiology continue to be defined by taxonomic lines? How will yeasts be related to *E. coli*, on the one hand; to nematodes or to human cells in culture, on the other? Will there be any logic to defining "microbiological" studies as those entailing the use of a microscope and culture media? It is testimony to the success of the microbiologist's perspective that this mode of thinking, embodied by cell culture methodology, pervades all of biology today.

The fissions and fusions will doubtless continue, accompanied by energy releases testifying to the intense dynamism of scientific progress in ways that blur all the boundaries.

## GENERAL REFERENCES

### Biography

For biographical data, see the biographical memoir series of the U.S. National Academy of Sciences and of the Royal Society (London). For biographical data over historic times, see the *Dictionary* (really encyclopedia) *of Scientific Biography* (Scribners, New York, N.Y., 1981).

### History of Microbiology

A broad-ranging history of microbiology up to current times would be a daunting task, and it is difficult to find such works more recent than Patrick Collard's *The Development of Microbiology* (Cambridge University Press, Cambridge, U.K., 1976). Most major textbooks will have introductory chapters on the history of the field. There are many other specialized works, especially on molecular genetics and DNA.

### Internet Resources

The World Wide Web has much to offer, including hot links to many external sources, e.g., http://www.profiles.nlm.nih.gov and the American Society for Microbiology site, http://www.asmusa.org/.

### *The Excitement and Fascination of Science*, vol. 1-5

Published by Annual Reviews, Inc., Palo Alto, Calif., these volumes embrace several hundred short memoirs, usually autobiographical, including those of many microbiologists.

### Overall Perspectives on Microbiology

For overall perspectives on microbiology, the following monographs and treatises are among the most comprehensive:

**Annual Reviews, Inc.** *Annual Review of Microbiology.* Annual Reviews, Inc., Palo Alto, Calif.(Volume 1 was published in 1947, and this series has been published annually to date.)

**Balows, A.** 1992. *The Prokaryotes: A Handbook on the Biology of Bacteria: Ecophysiology, Isolation, Identification, Applications*, 2nd ed. Springer-Verlag, New York, N.Y.

**Brock, T. D.** 1998. *Milestones in Microbiology*. ASM Press, Washington, D.C.

**Brock, T. D.** 1998. *Robert Koch: A Life in Medicine and Bacteriology*. ASM Press, Washington, D.C.

**Burnet, F. M., and W. M. Stanley (ed.).** 1959. *The Viruses: Biochemical, Biological, and Biophysical Properties*. Academic Press, Inc., New York, N.Y.

**Dubos, R.** 1998. *Pasteur and Modern Science*. ASM Press, Washington, D.C.

**Gunsalus, I. C., and R. Y. Stanier (ed.).** 1960. *The Bacteria: A Treatise on Structure and Function. Structure*. Academic Press, Inc., New York, N.Y.

**Lederberg, J. (ed. in chief).** 1992. *Encyclopedia of Microbiology*. Academic Press, Inc., San Diego, Calif.

**Neidhardt, F. C., R. Curtiss III, John L. Ingraham, E. C. C. Lin, K. Brooks Low, Jr., B. Magasanik, W. S. Reznikoff, M. Riley, M. Schaechter, and H. E. Umbarger (ed.).** 1996. *Escherichia coli and Salmonella: Cellular and Molecular Biology*. ASM Press, Washington, D.C.

**Peruski, L. F., and A. H. Peruski.** 1997. *The Internet and the New Biology: Tools for Genomic and Molecular Research*. ASM Press, Washington, D.C.

**Webster, R. G., and A. Granoff (ed.).** 1994. *Encyclopedia of Virology*. Academic Press Ltd., London, U.K.

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