Microbial Diversity and Bioprospecting
Microbial Diversity and Bioprospecting

EDITED BY Alan T. Bull

ASM PRESS
WASHINGTON, D.C.
## CONTENTS

**Contributors**  •  ix  
**Foreword**  *Arnold L. Demain*  •  xiii  
**Preface**  •  xv  
**Acknowledgments**  •  xix  

### I. Introduction: the Rationale

1. **Biotechnology, the Art of Exploiting Biology**  •  3  
   *Alan T. Bull*

### II. Microbial Diversity: the Resource

2. **An Overview of Biodiversity—Estimating the Scale**  •  15  
   *Alan T. Bull and James E. M. Stach*

3. **Defining Microbial Diversity—the Species Concept for Prokaryotic and Eukaryotic Microorganisms**  •  29  
   *Ramon Rosselló-Mora and Peter Kämpfer*

4. **Speciation and Bacterial Phylospecies**  •  40  
   *James T. Staley*

5. **Approaches to Identification**  •  49  
   *Fergus G. Priest*

6. **Eukaryotic Diversity—a Synoptic View**  •  57  
   *Laura A. Katz*

### III. Microbial Ecology: the Key to Discovery

7. **How To Look, Where To Look**  •  71  
   *Alan T. Bull*

8. **Culture-Dependent Microbiology**  •  80  
   *John C. Fry*

9. **Culture-Independent Microbiology**  •  88  
   *Kornelia Smalla*

10. **Resuscitation of “Uncultured” Microorganisms**  •  100  
    *Douglas B. Kell, Galya V. Mukamolova, Christopher L. Finan, Hongjuan Zhao, Royston Goodacre, Arseny S. Kaprelyants, and Michael Young*

11. **Soils—the Metagenomics Approach**  •  109  
    *Jo Handelsman*

12. **Deep Biospheres**  •  120  
    *R. John Parkes and Pete Wellsbury*

13. **Earth’s Icy Biosphere**  •  130  
    *John C. Priscu and Brent C. Christner*

14. **Extremophiles: pH, Temperature, and Salinity**  •  146  
    *Constantinos E. Vorgias and Garabed Antranikian*

15. **Extremophiles: Pressure**  •  154  
    *Fumiyoishi Abe, Chiaki Kato, and Koki Horikoshi*
16. Life in Extremely Dilute Environments: the Major Role of Oligobacteria • 160
   D. K. Button

17. Anaerobes: the Sulfate-Reducing Bacteria as an Example of Metabolic Diversity • 169
   Giry Fauque and Bernard Ollivier

18. Microbes from Marine Sponges: a Treasure Trove of Biodiversity for Natural Products Discovery • 177
   Russell T. Hill

19. Invertebrates—Insects • 191
   John A. Breznak

20. Microbial Symbioses with Plants • 204
   Peter Jeffries

IV. Biogeography and Mapping Microbial Diversity

Preamble • 213
   Alan T. Bull

21. Ubiquitous Dispersal of Free-Living Microorganisms • 216
   Bland J. Finlay and Genoveva F. Esteban

22. Microbial Endemism and Biogeography • 225
   Brian P. Hedlund and James T. Staley

23. Mapping Microbial Biodiversity Case Study: the Yellowstone National Park Microbial Database and Map Server • 232
   Daphne L. Stoner, Randy Lee, Luke White, and Ron Rope

V. The Paradigm Shift: Bioinformatics

Preamble • 239
   Alan T. Bull

24. The Paradigm Shift in Microbial Prospecting • 241
   Alan T. Bull

25. Genomics • 250
   Karen E. Nelson

26. Bacterial Proteomics • 260
   Phillip Cash

27. Phenomics • 280
   Jennifer L. Reed, Stephen S. Fong, and Bernhard Ø. Palsson

28. Phylogeny and Functionality: Taxonomy as a Roadmap to Genes • 288
   Alan C. Ward and Michael Goodfellow

VI. Prospecting: the Targets

Preamble • 317
   Alan T. Bull

29. Sectors and Markets • 319
   Alan T. Bull

30. Screening for Bioactivity • 324
   Hans-Peter Fiedler

31. Antimicrobials • 336
   William R. Strohl

32. Pharmacologically Active Agents of Microbial Origin • 356
   Stephen K. Wrigley

33. Bioprospecting for Industrial Enzymes: Importance of Integrated Technology Platforms for Successful Biocatalyst Development • 375
   Thomas Schäfer and Torben Vedel Borchert

34. Plant Growth-Promoting Agents • 391
   James M. Lynch

35. Biotreatment • 397
   Linda Louise Blackall and Christine Yeates

36. Bioprospecting Novel Antifoulants and Anti-Biofilm Agents from Microbes • 405
   Carola Holmström, Peter Steinberg, and Staffan Kjelleberg

VII. Conservation of Microbial Gene Pools

Preamble • 415
   Alan T. Bull

37. Extinction and the Loss of Evolutionary History • 417
   Alan T. Bull
38. What Is the Evidence for the Loss of Microbial Diversity? • 421
James Borneman

VIII. Convention on Biological Diversity: Implications for Microbial Prospecting

Preamble • 429
Alan T. Bull

39. The Convention on Biological Diversity and Benefit Sharing • 431
Kerry ten Kate

40. The Historical Context of Present Bioprospecting—Four Cases • 440
Hanne Svarstad

41. Biodiversity Prospecting: the INBio Experience • 445
Giselle Tamayo, Lorena Guevara, and Rodrigo Gámez

42. Contracts for Bioprospecting: the Yellowstone National Park Experience • 450
Holly Doremus

43. Natural Products Research Partnerships with Multiple Objectives in Global Biodiversity Hot Spots: Nine Years of the International Cooperative Biodiversity Groups Program • 458
Joshua P. Rosenthal and Flora N. Katz

IX. Conclusion

44. The Value of Biodiversity • 469
David W. Pearce

Index • 477
CONTRIBUTORS

F. Abe
The DEEPSTAR Group, Japan Marine Science and Technology Center (JAMSTEC), 2-15 Natsushima-cho, Yokosuka 237-0061, Japan

G. Antranikian
Technical University of Hamburg-Harburg, Biotechnology/Technical Microbiology, Kasernenstrasse 12, D-21071 Hamburg, Germany

Linda L. Blackall
Advanced Wastewater Management Centre, Department of Microbiology and Parasitology, The University of Queensland, Brisbane, 4072 Queensland, Australia

Torben Vedel Borchert
Novozymes A/S, Krogshøjvej 36, 2880 Bagsværd, Denmark

James Borneman
Department of Plant Pathology, Boyce Hall 3489, University of California, Riverside, Riverside, CA 92521

John A. Breznak
Department of Microbiology and Molecular Genetics, 6190 Biomedical and Physical Sciences, Michigan State University, East Lansing, MI 48824-4320

Alan T. Bull
Research School of Biosciences, University of Kent, Canterbury, Kent CT2 7NJ, United Kingdom

D. K. Button
Institute of Marine Science, University of Alaska, Fairbanks, AK 99775

Phillip Cash
Department of Medical Microbiology, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, United Kingdom

Brent C. Christner
Department of Land Resources and Environmental Sciences, 304 Leon Johnson Hall, Montana State University, Bozeman, MT 59717

Arnold L. Demain
Charles A. Dana Research Institute (R.I.S.E.), HS-330 Drew University, Madison, NJ 07940

Holly Doremus
University of California at Davis, School of Law, 400 Mrak Hall Drive, Davis, CA 95616

Genoveva F. Esteban
Center for Ecology and Hydrology, Dorset, Winfrith Newburgh, Dorchester, Dorset DT2 8ZD, United Kingdom

Guy Fauque
UR 101 Extrêmophiles, Institut de Recherche pour le Développement IFR-BAIM, Universités de Provence et de la Méditerranée, ESIL, Case 925, 163 avenue de Luminy, F-13288 Marseille Cedex 09, France

Hans-Peter Fiedler
Mikrobiologisches Institut, Universität Tübingen, Auf der Morgenstelle 28, D-72076 Tübingen, Germany

Bland J. Finlay
Center for Ecology and Hydrology, Dorset, Winfrith Newburgh, Dorchester, Dorset DT2 8ZD, United Kingdom
CONTRIBUTORS

Christopher L. Finan
Institute of Biological Sciences, University of Wales, Aberystwyth, Aberystwyth SY23 3DD, United Kingdom

Stephen S. Fong
Department of Bioengineering, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0419

John C. Fry
Cardiff School of Biosciences, Main Building, Cardiff University, Park Place, Cardiff CF10 3TL, United Kingdom

Rodrigo Gámez
Instituto Nacional de Biodiversidad, 3100 Santo Domingo, Heredia, Costa Rica

Royston Goodacre
Institute of Biological Sciences, University of Wales, Aberystwyth, Aberystwyth SY23 3DD, United Kingdom

Michael Goodfellow
School of Biology, University of Newcastle, Claremont Road, Newcastle upon Tyne NE1 7RU, United Kingdom

Lorena Guevara
National Institute of Biodiversity (INBio), 3100 Santo Domingo, Heredia, Costa Rica

Jo Handelsman
Department of Plant Pathology, University of Wisconsin, 1630 Linden Drive, Madison, WI 53706

B. P. Hedlund
Department of Biological Sciences, University of Nevada, Las Vegas, 4505 Maryland Parkway, Las Vegas, NV 89154-4004

Russell T. Hill
Center of Marine Biotechnology, University of Maryland Biotechnology Institute, Columbus Center Suite 236, 701 East Pratt Street, Baltimore, MD 21202-4031

Carola Holmström
Department of Microbiology and Immunology, School of Biotechnology and Biomolecular Sciences, University of New South Wales, Sydney, NSW 2052, Australia

Koki Horikoshi
The DEEPSTAR Group, Japan Marine Science and Technology Center (JAMSTEC), Yokosuka 237-0061, Japan

Peter Jeffries
Department of Biosciences, University of Kent, Canterbury, Kent CT2 7NJ, United Kingdom

Peter Kämpfer
Institut für Angewandte Mikrobiologie, Justus-Liebig Universität Giessen, Heinrich-Buff-Ring 26-32, D-35392 Giessen, Germany

Arseny S. Kaprelyants
Bakh Institute of Biochemistry, Leninskii Prospekt 33, 117071 Moscow, Russia

Chiaki Kato
Department of Marine Ecosystems Research, Japan Marine Science and Technology Center (JAMSTEC), Yokosuka 237-0061, Japan

Flora N. Katz
Fogarty International Center, National Institutes of Health, 31 Center Drive, Bethesda, MD 20892-2220

Laura A. Katz
Department of Biological Sciences, Smith College, Northampton, MA 01063

Douglas B. Kell
Department of Chemistry, Faraday Building, Sackville Street, UMIST, P.O. Box 88, Manchester M60 1QD, United Kingdom

Staffan Kjelleberg
Department of Microbiology and Immunology, School of Biotechnology and Biomolecular Sciences, University of New South Wales, Sydney, NSW 2052, Australia

Randy Lee
Ecological and Cultural Resources, Idaho National Engineering and Environmental Laboratory, Idaho Falls, ID 83415-2213

James M. Lynch
Forest Research, Alice Holt Lodge, Farnham, Surrey GU10 4LH, United Kingdom
Galya V. Mukamolova
Institute of Biological Sciences, University of Wales, Aberystwyth, Aberystwyth SY23 3DD, United Kingdom

Karen E. Nelson
Institute of Genome Research TIGR, 9712 Medical Center Drive, Rockville, MD 20850

Bernard Ollivier
Directeur UR101 Extrémophiles, Institut de Recherche pour le Développement, IFR-BAIM, Universités de Provence et de la Méditerranée, ESIL, Case 925, 163 avenue de Luminy, F-13288 Marseille Cedex 09, France

Bernhard O. Palsson
Department of Bioengineering, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0419

R. J. Parkes
Department of Earth Sciences, University of Cardiff, Main Building, P.O. Box 914, Cardiff CF10 3YE, United Kingdom

David W. Pearce
Department of Economics, University College London, Gower Street, London WC1E 6BT, United Kingdom

Fergus G. Priest
School of Life Sciences, John Muir Building, Heriot-Watt University, Riccarton, Edinburgh EH14 4AS, United Kingdom

John C. Priscu
Department of Land Resources and Environmental Sciences, 309 Leon Johnson Hall, Montana State University, Bozeman, MT 59717

Jennifer L. Reed
Department of Bioengineering, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0419

Ron Rope
Ecological and Cultural Resources, Idaho National Engineering and Environmental Laboratory, Idaho Falls, ID 83415-2213

Joshua P. Rosenthal
Fogarty International Center, National Institutes of Health, 31 Center Drive, Bethesda, MD 20892-2220

Ramon Rosselló-Mora
Group d'Oceanografia Interdisciplinar, Institut Mediterrani d'Estudis Avancats (CSIC-UIB), Miquel Marques 21, E-07190 Esportes (Illes Balears), Spain

Thomas Schäfer
Novozymes A/S, Krogshøjvej 36, 2880 Bagsvaerd, Denmark

Kornelia Smalla
Federal Biological Research Centre for Agriculture and Forestry, Institute for Plant Virology, Microbiology and Biosafety, Messeweg 11-12, D-38104 Braunschweig, Germany

James E. M. Stach
Research School of Biosciences, University of Kent, Canterbury, Kent CT2 7NJ, United Kingdom

James T. Staley
Department of Microbiology, University of Washington, Seattle, WA 98195

Peter Steinberg
Centre for Marine Biofouling and Bio-Innovation, School of Biological Science, University of New South Wales, Sydney, NSW 2052, Australia

Daphne L. Stoner
Biotechnology Department, Idaho National Engineering and Environmental Laboratory, P.O. Box 1625, Idaho Falls, ID 83415-2203

William R. Strohl
Department of Biologics Research, Merck Research Laboratories, P.O. Box 2000, Mail drop RY80Y-215, Rahway, N.J. 07065

Hanne Svarstad
NINA, P.O. Box 736 Sentrum, 0105 Oslo, Norway

Giselle Tamayo
National Institute of Biodiversity (INBio), 3100 Santo Domingo, Heredia, Costa Rica
Kerry ten Kate
Insight Investment, 33 Old Broad Street, London EC2N 1HZ, United Kingdom

Constantinos E. Vorgias
National and Kapodistrian University of Athens, Faculty of Biology, Department of Biochemistry-Molecular Biology, Panepistimiopolis-Zographou, 15701 Athens, Greece

Alan C. Ward
School of Biology, University of Newcastle, Claremont Road, Newcastle upon Tyne NE1 7RU, United Kingdom

Pete Wellsbury
Department of Earth Sciences, University of Bristol, Bristol BS8 1RJ, United Kingdom

Luke White
Programmatic Software Development, Idaho National Engineering and Environmental Laboratory, Idaho Falls, ID 83415-3419

Stephen K. Wrigley
Cubist Pharmaceuticals (UK) Ltd., 545 Ipswich Road, Slough, Berkshire SL1 4EQ, United Kingdom

Christine Yeates
Advanced Wastewater Management Centre, The University of Queensland, St. Lucia, Queensland 4072, Australia

Michael Young
Institute of Biological Sciences, University of Wales, Aberystwyth, Aberystwyth SY23 3DD, United Kingdom

Hongjuan Zhao
Institute of Biological Science, University of Wales, Aberystwyth, Aberystwyth SY23 3DD, United Kingdom
This is an exciting time for those involved in bioprospecting, especially in the pharmaceutical area; indeed this field is at a crossroads in its development. Whereas ingenuity, innovation, and product introduction have been deaccelerated by the mega mergers of the pharmaceutical industry, the new opportunities now available for the development of new drugs are staggering. Indeed, the high cost of these novel opportunities to "big pharma" has in part contributed to the downgrading of natural product research and development. The loss of interest in this most important aspect of new drug innovation is of course only temporary because its replacement by combinatorial chemistry, genomics, and high-throughput screening has not been productive. This opinion is not a conclusion arrived at by biologists; rather, it has been stated publicly by prominent medicinal chemists. So what is to be done? The answer is a synergistic combination of the traditional and the new, i.e., combining intelligent bioprospecting of nature's diversity with the novel techniques of genomics, proteomics, metabolomics, metagenomics, combinatorial chemistry, combinatorial biosynthesis, high-throughput screening, and bioinformatics. We are fortunate that, during this period of downgrading of natural products by the major drug companies, a number of smaller biotechnology companies have picked up the slack by entering the arena of natural product discovery. They are using some of the newer techniques in their efforts as well as expanding the search to relatively ignored environments such as the ocean.

When one speaks about natural products, included are biopharmaceutical (i.e., erythropoietin) primary metabolites such as amino acids and vitamins, secondary metabolites (penicillin G), products discovered in nature but made by chemical synthesis (thienamycin), and chemical derivatives of natural products (clarithromycin). Successful applications have included antibiotics, antitumor agents, enzyme inhibitors, antiparasitic agents, bioherbicides, algicides, and bioinsecticides. Of great importance for pharmaceutical discovery are new targets such as receptor-ligand binding, reporter genes, adhesion, proteosome action, signal transduction, and cell-to-cell communication. For antitumor agents, recent targets have included protein kinase C, farnesyl protein transferase, P53-related targets, proteosomes, and telomerase.

Many of the new developments in industrial microbiology derive from the birth of molecular biology in the 1950s and of recombinant biotechnology in the 1970s. Of special interest is the area of industrial enzymes that has made major strides because of cloning and the complementary techniques of protein engineering and directed molecular evolution. These enzymes have great use in food processing, detergents, cleaning of contact lenses, biosensors, and molecular biology (DNA polymerase for the polymerase chain reaction, and restriction enzymes). Enzymes and cellular bioconversions have been applied in the preparation of chiral drugs that are currently desired by industry and health authorities. Many industrial enzymes are derived from thermophilic, alkaliophilic, or psychrophilic microbes ("extremophiles") from areas of high biodiversity interest. Environments of interest for bioprospecting are soil, the marine environment including the deep biosphere, the icy biosphere, marine sponges, and insects. Plants harbor many microbial symbionts that are a good source of alkaloids and other drugs, biocontrol agents, plant growth stimulators, agents protecting plants from abiotic stress, and for ecosystem restoration. Other current or potential benefits of exploring microbial diversity include (i) the economical and environmentally important replacement of chemical processes by biological procedures in the manufacture of riboflavin, acrylicamide, 7-aminoccephalosporanic acid, and 7-amino-6-deacetoxycephalosporanic acid; (ii) control of agricultural pollution by the use of feed enzymes such as...
phytase; (iii) replacement of petroleum, plastics, and other materials by bioprocessing of renewable raw materials; (iv) bioremediation and biodegradation of polluting materials; (v) discovery of new plant growth promoting microbes; and (vi) novel antifoulants and antibiofilm agents. In relation to the antifoulants, it was surprising for me to read in the present book that biofouling, i.e., the colonization of surfaces in aqueous environments by living organisms, costs the shipping industry over five billion dollars per year!

There is no doubt that biodiversity is being lost throughout the world. This is unfortunate because we need biodiversity to provide novel microbes and novel products. We are told that only 0.5 to 1% of living bacterial species and 5% of living fungal species have been cultured. Of great interest are new methods that allow isolation of previously uncultured microbes, e.g., low-nutrient media, long incubation times, dilution to extinction, ecosystem mimicry, syntrophy, and cell-to-cell communication. Of use in these efforts have been micromanipulation, optical tweezers, atomic force microscopy, and density gradient centrifugation. The newly cultured species may not do very well in industrial fermentors, but cloning of their production and regulatory genes into industrial bacteria and fungi would allow scale-up and industrial production. The metagenomics approach is a complementary development that allows expression of environmental DNA and mRNA. This very exciting area has already yielded known antibiotic products such as violacein, indirubin, and fatty dienic alcohols and new antibiotics such as acyltyrosines, terragine, and turbomycin. In addition to these secondary metabolites, new enzymes, antiporter and antibiotic resistance determinants, have been isolated from environmental nucleic acids.

It is clear that the large pharmaceutical companies will soon adapt their genomic, combinatorial chemistry, and high-throughput screening efforts to new natural product scaffolds. Such novel structures are sorely needed and will be provided by the proper utilization of biological diversity. It is extremely fortunate for the field that this book has been assembled at this time with contributions from the desks of the world's best minds of microbial diversity and bioprospecting. Of course, microbes are not the only source of remarkable drugs, but inclusion of plants and other life forms would have required much greater time and effort and would have delayed publication of this useful compilation, which is needed Now!

Arnold L. Demain
Madison, New Jersey
PREFACE

ORIGINS

This book is born out of a lifetime's fascination for microorganisms, a fascination that has been nurtured by many people and many experiences and, not the least, by undergraduate courses in systematic biology, an increasingly rare feature of degree curricula. Serendipity, I freely confess, has played a major role in sustaining this fervor for microbiology, and a significant turning point came in the 1970s when I joined the then Panel on Applied Microbiology of the United Nations Environment Programme and the United Nations Educational, Scientific, and Cultural Organization. This U.N. involvement enabled me to work with a group of extraordinarily committed humanitarian and knowledgeable microbiologists from the world over. The effect of working with Martin Alexander, Goran Heden, Roger Porter, David Pramer, Maurits la Riviere, Jacques Senez, and H. Taguchi, and others too numerous to name, was electrifying and permanent in so many ways but especially in revealing how microbiology can be developed for the common good. The panel experience had a variety of consequences for me, among them an entrée into international science and opportunities to see first hand a wide range of microbial technology being exploited in developing countries for both traditional and innovative processes. Years later this amalgam of experience led to two particular opportunities to bring microbial diversity and bioprospecting together in quite dramatic fashion—one in Indonesia that was relatively low tech and the other in Japan that was decidedly high tech.

Alfred Russel Wallace, "one of the neglected giants of the history of science and ideas," has long been one of my heroes, for, as Peter Raby concludes in his splendid biography of Wallace (P. Raby, Alfred Russel Wallace: A Life, Princeton University Press, 2001), "There is, finally something heroic about a man who independently constructs a theory of natural selection . . . and spends the rest of his life proclaiming the ideals of co-operation and altruism as the way to hasten the perfecting of the human." Consequently the chance to retrace a few of Wallace's steps in the Malay Archipelago intermittently over a period of 15 years, but collecting microorganisms rather than insects or birds of paradise, came as a piece of tremendous good fortune. Results of the ensuing biotechnology training and research program, which included mycorrhizal inoculant technology, bioremediation, biopesticides, and applied microbial taxonomy, are summarized elsewhere (Indones. J. Biotechnol., Special Issue, June 2000), but the enduring memory is of the spectacular biodiversity of that remarkable archipelago. At the westernmost peninsula of Java, facing the Sunda Strait, lies Ujung Kulon, an area that was inundated by 10- to 15-m tidal waves in 1883 following the eruption of Krakatau. Ujung Kulon now is a national park devoid of human inhabitants and notable for containing the remaining (very small) population of Javan rhino. It was here some years ago that I witnessed a glittering display of bioluminescence. Our camp, where evenings were shared with an assortment of macaques, deer, monitor lizards, geckos, and bats, was close to the shore which, on one occasion, was intensely illuminated as teeming populations of microinvertebrates were oxygenated in the breaking tide. However, a few years later even this microbiological display was eclipsed by the coral reef communities off the north coast of North Sulawesi. These reefs are one of the most spectacular in the whole Indo-Pacific region, and the realization that a very high proportion of their invertebrate biomass comprised microorganisms about which so little was known was a forceful reminder of how fragmented and incomplete was our knowledge of microbial diversity. The English naturalist Sidney Hickson, following his observations of these ecosystems, wrote "A coral reef cannot be properly described. It must be seen to be thoroughly appreciated" (Hickson, A Naturalist in North Celebes,

xv
Murray, 1889); how right he was! Readers will not be surprised to find marine invertebrates and their microbial symbionts featured in this book. Geothermal and other extreme environmental locations also are common in many parts of the archipelago and have provided further insights to the diversity of the microbial world. However, the opportunity to prospect microorganisms of truly extreme habitats was presented when Koki Horikoshi invited us to collaborate with the DeepStar program of the Japan Marine Science and Technology Agency (http://www.jamstec.go.jp). Our interest has been on the actinomycete diversity in very deep-sea sediments including those below the seafloor, where the extent of taxonomic diversity again is remarkably high. The exploration of these newly discovered biospheres is exciting and promising for bioprospecting, and various aspects of this novel field are contained in this book.

Edward Wilson probably has done more than any other individual to awaken the interest of both scientists and the public in biodiversity and why it should be promoted to a front page issue. His writings are rich in knowledge, challenging questions, and memorable imagery, and provide an especially prevailing sense of wonder. Wonder, that emotion excited by what surpasses expectation and the desire to know, is something I very much hope that readers will encounter throughout the course of this book, for, as Francis Bacon declared, “For all knowledge and wonder (which is the seed of knowledge) is an impression of pleasure in itself” (F. Bacon, Proficiency and Advancement of Learning Book I.i.3, 1605).

**REVOLUTION**

During the lifetime of my generation there has occurred an unprecedented change in which biological systems—from cell to biome—are viewed and investigated. As I attempt to show in chapter 24, this has been a revolution of genuinely Kuhnian proportions. Within the span of 50 years we have progressed from speculative debates about the organization of DNA in bacteria (see, for example, E.T.C. Spooner and B.A.D. Stocker [eds.], Bacterial Anatomy, Cambridge University Press, 1956) to a position in which students can manipulate, with facility and rationality, the DNA within and between species, and even domains! The introduction and adoption of the techniques of molecular biology have occurred with unbelievable rapidity and ease such that they now permeate the whole spectrum of biological research. Questions can now be posed, and answered, that were inconceivable and/or had minimal expectation of being resolved prior to the molecular biology era. The impact on our approach to and understanding of phylogeny and evolution, biodiversity and ecology, infection and therapy has been immense; the impact on the ways in which we exploit genetic resources in the context of biotechnology is no less impressive. In short we are of a generation that has seen the emergence of a new and powerful discipline, albeit with ill-defined boundaries, called bioinformatics. A word of caution is necessary here: bioinformatics, powerful though it is, is not the sole technoscientific driver of biotechnology; innovative developments in chemistry, chemical and biochemical engineering, computer science, and nanotechnology, for example, all have engaged with biology in transforming the search for novel drugs, chemicals, materials, and so on. Nevertheless, there has been a demonstrable paradigm shift in the way in which we do, or can do, search and discovery in biotechnology, that is, the shift from traditional biology based on specimen collection, observation, and experimentation to bioinformatics based on data collection, storage, and mining. One of the questions emerging from this paradigm shift is whether bioinformatics, in concert with approaches such as combinatorial chemistry, will displace the traditional biological approach or will exist in synergy with it. Present evidence strongly suggests that a synergy will become established.

The extent to which we are able to integrate diverse technical and analytical capabilities will be critical for the future of microbiology and biotechnology. The multidisciplinary approach has long and widely been appreciated as an essential underpin for successful biotechnology, but a comparable recognition in microbiology and among microbiologists has been slower to emerge. Recently this point was made very clear by Ed DeLong, who concluded that, “The challenge to future microbial biologists is that they must become as conversant in Earth science as nanotechnology, as familiar with systems ecology as genomes, and as well versed in global information systems as bioinformatics” (E. F. DeLong, Towards microbial systems science: integrating microbial perspective, from genomes to biomes. *Environ. Microbiol.* 4:9–10, 2002). Just as integrated technology approaches are seen as increasingly necessary for addressing the big questions in microbiology, there is a growing sense that severe reductionist science, epitomized by molecular biology, has deflected attention away from an understanding of the complexities of biological system properties. I am pleased, therefore, that many of the contributions in this book directly confront or elude to these issues of technology integration and the holistic perspective.
MICROBIAL DIVERSITY AND BIOPROSPECTING

Although this book has had a long gestation, now seems to be the appropriate time to bring together its principal themes and ideas. Equipped with a formidable set of new tools based on molecular biology, chemometrics, computing, statistics, and so on, and firmly fixed in the postgenomics era, we can begin to evaluate the effects that developments made possible by these tools are having on the way we go about exploring microbial diversity and searching for exploitable biology. The scope of this book is broad so that, in addition to those topics that might be anticipated, the reader will find other topics that are rarely considered in the context of microbial search and discovery, among them questions of biogeography, extinction, and the value of biodiversity. We also consider the implications of the Convention on Biological Diversity for microbial prospecting activities.

The book is organized in nine sections that deliberate on biotechnology and the case for natural product discovery; the resource that the microbial world presents for biotechnology; why it is important to take an ecological perspective when engaging in search and discovery; the distribution of microorganisms at the global scale and early attempts at microbial biocartography; the paradigm shift embodied in bioinformatics; some illustrations of microbial prospecting activities and their results in a range of high and not so high-added-value industries; the loss of evolutionary history and the conservation of microbial gene pools; microbiology, biotechnology innovations, and the Convention on Biological Diversity; and, finally, what we perceive as the value of biodiversity and how valuations might be made. Such a book is very unlikely to be exhaustive in its coverage; this one naturally reflects a personal survey of the landscape, and I would be pleased to have readers' thoughts on omissions and amendments that might be made. Readers also will be aware of the problems that often beset multiauthored books. Consequently, with the exception of the first and last sections, I have attempted to set the scene and provide continuity within and between the sections by way of short preambles. A few topics and authors have been lost along the way, but overall it has been possible to keep to the original plan and content.

QUAERENDO INVENIETIS!

If the reader will indulge me briefly, I wish to switch, finally and hopefully to some purpose, from microorganisms to music and in particular to Johann Sebastian Bach. A significant part of Bach's life overlapped with those of van Leeuwenhoek and Linnaeus, but this narrative concerns Frederick the Great rather than either of these notable biologists. Bach enthusiasts will recall that Frederick and Bach eventually met at Potsdam in 1747 and how the king invited Bach to improvise on a "royal theme," the result being one of the grandest and most complex inventions in the history of music— _The Musical Offering_. This composition of two fugues, ten canons, and a trio sonata was inscribed _Regis Jussu Cantio Et Reliqua Canonica Arte Resoluta_ (at the king's command, the song and the remainder resolved with canonic art). The acronym of Bach's dedication reveals "ricercar," the term for an earlier composition in the style of a fugue incorporating the most extreme devices of counterpoint, but also an adroit message in Italian—to seek out, with an implication of effort required in the search. The second ricercar of _The Musical Offering_ is an astonishing six-part fugue, astonishing to the extent that Douglas Hofstadter likened it to "the playing of sixty simultaneous blindfold games of chess, and winning them" (D. Hofstadter, _Gödel, Escher, Bach_, Vintage Books, 1980). Moreover, among the canons, which were presented to the king as uncompleted musical puzzles, is one marked _quaerendo invenietis_—by seeking, you will discover. I like to think of the totality of this musical composition as the apt metaphor for biodiversity, biocomplexity, and bioproSpecting, the more so because Bach and many of his contemporaries regarded music as a science; indeed Bach became a member of Lorenz Mizler's Society for Musical Sciences at the time of the _Offering's_ composition. This exhortation is emphasized by Bill Strohl in the epilogue to his chapter and this, in essence, is the theme of this book.
ACKNOWLEDGMENTS

The immediate precursor of this book was an article invited by Roy Doi for *Microbiology and Molecular Biology Reviews* (A. T. Bull, A. C. Ward, and M. Goodfellow, search and discovery strategies for biotechnology: the paradigm shift, 64:573–606). My first thanks, therefore, to Roy for his encouragement and to Alan Ward and Mike Goodfellow for many years of stimulating and eclectic discussion and productive collaboration. As mentioned in the preface, I have incubated the contents and ideas contained in these pages for several years, and in consequence many people either wittingly or unwittingly have contributed to my thinking and to keeping fun firmly on our agenda. So many thanks to the generations of graduate students and postdocs and colleagues in various organizations and places who have helped to keep me enthused and enlightened on microorganisms.

I thank Frank Bisby for his kind gift of the *Catalogue of Life* 2002 annual checklist; and Iain Prance and Dan Simberloff, my editors for *Biodiversity and Conservation*, for helping to sustain my commitment to biological diversity in the wider context and for their staunch support of the journal since its foundation. David Wynn-Williams of the British Antarctic Survey, a generous friend and fine microbiologist, was killed during the preparation of this book (see *Extremophiles* 6:265–266, 2002); I am especially pleased, therefore, that the book contains an excellent account of the “icy biosphere” with which David’s career was so closely concerned.

The enthusiastic interactions that I have enjoyed with the contributors to this book have been marvelous, and I am greatly indebted to them for preparing such thoughtful and timely accounts of their specialist subjects—my warmest thanks to you all. It is a pleasure to acknowledge the support for my own research into microbial diversity and biotechnology, some of which is mentioned in this book, from the Biotechnology and Biological Sciences Research Council and the Natural Environment Research Council (U.K.), The British Council, the Department for International Development (U.K.), the International Institute for Biotechnology, and the Japan Marine Science and Technology Center.

Greg Payne has been the ideal editor with whom to work—ever solicitous, patient, and enthusiastic; to him and the production team at the ASM Press I wish to convey very special thanks and appreciation for all their efforts in bringing this book to fruition.

Finally, I want to dedicate this book to my wife Jenny for her steadfast support over the years and not the least during the preparation of this book.

Alan T. Bull
Canterbury, January 2003
SUBJECT INDEX

A
Abscisic acid, 392
Acarbose, 370–371
ACC deaminase, 395
Access and Benefit Sharing partnerships, 436–438
Access regulation, 432–433, 462–463
Accretion ice, 139
Acellular slime molds, 63
Acetobacter diazotrophicus, 206
Acetogens, 124
N-Acetylneuraminate lyase, 298
Acid precipitation, 422
Acidianus, 146–147
Acidianus in femus, 147
Acidithiobacillus ferrooxidans, 246
Acidobacterium, 21, 82–83, 132–133
Acidophiles, 146–147
Acidovorax, 205
Acinetobacter, 137, 338, 401
Aclacinomycin, 330
Aclarubicin, 349
Acremonium chrysogenum, 326, 337
Acrylamide, 5–6
Actinobacteria, 20, 132–133
Actinoleukin, 329
Actinomadura carminata, 349
Actinomadura, 7, 74–76
Actinomadura madurae, 349
Actinomyces, 7, 325–326, 340–342
Actinomycetes, 74–76
Actinorhodin gene cluster, 304, Color Plate 9
Actinoplanes, 330, 370–371
Actinoplanic acid, 366
Actinorhodin gene cluster, 304, Color Plate 9
Activated sludge, 400–402
Acyl tyrosines, 115–117
Adenyl sulfate, 170
Adriamycin, 330
Aeropyrum pernix, 149, 296
Aerothionin, 183
African violet, see Saintpaulia
Agar plate diffusion assay
antibacterial, 324–325
based on spheroplast formation, 327
compounds detected, 325–327
narrow-spectrum screening concept, 327
screen against permeation barrier, 327–328
antifungal, 328
 Agriculture, 319–320, 421, 474
Agrobacterium, 394
Agrobacterium tumefaciens, 392
Air pollution, 422
Airborne microbes, 137
Akkadix-INBio RCA, 447–448
Algae, 61, 133–136, 341, 346
Algidines, 407
assays, 332
Algorithm sampling plan, 73
Alicyclobacillus acidocaldarius, 147
Alkaliphiles, 147, 151
All Species Foundation, 16
Allopatric speciation, 41, 219
Allorhizobium, 205
α-Diversity, 73, see also Species richness
Alternaria, 345
Alteromonas, 346, 407
Alteromonas haloplanctis, 148
Altohyrtins, 183
Alveolates, 59–61
Amanita, 207
Ambrosia beetles, 198–199
Ambrosiella, 199
Ambruticin, 349
Amebae, 219, 227
Aminoglycosides, 341
Ammonia monooxygenase, 296–297
Ammonium-oxidizing bacteria, 76, 94
amoA gene, 90
Amphimedon, 183, 185
Amphimedon viridis, 178
Amphotericin B, 328, 336–337, 339, 341, 348
Amycolatopsis mediterranei, 296, 326
Amylases, 378, 382–383
Anaerobes, sulfate-reducing bacteria, 69, 169–176
Anaerobranca gottschalkii, 147
Anaerobranca horikoshii, 147
Andrimid, 182
Anidulafungin, 340
Animal(s)
speciation, 40–41
transport of microbes, 221
Animal feed, 6
Annotation, 251–252
Ant(s), fungus-cultivating, 198
Antarctic lake ice, 132–135
Anthracycyclines, 344
Anthropogenic activities, 424
causing increase in microbial diversity, 422
causing reduction in microbial diversity, 421–422
with no effect on microbial diversity, 422
Antibacterials, 336, 338–340
antifoulants, 407
assays, 324–328
pediatric, 339
searching for new drugs, 246
sources for future drugs, 347–348
synergism between, 348
targets, 350
Anti-biofilm agents, 405–412
Antibiosis, 71
Antibiotics, 7
resistance, see Drug resistance
semisynthetic, 6
soil metagenomic libraries, 115–117
AntFifoulants, 405–412
future, 409
from Pseudoalteromonas, 406–407
technology development, 408
Antifungals, 336, 338–340
antifoulants, 407
assays
agar plate diffusion assay, 328
for inhibition of cell wall synthesis, 329
for morphological changes of hyphae, 328
sources for future antibiotics, 348–349
Antimicrobials, 317–318, 336–355
assessing DNA diversity, 346–347
bacterial diversity in production, 342–345
chemical versus biological diversity, 340–342
fungal diversity, 345–346
marine microbes, 346
need for new natural product antibiotics, 338–340
world sales, 338–339
Antiparasitic assays
in vitro, 331
in vivo, 331
Antitumor agents, 182, 336, 340, 346, 351, 356, 363–368
assays
in vitro, 329–330
in vivo, 330
sources for future drugs, 349–350
Aphids, 195–196
API20E system, 54
Apicomplexans, 59–61, 245
Aplysina aerophoba, 179, 182
Aplysina fistularis, 178
APS reductase, 169–171
Aquaculture, 421
antifoulants for, 408
sponges, 187
Aquaspirillum arcticum, 148
Aquifex, 148–149
Aquifex pyrophilus, 149
Aquificales, 84
Arbuscular mycorrhizal fungi, 74, 204, 207
Arbutroid mycorrhiza, 207
Arbutus, 207
Archaea, 20, 22
insect-associated, 194
sponge-associated, 181
Archaeal-like genes, 254–255
Archaeoglobus, 148–149, 228, 297
Archaeoglobus fulgidus, 149, 170, 293
Archaeoglobus lithotrophicus, 149
Arenastatin A, 184
Armorilla mellea, 207
Arsenic, reduction by sulfate-reducing bacteria, 173
Arsenic contamination, 422
Arsenobobus nasoniae, 195
Arsenobobus triatominaria, 196–197
Arthrobacter, 137, 141
Arthrobacter agilis, 141
Arthrobacter glacialis, 148
Arthropod diversity, 17–18, 21, 73
Arthrosira, 217–218
Ascomycetes, 62–63
Ascomycin, 300
Aspergillus, 6, 208, 341, 345, 378
Aspergillus aculeatus, 369
Aspergillus alliaceus, 377
Aspergillus terreus, 331, 356, 368–369
Asperlicin, 357
Asperuginus, 346
Atorvastatin, 368
Avarol, 183
Avermectins, 331–332, 341, 351
Avilamycin, 337, 341
Axinella mexicana, 181
Azithromycin, 350
Azocrinus, 295
Azorhizobium, 205
Azospirillum, 391
Azospirillum amazonense, 393–394
Azospirillum brasilense, 393–394
Azospirillum halopraeferens, 394
Azospirillum irakense, 393–394
Azospirillum lipoferum, 393–394
Azotobacter, 394
Azotobacter chroococcum, 295
Bacillus, 50, 149, 182, 185, 205, 337, 341, 378, 394
alkaliphilic, 147
biogeography, 229
desert-dwelling, 229
Bacillus acidocaldarius, 149
Bacillus anthracis, 50–52, 256, Color Plate 1
Bacillus brevis, 325, 337
Bacillus cereus, 51, 148, Color Plate 1
Bacillus halodurans, 296, 305
Bacillus lateosporus, 361
Bacillus licheniformis, 337
Bacillus mojavensis, 50, 229
Bacillus polymyxa, 337
Bacillus psychrosaccharolyticus, 148
Bacillus sphaericus, 50
Bacillus stearothermophilus, 149
Bacillus subtilis, 5, 46, 50, 229, 263–264, 296, 305, 344, 379, Color Plate 1
Bacillus thuringiensis, 51, Color Plate 1
Bacitracin, 337
Bacteria, see also Prokaryotes
species concept, 32–37, 41–42
phyllospecies, 42–43
Bacterial artificial chromosome, 409
Bacterial diversity, see Microbial diversity
Bacterial speciation, 13, 40–48
biological factors, 44
chemical and physical factors, 43–44
constraints on genetic fluidity, 45–46
cospeciation, 44
dispersal and, 43
environmental factors, 43–44
 genetic exchange and, 43
 genome size and, 46–47
 geographic factors, 43–44
 growth rates and, 43, 45
 haploidy and, 45
 horizontal gene transfer and, 44–45
 intrinsic factors, 44–45
 mutation and, 45
 oligobacteria, 162–163
 population sizes and, 45
 Bacteriocyte, 192, 195
 Bacteriome, 192, 195
 Baicalin, 348
 Balanol, 366
 Ballast water, 222
 Bark beetles, 198–199
 Barophiles, see Piezophiles
 Basalt rocks, 125
 Basidiomycetes, 62–63
 Benefit sharing, 429–439, 462–463
 INBio in Costa Rica, 429–430, 445–449
 in practice, 436–437
 β-Diversity, 15
 β-Lactams, 345, 348
 Bialaphos, 341, 344
 Bioactivity, screening for, 317–318, 324–335
 Biocartography, 232–236
 Biocatalysts, 4–5, see also Enzymes
development, 317–318, 375–390
Biochemical systems theory, 282
Biocontrol agents, 205
antifoulants, 408
bacterial, 206
fungal, 208
Biodiversity, 290, see also Microbial diversity
bioprospecting for industrial enzymes, 376–381
conferred value, 430
Convention on Biological Diversity, 429–439
definition, 15
economic benefits, 472
economic valuation, 469–470
 biodiversity as information, 474
 equation of well-being, 470–472
 in practice, 474
 techniques, 475
ecosystem functioning and, 423–424
effect of anthropogenic activities
 increase in microbial diversity, 422
 lack of, 422
 reduction of microbial species, 421–422
 estimation, 16–19, 29, 424
 extinction, see Extinction
 hot spots, 77, 419, 458–466
 International Cooperative Biodiversity Groups,
 458–466
 loss of, 469
 evidence for, 415–416, 421–425
 irreversibility, 474
 significance, 422–423
 loss of evolutionary history, 415–420
 overview, 15–28
 Biofilms, 94–95, 110, 398
 anti-biofilm agents, 405–412
 Bio fouling, 405–412
 Biofuels, 3
 Biogeochemical cycles, 109
 Biogeography, 288, 419
 body size and, 225–227
 dispersal of free-living microbes, 213–214, 216–224
 microbial endemism, 213–214, 223–231, 419
 studies of small-subunit RNA, 228–229
 Yellowstone National Park Microbial Database and
 Map Server, 214, 232–236, Color Plates 3
 through 7
Bioinformatics, 4, see also Genomics; Phenomics;
 Proteomics
definition, 241–242
environmental and industrial applications, 246–247
 enzyme discovery, 379
impact on biological research, 243
integration and interoperability, 243–244
medical applications, 244
paradigm shift in microbial prospecting, 239–249
pharmaceutical applications, 245–246
Bilog methodology, 54
Biological species concept, 31–32, 40
Biomaterials, 321–322
Biomimetics, 321–322
Biopiracy, 434, 442–443
Bioprospecting
colonial, 440–441
definition, 445
discursive icons related to, 442
effect of species loss, 423
historical context, 429–430, 440–444
how to search, 69, 71–78, 306
INBio experience, 429–430, 445–449
International Cooperative Biodiversity Groups,
 458–466
major lineages as prolific producers, 305
paradigm shift, 239–249
postwar, 441
scope and issues, 6–9
taxonomy as roadmap, 239–240, 288–313
where to look, 76–77
Yellowstone-Diversa agreement, 429–430, 450–457
Bioprospecting targets
anti-biofilm agents, 317–318, 405–412
antifoulants, 317–318, 405–412
antimicrobials, 317–318, 336–355
biotreatment, 317–318, 397–404
enzymes, 317–318, 375–390
pharmacological agents, 317–318, 356–374
plant growth-promoting agents, 317–318, 391–396
screening for bioactivity, 317–318, 324–335
Bioreactor design, 398
Bioremediation, 173, 246, 397
Bioscreen C system, 281–282
Biosensors, 322
Biotechnology
applications, 3
clean, 5
contribution to sustainable industry, 5
sectors and markets, 317–323
Biotin synthesis, 382
Biotransformation, linking microbial community structure with function, 93–95
Biotreatment, 173, 317–318, 397–404
ex situ, 398
in situ, 397
novel microbes, 399–400
Bisabosquals, 369
Bisulfite reductase, 169–170
Black smokers, 148
Blasticidin S, 349
Buchnera, 46, 297
Buchnera aphidicola, 195–196
Bacillus subtilis, 366–367
Bacillus thuringiensis, 366–367
Bacillus subtilis, 366–367
Bacillus subtilis, 366–367
Bacillus thuringiensis, 366–367
Bacillus subtilis, 366–367

Chromatium, 147
Chromium, reduction by sulfate-reducing bacteria, 173
Chromobacterium violaceum, 337
Chytrids, 62
Ciliates, 21, 59–60, 193, 217–221, 227
Cilofungin, 329
Cinachyras, 183
Cinachyrolide A, 183
Cinchona, 441
CJ-14,897, 362–363
CJ-15, 369
Cladistics, 19
Cladosporium, 362–363
Clarithromycin, 350
Clavariadelphus truncatus, 366–367
Clavaric acid, 366–367
Claviceps, 341, 345
Claviceps purpurea, 205, 356
Clays, deep terrestrial, 124
Click chemistry, 322
Clostridium, 149
Clostridium acetobutylicum, 46
Clostridium botulinum, 148
Clostridium halophilum, 150
Clostridium pasteurianum, 295
Clostridium thermosulfurogenes, 149
Clotrimazole, 339–340
Coal refuse piles, 146
Clotrimazole, 339–340
Coal reservoirs, deep, 124
Coccidioides immitis, 339
Cochliobolus lunatus, 363
Coccolithophorida, 219
Cockroaches, 194, 196, 198, 200
Codon cube, 384
Cohesion species concept, 31
Cold biosphere, 130, see also icy biosphere
Cold-adapted microbes, 140–141, 147–148
Colletotrichum magna, 204, 208
Colonial bioprospecting, 440–441
Colonization, see also Biofilms
surfaces by bacteria, 406–408
Colpoda inflata, 218
Colwellia, 293, 306
Colwellia hadalensis, 155
Combinatorial chemistry, 7–8, 324, 429, 434
Common species, 15
Community diversity profile, 71
Community genomics, see Metagenomic libraries
Compactin, 208, 368
Comparative genome hybridization, 250, 255–256
Compatible solutes, 151
Competition, multispecies, 71–72
Complete gene random mutagenesis, 384
Complexity hypothesis, 299
Comprehensive Microbial Resource, 252
Conservation
discursive icons, 442
economic aspects, 469–475
Consumer’s surplus, 470
Continuous culture systems, 74–75
Convention on Biological Diversity, 429–440
access to genetic resources, 432–433
benefit sharing and, 431–439
key provisions, 432
move to fairer partnerships, 433–435
objectives, 429, 431, 450
recent developments, 435
Cooperative Research and Development Agreement, 451–457; see also Yellowstone-Diversa CRADA
Copeotrophs, 160
Core genes, 36
Correlations research, 73
Corynebacterium, 291–292
Corynebacterium diphtheriae, 103
Corynebacterium glutamicum, 103, 379
Coryneforms, 291–292
Cosmopolitan species, see Microbial cosmopolitanism
Cospinfection, 44
Costa Rica, INBio, 429–430, 437, 445–449
Crenarchaeota, 130
Cribrochalina, 185
Crickets, 193
Cryoconite holes, 135–136
Cryptic species, 20
Cryptococcus neoformans, 339
Cryptophycins, 184
Culturability, 100, 162
loss in laboratory cultures, 101–102
Culture collections, 378, 415–416, 434–435
Culture-dependent microbiology, 69, 73–76, 80–87,
241–242, 377–378
enrichment and micromanipulation, 83–84
extinction culture, 75–76, 82, 84–85, 163, 409
future, 85–86
media, 81
plating methods, 81–83, Color Plate 2
pure cultures, 80–81
Culture-independent microbiology, 74–76, 88–99,
241–242, 250, 256–257
analysis of environmental nucleic acids, 89–93
DNA extraction from environmental samples, 88–89
future, 96
horizontal gene pool analysis, 95–96
linking microbial community structure with function,
93–95
need for, 88
RNA extraction from environmental samples, 89
Curiosity-driven research, 76
Curve extrapolation methods, 23
Cuspopfungin, 337
Cyanobacteria, 341
alkaliphilic, 147
cryoconite holes, 135–136
icy biosphere, 132–135
Cyanophycin, 321
Cybernetic modeling, 282
Cycloclasticus oligotrophus, 75, 82, 85, 161-162, 166-167
Cycloserine, 326, 337, 341
Cyclosporin, 328, 345, 351, 356, 359-361, 429, 441-442
Cylinder plate assay, 325
Cytophaga, 341
Cytophagales, 133
Dactinomycin, 349
Dalfopristin, 348
Data mining, 243
Database, molecular biology, 243-244
Daunomycin, 356, 363
Daunorubicin, 300, 330, 344, 349
Deep biosphere, 69, 120-129
cold, 125-126
marine sediments, 120-124
petroleum and coal reservoirs, 124
significance, 126-127
terrestrial, 124-125
Deep-sea environment, 18-19, 25-26, 72, 75-76, 148, 154
Deep-sea subsea floor biosphere, 417-418
Deforestation, 422
Dehalococcoides ethenogenes, 399
Dehalogenase, 6
Deinococcus radiodurans, 256
Deletions, see Gene deletions
Denaturing gradient gel electrophoresis, 91-92
Dercitamide, 183-184
Dereplication, 9, 20, 343, 350, 357-358
pharmacological agents, 357-358
at species level, 305-306
Desert locust, 193
Desmids, 221
Desulfobacter, 172
Desulfobacterium, 171
Desulfobacterium autotrophicum, 172
Desulfobacterium catecholicum, 172
Desulfobacul a, 297
Desulfobacula toholica, 297
Desulfobulbus, 171-172
Desulfobulbus propionicus, 171-172
Desulfococcus, 149, 171
Desulfococcus multivorans, 172
Desulfomicrobium, 170, 172
Desulfomicrobium baculatum, 172
Desulfomicrobium norvegicum, 173
Desulfotomaculum, 170-172, 297
Desulfotomaculum auripigmentum, 173
Desulfotomaculum reducens, 173
Desulfotomaculum ruminis, 297
Desulfotomaculum thermocisternum, 297
Desulfovibrio, 169-172
Desulfovibrio aminophilus, 171
Desulfovibrio desulfuricans, 170-173, 296
Desulfovibrio fructosovorans, 171, 173
Desulfovibrio gigas, 170, 172-173
Desulfovibrio profundus, 123-124
Desulfovibrio sulfodismutans, 171
Desulfovibrio termididis, 172-173
Desulfovibrio vulgaris, 171, 173, 246
Deuteromycetes, 62-63
Developing countries, Convention on Biological Diversity, 431-439
2,4-Diacetylphloroglucinol, 349
Diagnostic species concept, 31
Diatoms, 60-61, 219-221, 322
Diazotrophs, icos biosphere, 135
Dicarboxylic acid acylase, 6
Dictyostelium, 63
Diethylstilbestrol, 292
Dihydromaltophilin, 349
Disocyanodociane, 183
Diketopiperazines, 182
Dilute environments, 69, 160-168
Dilution culture, see Extinction culture
Dimethyl sulfide, 162
Dimethyl sulfoxide reductase, 296-297
Dinoflagellates, 60-61, 217, 341
Dinophysis, 183
Diplomonads, 63-64
Directed evolution, 247-248
industrial enzymes, 383-386
candidates for basis of next generation, 385
coupling DNA mutants and protein variants, 384-385
DNA variation, 384
iterative aspect, 385-386
Dirithromycin, 350
Disciplinary matrix, 241
Discodermia, 179
Discodermia dissoluta, 185
Discodermolide, 184
Discounting, 471, 473
Dispersal, free-living microbes, 213-214, 216-224
Diversa Corporation
Diversa-INBio RCA, 447-448
Yellowstone-Diversa CRADA, 429-430, 450-457
DNA
environmental, 75, 88, 346-347
detecting unculturable bacteria, 22-23
dot blot hybridization and gene arrays, 92-93
extraction, 88-89
molecular analysis, 89-93
molecular fingerprinting, 91-92
PCR, cloning, and sequencing approach, 90-91
oligobacteria, 161-162
DNA sequencing, 9
environmental DNA, 90-91
methods, 250-251
whole-genome, 250-251, 297-298, 305
DNA shuffling, 247, 385
DNA-based typing methods, 35
DNA-DNA hybridization
delineation of bacterial species, 33–35
microbial identification, 50–51, 55
species concept based on, 41–42, 47
DNase, 382
Docetaxel, 349–350
*Doratomyces*, 208
Dormancy, 100–105
Dot blot hybridization, quantitative, 92–93
Doxorubicin, 349, 356, 363
*Drosophila*, 195
*Dunaliella*, 150
Dust storms, 221
*Dysidea*, 177
*Dysidea arenaria*, 184
*Dysidea avara*, 183
*Dysidea herbacea*, 177

**E**
E-CELL project, 247
Echinocandins, 328–329, 336, 340, 346, 349
Ecome, 243
Economics, environmental, 469–475
Ecosystem functioning, microbial diversity and, 423–424
Ecosystem functions, 472
Ecosystem resilience, 472, 474
Ecosystem restoration, 205, 207
*Ecteinascidia turbinata*, 186–187
Ecteinasidins, 186–187
Ectoines, 151
Ectomycorrhizal fungi, 206–207
*Edmonds Institute v. Babbitt*, 452–453
Elaophylin, 300, 302–303, 306
Elementary mode analysis, 282
*Emiliana huxleyi*, 217–218
*Encephalitozoon cuniculi*, 62
Endangered habitats, 416
Endemism, see Microbial endemism
Endophytes, 204
bacterial, 206
fungal, 18
of leaves, 208
Endosymbiont theory, 57
Energy yield, genome size and, 47
Enfumafungins, 346, 349
Enhanced biological phosphorus removal, 400–402
Enrichment methods, 83–84
*Entamoeba histolytica*, 58
*Enterobacter*, 391, 394
*Enterobacter cloacae*, 395
Enterococci, vancomycin-resistant, 338
Environmental DNA, see DNA, environmental
Environmental economics, 469–475
Environmental genomics, see Metagenomic libraries
Environmental impact statement, 452–453
Environmental permits, 437

**Enzymes**
chemotaxonomy, 291
enzyme inhibitory assays, 330
extremophiles, 4, 151–152
industrial, 4, 151–152, 317–320, 375–390
bioinformatics in enzyme discovery, 379
bioprospecting, 376–381
cloning from nonculturable microbes, 380–382
cloning to obtain enzymes for testing, 378
directed evolution, 383–386
genome analysis for novel genes, 379–380
manufacturers, 375
metagenomics approach, 380–382
molecular screening, 378–379
rational protein engineering, 381–383, 386
screening based on culturing of microbes, 377–378
screening programs, 375–376
worldwide use, 375

**Ephemeral habitats**, 416
Epigallocatechin gallate, 348
Epothilones, 349–350, 364–365
Epoxomicin, 368
*Epulopiscium fisheloni*, 256
Equation of well-being, 470–472
Erbstatin, 366
Ergokinin A, 349
Ergot, 356
Ergotamine, 345
Ericoid mycorrhiza, 207
*Erwinia*, 148
Erythromycin, 326, 336–337, 341
Erythromycin resistance, 274
*Escherichia coli*, 225, 296, 299, 305
comparison with primate host species, 42
environmental, 110
genome sequence, 20, 256, 298
genome size, 46
in silico strains, 247
phenomics, 283–286
proteome database, 263–264
specific affinity, 166
*Escherichia coli* O157:H7, 255
*Escovopsis*, 198
Esterases, 382, 453
Etherincins, 328
Ethnomedicine, 461
Ethylene, 391–392, 394
Euglenids, 62
Euglenozoa, 61–62
Eukaryotic microbes
alveolates, 59–61
biogeography, 226–227
definition, 57–59
diplomonads, 63–64
diversity, 21–22
early, 58
euglenozoa, 61–62
evolutionary relationships, 57–58
foraminiferans, 63
heterokonts, 61
lineages, 59–64
metabolism, 58
mycetozoans, 63
opisthokonts, 62–63
parbasalids, 63
photosynthetic, 58–59
species concept, 31–32
Eupenicillium, 208
Euplotes aediculatus, 218
Europa (moon of Jupiter), 131
Evaporite lagoons, 150
Evvinitomycin, 337
“Everything is everywhere” concept, 422–423
Evolution
cold-adapted species, 140–141
directed, see Directed evolution
eukaryotes, 57–58
on frozen earth, 131–132
loss of evolutionary history, 415–420
plant-microbe associations, 204
resuscitation-promoting factor, 105–106
understanding genomics, 254–255
Evolutionary species concept, 31
Ex situ programs, conservation of microbes, 416
Exiguobacterium, 141
Exploitable microbiology, 3–5, 7
expression of exploitable organisms, 7–8
Expression cloning, enzyme production, 378
Extinction, 415–420, 422–423, 434
habitat destruction, 419
random vs. nonrandom nature, 418–419
Extinction culture, 75–76, 82, 84–85, 163, 409
Extraterrestrial life, 125, 127, 130–131, 142
Extreme halophiles, 150–151
Extreme pathway analysis, 282
Extreme thermophiles, 149
Extremophiles, 69, 146–153
biocatalysis by, 4, 151–152
growing around boiling point of water, 148–149
growing around freezing point of water, 147–148
living at extreme salinity, 150–151
living at extreme pH, 146–147
living at high pressure, 154–159

F
FST, 25
Faerifungin, 339
Family shuffling, 247, 385–386
Fatty acid analysis, microbial identification, 53, 55
Fatty dienic alcohols, 115–117
Favolaschia pustulosa, 358–359
Feed enzymes, 6
Feedstocks, industrial, 3–4
Fermentation, by sulfate-reducing bacteria, 171
Fervidobacterium, 52, 149
Fervidobacterium pennivorans, 149
“Field of bullets” scenario, 418–419
Filter disk plate diffusion assay, 325
Fjord water, 82
FK506, 300, 341, 351, 360–361
Flagellates, 217–219
Flavobacterium, 166, Color Plate 2
Flexibacter polymorphus, 292–293
Fluconazole, 339–340
Fluorescent in situ hybridization, 84, 94
Fluvastatin, 368
Flux-balance analysis, 282–284
Fog particles, 137
Fourier-transform infrared spectroscopy, microbial identification, 53–55, 292
Francisella tularenis, 272–273
Free-living microbes
absolute abundance, 216–217
mechanisms of dispersal, 220
animals, 221
human activities, 221–222
wind and water, 220–221
ubiquitous dispersal, 213–214, 216–224
evidence from genotypes, 217–219
evidence from morphospecies, 217
evidence from sibling and physiological species, 218–219
indirect evidence, 219
Friedmaniella antarctica, 141
Friedmaniella spumicola, 141
Fumagillin, 364–365
Functional diversity, 15
Functional genomics, 250, 252, 255–256, 260
Functional redundancy, groups of microbes, 415
Functional screening assays, enzymes, 376
Fungi, 62–63
aerial transport, 221
antimicrobials from, 341, 345–346, 351
diversity, 17–18, 22
insect-associated, 198–199
plant-associated, 205–208
spore-associated, 182
Fungus-cultivating insects, 198–199
Fusaric acid, 392
Fusarium, 345, 378
Fusarium oxysporum, 208
Fusidic acid, 337, 341, 345
Fusidium coccineum, 337
G
G+C content, 35, 42
γ-Diversity, 15
Gas hydrate sediments, 121–122
Gasoline contamination, 421–422
Gemtuzumab ozagaminic, 364
Gene(s)
identification, 251–252
inferring from biomarkers, 291–292
lineage-specific loss, 22
taxonomy and, 291–298
Gene deletions, flux-balance analysis, 284
INDEX 485

Gene expression, 260, 288, see also Proteomics
drug-induced, 275
in vivo expression technology, 270–273
studies of, 256
Gene pool, microbial, loss of, 415
Gene trapping methods, 380
Genetic diversity, 23–25
Genetic fluidity, 45–46
Genetic headroom, 20
Genetic resources, 3
Genome
oligobacteria, 161–162
species genome, 20, 36
Genome sequencing, 250–252, 297–298, 305
Genome size, 76
bacteria, 46–47
Buchnera, 195–196
upper limit, 47
Genome species concept, 297, 306
Genomics, 241, 243, 249–259
bioinformatics analysis of genome sequence, 251–252
eukaryotic, 254
functional, 250, 252, 255–256, 260
insights into metabolic diversity, 252–254, Color Plate 8
limitations, 260, 280
sequencing methods, 250–251
tools for comparing genomes, 252–254
unculturable species, 250, 256–257
understanding evolution, 254–255
Genotype-phenotype relationship, 280–287
Geobacter metallireducens, 296
Geographic information systems, Yellowstone National Park Microbial Database and Map Server, 214, 232–236, Color Plates 3 through 7
Geography, bacterial speciation and, 43–44
Giardia, 58
Giardia lamblia, 63–64, 295
Gibberella fujikuroi, 392
Gibberellins, 392, 394
Glaciers, 125–126, 136–138, 148
Glarea lozoyensis, 337
Gidobactin, 349
Glucose isomerase, 4
Glucosidase inhibitors, 330
Glyceraldehyde phosphate dehydrogenase, 274
Glycogen-accumulating organisms, 400–402
Glycosidases, 453
Gonium pectorale, 218
Gordionia, 292
Gramicidin, 337, 341
Green fluorescent protein, 94–95
Griseofulvin, 328
Growth rate, 280
bacteria, 43, 45, 81, 160
Gut microbes, insect-associated, 192–194, 200
Gymnoascus, 208
Gymnodinium, 218
Gymnodinium catenatum, 217
H
Habitat destruction, 416, 419
Habitat simulation, 74
Haemophilus influenzae, 225, 246, 267, 274
genome sequence, 250
proteome database, 263–265
Halangiycin, 349
Halichondria melanodocia, 183
Halichondria okadai, 183, 185
Halichondria panicea, 182
Halichondrin B, 184
Haliclonia, 183, 185
Haloalkaliphiles, 147
Haloanaerobium praevalens, 150
Halotarctia marismortui, 296, 299
Halobacteria, 150
Halobacterium denitrificans, 150
Halofexax vulcanii, 150
Halophiles, 150–151
Haploidy, bacterial speciation and, 45
“Hardangervidda fungus,” 441–442
Heavy metal contamination, 422
Hebeloma, 207
Helicobacter pylori, 245, 267–268, 273–274, 284, 305
drug-induced gene expression, 275
genome sequence, 256
proteome database, 263, 265–266
Herbaspirillum, 205
Herbicides, 422
assays, 331–332
Heterokonts, 61
Heterotrophs, icy biosphere, 135
Hierarchical Classification System, 244
High-pressure environment, 154–159
High-fructose syrup, 4
High-throughput screening, 324, 356–357
Hindgut microbes, 192–193
Histoplasma capsulatum, 339–340
HMG-CoA reductase inhibitors, 330–331, see also Statins
Holophaga, 132
Homocacetogens, 125
Homaoerothionin, 183
Horizontal gene pool, culture-independent study, 95–96
Horizontal gene transfer, see Lateral gene transfer
Hot fumaroles, 148
Hot spots, biodiversity, 77, 419, 458–466
Hot springs, 146, 148
Human genome, 298
Hurricanes, 221
Hyatella, 182
Hydrogen sulfide, 172
Hydrogenase, 169–173
Hydrothermal vents, 83, 148, 154, 227–228
4-Hydroxybutyrate dehydrogenase, 382
Hygromycin, 344
Hyaluronan synthase, 298
Hymenoscyphus ericae, 207
Hypaphorine, 341
Hypersaline sites, 76, 147
Hyperthermophiles, 148–149, 151, 227–228
Hypomyces, 208
Hypothesis-driven science, 243
Hypoxylon, 345
Hyritios altum, 183

I
Iceobacter, 217
Icy biosphere, 130–145
cold deep biosphere, 125–126
cold-adapted species, 140–141
cryoconite holes, 135–136
evolution on frozen earth, 131–132
extraterrestrial life, 130–131
glacial ice, 136–138
microbes growing around freezing point of water, 147–148
permanent Antarctic lake ice, 132–135
subglacial lakes, 139–140
Idarubicin, 349
Igneococcus, 148
Igneous rock, 125
Iglnicoccus, 228
Illicicolin, 349
Imipenem, 327, 336–337
Immunocompromised patients, 339
Immunosuppressive agents, 359–363
Impatiens sultani, see Busy Lizzie
In silico strains, 247
In situ hybridization, whole cells, linking microbial community structure with function, 94
In situ programs, conservation of microbes, 416
In vivo expression technology, 270–273
INBio (Costa Rica), 429–430, 437, 445–449
achievements of bioprospecting, 448
Akkadix-INBio RCA, 447–448
Chagas space program, 448
Diversa-INBio RCA, 447–448
future, 449
La Gavilana RCA, 448
Merck & Co-INBio RCA, 445, 447–449
microbial bioprospecting agreements, 447–448
research collaborative agreements, 445–447
Indigenous peoples, 462–463
Indirubin, 115–117
Indoleacetic acid, 394
Indole-3-glycerol phosphate synthase, 248
Industrial sectors, penetration of biotechnology, 319–320
Infrared spectroscopy, microbial identification, 53–55, 292
Insect-associated microbes, 191–203
bioprospecting within, 199–200
ectosymbionts, 198–199
extracellular endosymbionts, 192–194
intracellular endosymbionts, 194–198
terminology, 191–192
Insulin mimetic, 371
Intellectual property rights, 437, 462–463
Intercontinental trade, 221–222
International Agricultural Research Centres, 435
International Cooperative Biodiversity Groups (ICBG), 429–430, 458–466
access, intellectual property rights, and benefit sharing, 462–463
bioinventory results, 460–461
bioprospecting results, 461–462
capacity and capability accomplishments, 463
conservation outcomes
capacity-building efforts, 464
dissemination of findings, 465
ex situ botanical conservation, 464
integrated conservation and development, 464–465
natural resources management, 464
interactions with industrial partners, 462
program summaries, 458–460
International law, 429
International Treaty on Plant Genetic Resources for Food and Agriculture, 434–435
Intertidal sediments, 74
Inventive problem solving, 321
Inventory project, 73
Inverse flux analysis, 282
Invertebrates, marine, 186–187
Ionophores, rhizosphere, 392–393
Irpinia, 185
Irroinotecan, 349–350
Iron-reducing bacteria, 94, 173
Isaria sinclairii, 361–362
Isopentyladenine, 392
Isoprenoids, 291, 293–295, 341
Isotope-coded affinity tags, 262
K
Kanamycin, 337
Kasugamycin, 341
Keratinase, 382
Ketoconazole, 339–340
Kinetoplastids, 62
Kissing bugs, 196–197
Kitasatosporia, 394
Klebsiella, 394
Klebsiella oxytoca, 193, 296
Klebsiella pneumoniae, 296, 305
Kluyvera ascorbata, 395

L
L-671,776, 358–359
L-783,281, 370–371
La Gavilana S.A., 448
Labyrinthula macrocystis, 61
Labyrinthulids, 61
Lactacystin, 367–368
Lactic acids, chiral, 4
Lactobacillus casei, 50
Lactobacillus paracasei, 50
Lactococcus lactis, 337
Ladybird beetles, 195
Lake Vostok, Antarctica, 126, 130, 139–140
Land tenure, 437
Landfills, 398
Latency, 100
Lateral gene transfer, 22, 32, 57–58, 254–255, 288, 293–300, 305
bacterial speciation and, 44–45
prokaryotes, 35–36
Latrunculins, 183
Laulimalide, 350
Legionella pneumophila, 271
Leishmania, 246
Leishmania donovani, 272
Leishmania major, 62
Leninus edodes, 206
Leptodontium elatius, 368
Letters of intent, 437
Liblomycin, 329
Lichens, 207
LightCycler, 52
Lincomycin, 336–337, 341
Linezolid, 350
Lipases, 382–383
Lipids, membrane, under pressure conditions, 154–155
Lipopolysaccharides, 291
Lipstatin, 370–371
Lissodendoryx, 184
Listeria monocytogenes, 148, 267, 271
Lovastatin, 330–331, 341, 351, 368–369
Lucilactaene, 366
Luffisphaera, 219
Lyngbia, 346
Magainins, 322
Magnaporthe grisea, 205
MALDI-TOF mass spectrometry, 54
Manganese, reduction by sulfate-reducing bacteria, 173
Manufacturing industries, 319–320
Manzamines, 180, 185–186
MAR1, 343
Marasmiellus, 362–363
Marine environment, 8, 18–19, 81–82, 84–85, 419
bacterial diversity, 25–26, 346, 405–412
invertebrates, 186–187
Marine industries, biofouling, 405–412
Marine saltern, 150
Marine sediments
basement rock beneath, 123
depth, 120–124
Marine sponges, see Sponge(s)
Marinobacter arcticus, 165
Marker genes, 94–95
Market(s), for biotechnology products, 321
Market forces, 470
Mars, life on, 130–131
Mass extinction, 417–419
Mass spectrometry, 262, see also specific types of mass spectrometry
Material Transfer Agreement, 436–437
Matsuebacter chitosanotabidus, 82–83
McMurdo Dry Valleys, 132–135
Mealybugs, 196–197
Media, 81
Methanobrevibacter, 194
Methanococcus jannaschii, 46, 149, 155
Methanogens, deep biosphere, 124–125
Methanopyrus, 148–149
Metal reduction, sulfate-reducing bacteria, 173
Metallosphaera, 147
Meteorological events, extreme, 221
Methane, 162
Methanothermus fervidus, 146, 149
9-Methoxystrobilurin E, 358–359
Microautoradiography, 94
Microbacterium, 182
MicrobeLynx system, 55
Microbial area-species curve, 73
Microbial cosmopolitanism, 225–226
eukaryotic microbes, 226–227
prokaryotic microbes, 227–228, 230
Methylotrophs, 194
Methylobacterium extorquens, 246
Mevinolin, 208, 330–331, 356
Micafungin, 340
Microarray technology, 243–244, 246, 250, 255–256, 424, Color Plate 1
analysis of environmental nucleic acids, 92–93
Microautoradiography, 94
Microbacterium, 182
MicrobeLynx system, 55
Microbial area-species curve, 73
Microbial cosmopolitanism, 225–226
eukaryotic microbes, 226–227
prokaryotic microbes, 227–228, 230
Microbial diversity, 4, 340, *see also* Biodiversity
bacterial speciation, 13, 40–48
defining, 13, 29–39
disproportionate taxonomic effort, 21
estimating and comparing uncountable species, 22–25
eukaryotic, 13, 57–65
mapping, 214, 232–236
 marine bacteria, 25–26
microbial identification, 13, 49–56
numbers and diversity, 20–21
phylogenetic framework, 21–22
supersaturated coexistence, 71–72
unit of count, 19–20

Microbial ecology
deep biospheres, 69, 120–129
dilute environments, 69, 160–168
extremophiles, 69, 146–159
icy biosphere, 130–145
insect-associated microbes, 191–203
plant symbionts, 69, 204–210
resuscitation of uncultured microorganisms, 100–108
soil metagenomics, 69, 109–119
sponge-associated microbes, 177–190
sulfate-reducing bacteria, 69, 169–176

Microbial endemism, 213–214, 220, 223–231, 419
argument for, 225
future directions, 229–231

Microbial identification, 13, 49–56
approaches, 49
cell composition, 53–55
DNA-DNA hybridization, 50–51, 55
fatty acid analysis, 53
Fourier-transform infrared spectroscopy, 53–55, 292
mass spectrometry, 54
nucleic-acid-based procedures, 49–52
PCR-based procedures, 51–52, 54–55
physiology-based methods, 54–55
protein analysis, 52–53
ribotyping, 52
*Micrococcus*, 182
*Micrococcus cryophilus*, 148
*Micrococcus luteus*
dormancy and resuscitation, 101
resuscitation-promoting factor, 102–105

Microcolony technique, 81

*Microcystis*, 217

*Microdochium caespitosum*, 366–367

Microfossils, 417

Micromanipulation, 83–84

*Micromonospora*, 350, 361

*Micromonospora carbonacea*, 337

*Micromonospora chalcea*, 340

*Micromonospora echinospora*, 364–365

Microorganisms Sustainable Use and Access Regulation
International Code of Conduct (MOSAICC), 435–436

MicroSeq 500 Bacterial Identification System, 50

*Microsphaeropsis*, 182

Microsporidians, 62

Mining practices, effect on microbial diversity, 421

Mithramycin, 349, 363

Mitomycin C, 341, 349, 356, 363

Mitoxantrone, 349

Mobile genetic elements, culture-independent study, 95–96

Moderate halophiles, 150

Moderate thermophiles, 148–149

Molecular complexity index, 8

Molecular ecology, 290

Molecular phylogeny, 17, 75

Molybdenum, reduction by sulfate-reducing bacteria, 173

*Monascus*, 208, 345

*Monascus ruber*, 331

Monensin, 337, 341

Monophyletic species concept, 31, 34

Monorden, 358–359

Monotropoid mycorrhiza, 207

Morphologic species concept, 31–32, 40, 217

*Mycetocyte*, 192

*Mycetome*, 192

*Mycetozaens*, 63

*Mycobacterium*, 291–292

*Mycobacterium avium*, 103, 272

*Mycobacterium bovis*, 103, 269–271, 296

*Mycobacterium leprae*, 76, 103

*Mycobacterium smegmatis*, 272

*Mycobacterium tuberculosis*, 76, 103, 268–273, 296, 345
drug-induced gene expression, 275
drug-resistant, 339
proteome database, 263, 266

Mycolic acids, 291–292

Mycopropholic acid, 345, 361

*Mycoplasma*, 267

*Mycoplasma genitalium*, 247, 250

*Mycoplasma pneumoniae*, 263, 268

Myriocins, 361–362

Myxalamide, 349

Myxin, 349

Myxobacteria, 343, 349, 351

*Myxococcus*, 46

N

NADH oxidase, 172

“Nanoarchaeum equitans,” 46, 228

Natamycin, 349

National Environmental Policy Act, 452–453
National Park Service bioprospecting on federally owned land, 450–457
  current state of bioprospecting in parks, 453–454
  evaluation of bioprospecting in parks, 454–456
Natural products, 3, 7–8
  biosynthesis, taxonomic distribution, 299
dereplication methods, see Dereplication
gene libraries, 346–347
  marine, 8, 346
  pharmacological agents, 317–318, 356–374
  screening for bioactivity, 317–318, 324–335
taxonomy as roadmap to genes, 239–240, 288–313
Navicula pelliculosa, 322
Negombata magnifica, 183
Neisseria gonorrhoeae, 267
Neisseria meningitidis, 225, 256, 267, 297, 305
Nematode diversity, 21
Neomycin, 336–337
Nigericin, 302–303, 306
Nikkomycin, 328, 340–341, 349
Nisin, 337, 341
Nitrate reductase, 172, 296–297
Nitrate reduction, dissimilatory, by sulfate-reducing bacteria, 172
Nitrile hydratase, 5–6
Nitrite reductase, 172
Nitrite-oxidizing bacteria, 94
Nitrobacter, 400
Nitrogen, removal from wastewater, 398–399
Nitrogen fixation
  icy biosphere, 133, 135
  rhizobia, 205–206
  sulfate-reducing bacteria, 172
taxonomic significance, 295
Nitrogenase, 295
Nitrospira, 297, 399
Nocardia, 291–292
Nocardia lactamurans, 327, 337
Nodulisporic acid, 327, 337
Nodulisporium, 208, 345
Nonactin, 344
“Nonculturable” organisms, see Unculturable/uncultured microbes
Nonparametric estimators, 24
Nonproportionate sampling, 73
Nonuse value, 472
Nosocomial infections, 338
Novobiocin, 326, 337
Nramp gene, 272–273
NtrB–NtrC system, pressure-regulated, 157–158
Nuclear dualism, 59
Numerical taxonomy, 19, 33
Nyctotherus ovalis, 58, 193
Nystatin, 328, 336–337, 339, 348
O
O-antigens, 297, 306
Ocean circulation, 221
Oceanapia sagittaria, 183
Octadecabacter, 227
Oidiodendron, 207
Oidiodendron griseum, 363
Okadaic acid, 183
Oligobacteria, 69, 160–168
  activity control by substrate concentration, 163–167
  composition, 161
  metabolism, 162
  speciation, 162–163
  transporters, 162–167
  viability, 163
Oligomycin, 349
Oligonucleotide fingerprinting, 51–52, 424
Oligonucleotide microarray, 51, Color Plate 1
Oomycetes, 61
Open reading frame analysis, 251–252, 260
Operational taxonomic unit, 19, 23
Ophiostoma, 199
Opisthokonts, 62–63
Opportunity costs, 469–470
Optical tweezers, 84
Option agreements, 437
Orbulina universa, 218, 221
Oreganic acid, 366
Origins of life, 131–132, 142
Orlistat, 371
Oscillatoria chalybea, 296
Oscillatoria spongelliae, 177
Outer-membrane proteins, piezophiles, 156
Oxygen
  reduction by sulfate-reducing bacteria, 172–173
  uptake rate, 280
Oxygenase, 382
Oxytetracycline, 337, 341
P
P test, 25
Pachyphyllina, 185
Paclitaxel, 349–350
Paenibacillus, 295
Paenibacillus validus, 74
Palaeococcus ferrophilus, 155
Pamamycin, 349
Pantoera agglomerans, 193
Parabasalids, 63
Paracoccus denitrificans, 296
Paradigm shift, microbial prospecting, 239–249
“Paradox of the plankton,” 71
Paramecium aurelia, 218
Paramecium primaurelia, 218
Paramecium tredecaurelia, 218
Paraphysomonas, 219, 227
Patenting, 442–443, 453, 456
Pathogenesis
  in vivo-induced protein synthesis, 270–273
  investigations at proteome level, 268–273
Pathogens, biogeography, 225
<table>
<thead>
<tr>
<th>Keyword</th>
<th>Page(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR-based analysis</td>
<td>490</td>
</tr>
<tr>
<td>environmental nucleic acids</td>
<td>90-91</td>
</tr>
<tr>
<td>microbial identification</td>
<td>51-52, 54-55</td>
</tr>
<tr>
<td>Taq polymerase</td>
<td>450-451</td>
</tr>
<tr>
<td><em>Pedicoccus</em></td>
<td>52</td>
</tr>
<tr>
<td><em>Pellina</em></td>
<td>185</td>
</tr>
<tr>
<td>Peloride A</td>
<td>350</td>
</tr>
<tr>
<td>Penicillin</td>
<td>324, 336-337, 341, 345</td>
</tr>
<tr>
<td>Penicillin G expandase</td>
<td>6</td>
</tr>
<tr>
<td>Penicillin resistance</td>
<td>274</td>
</tr>
<tr>
<td><em>Penicillium</em></td>
<td>208, 341, 345</td>
</tr>
<tr>
<td><em>Penicillium brevicalectum</em></td>
<td>331, 368-369</td>
</tr>
<tr>
<td><em>Penicillium chrysogenum</em></td>
<td>6</td>
</tr>
<tr>
<td><em>Penicillium citrinum</em></td>
<td>368-369</td>
</tr>
<tr>
<td><em>Penicillium griseofulvum</em></td>
<td>328</td>
</tr>
<tr>
<td><em>Penicillium notatum</em></td>
<td>324, 337</td>
</tr>
<tr>
<td>Pentostatin</td>
<td>349</td>
</tr>
<tr>
<td>Peptaibol</td>
<td>349</td>
</tr>
<tr>
<td>Peptide mass fingerprinting</td>
<td>262</td>
</tr>
<tr>
<td>Peptide synthetases, nonribosomal</td>
<td>341</td>
</tr>
<tr>
<td>Peptidoglycans</td>
<td>291-292</td>
</tr>
<tr>
<td>Perchlorate-reducing bacteria</td>
<td>219</td>
</tr>
<tr>
<td>Periodicity atlas</td>
<td>252</td>
</tr>
<tr>
<td>Periwinkle</td>
<td>349, 441-443</td>
</tr>
<tr>
<td>Permafrost</td>
<td>130</td>
</tr>
<tr>
<td><em>Pestalotiposis microspora</em></td>
<td>205</td>
</tr>
<tr>
<td>Petroleum reservoirs</td>
<td>124</td>
</tr>
<tr>
<td><em>Petrosia</em></td>
<td>185</td>
</tr>
<tr>
<td><em>Pfiesteria piscicida</em></td>
<td>218</td>
</tr>
<tr>
<td>Phage display technology</td>
<td>322</td>
</tr>
<tr>
<td>Pharmacogenomics</td>
<td>245</td>
</tr>
<tr>
<td>Pharmacological agents</td>
<td>3, 8, 317-318, 356-374</td>
</tr>
<tr>
<td>development using proteomics</td>
<td>273-275</td>
</tr>
<tr>
<td>diversity, reactivity, and toxicity of natural products</td>
<td>358-359</td>
</tr>
<tr>
<td>high-throughput screening</td>
<td>356-357</td>
</tr>
<tr>
<td>sample presentation and chemical dereplication</td>
<td>357-358</td>
</tr>
<tr>
<td>searching for new drugs</td>
<td>245-246</td>
</tr>
<tr>
<td>sponge-associated microbes</td>
<td>181-182</td>
</tr>
<tr>
<td>trends and prospects</td>
<td>371-372</td>
</tr>
<tr>
<td>Phenazine-1-carboxylic acid</td>
<td>206</td>
</tr>
<tr>
<td>Phenetetic (polythetic) species concept</td>
<td>31, 33-34</td>
</tr>
<tr>
<td>Phenome</td>
<td>243</td>
</tr>
<tr>
<td>Phenomics</td>
<td>239-241, 280-287</td>
</tr>
<tr>
<td>flux-balance analysis</td>
<td>282-284</td>
</tr>
<tr>
<td>gene deletions</td>
<td>284</td>
</tr>
<tr>
<td>impact on biotechnology</td>
<td>285-286</td>
</tr>
<tr>
<td>measurement tools</td>
<td>281-282</td>
</tr>
<tr>
<td>phenotypic measurements</td>
<td>35, 280-281</td>
</tr>
<tr>
<td>phenotypic phase plane analysis</td>
<td>284-285</td>
</tr>
<tr>
<td>predicting and analyzing data</td>
<td>282-285</td>
</tr>
<tr>
<td>Phenotype Microarrays</td>
<td>281</td>
</tr>
<tr>
<td>Phenotypic phase plane analysis</td>
<td>284-285</td>
</tr>
<tr>
<td>Phespertpepins</td>
<td>368</td>
</tr>
<tr>
<td>Phromones, bacterial</td>
<td>102</td>
</tr>
<tr>
<td>Phleomycins</td>
<td>329</td>
</tr>
<tr>
<td>Phoma</td>
<td>76-77, 208, 345, 363, 369</td>
</tr>
<tr>
<td>Phomopsis</td>
<td>363</td>
</tr>
<tr>
<td>Phosphoribosylantranilate isomerase</td>
<td>248</td>
</tr>
<tr>
<td>Phosphorus, removal from wastewater</td>
<td>400-402</td>
</tr>
<tr>
<td><em>Photobacterium profundum</em></td>
<td>155-156</td>
</tr>
<tr>
<td>Photorhodopsin gene</td>
<td>113</td>
</tr>
<tr>
<td>Photosynthesis, eukaryotic microbes</td>
<td>58-59</td>
</tr>
<tr>
<td>Phototrophic microbes, icy biosphere</td>
<td>135</td>
</tr>
<tr>
<td>Phyletic gradualanism</td>
<td>41</td>
</tr>
<tr>
<td>Phyllogeographic studies</td>
<td>76</td>
</tr>
<tr>
<td>Phylome</td>
<td>252, 255</td>
</tr>
<tr>
<td>Phyllogenetic species concept</td>
<td>34</td>
</tr>
<tr>
<td>Phylospecies</td>
<td>42-43, 47</td>
</tr>
<tr>
<td>Phylogenome</td>
<td>243</td>
</tr>
<tr>
<td>Phenomenon</td>
<td>133</td>
</tr>
<tr>
<td><em>Planococcus mcmekineii</em></td>
<td>141</td>
</tr>
<tr>
<td><em>Planococcus okeaoikeotes</em></td>
<td>141</td>
</tr>
<tr>
<td><em>Planococcus psychrotoleratus</em></td>
<td>141</td>
</tr>
<tr>
<td>Plant(s), speciation</td>
<td>40-41</td>
</tr>
<tr>
<td>Plant growth-promoting agents</td>
<td>317-318, 391-396</td>
</tr>
<tr>
<td>ACC deaminase</td>
<td>395</td>
</tr>
<tr>
<td>from <em>Azospirillum</em></td>
<td>393-394</td>
</tr>
<tr>
<td>ionophores</td>
<td>392-393</td>
</tr>
<tr>
<td>from <em>Trichoderma</em></td>
<td>394-395</td>
</tr>
<tr>
<td>Plant growth-promoting bacteria</td>
<td>205</td>
</tr>
<tr>
<td>Plant growth-promoting fungi</td>
<td>207-208</td>
</tr>
<tr>
<td>Plant-associated microbes</td>
<td>69, 204-210</td>
</tr>
<tr>
<td>eukaryotic symbiosis</td>
<td>206-208</td>
</tr>
<tr>
<td>prokaryotic symbiosis</td>
<td>205-206</td>
</tr>
<tr>
<td>prospects for exploitation</td>
<td>208-209</td>
</tr>
<tr>
<td>Plasmids</td>
<td>95-96</td>
</tr>
<tr>
<td>culture-independent study</td>
<td>95-96</td>
</tr>
<tr>
<td>transfer in mixed communities</td>
<td>95-96</td>
</tr>
<tr>
<td><em>Plasmodium falciparum</em></td>
<td>60, 245-246, 253-254, Color Plate 8</td>
</tr>
<tr>
<td>Plate reader</td>
<td>281-282</td>
</tr>
</tbody>
</table>
Plating methods, 81–83, Color Plate 2
Picamycin, 349
Pluramycins, 329
pmoA gene, 90
Pneumocandin, 341
Pneumocystis carinii, 63, 339–340
Polaribacter, 227
Polyenes, 302, 328
Polyethylene terephthalate, 3–4
Polyethyleneglycol, 329
Polyketide(s), 341
Polyketide keto synthase, 299–300
Polymyxin B, 337
Polyphasic species, 20
Polyphasic taxonomy, 13, 35, 289–290
Polyphosphate-accumulating organisms, 400–402
Polythetic species concept, see Phenetic (polythetic) species concept
Polyunsaturated fatty acid synthesis, taxonomic significance, 292–294
Porphyromonas gingivalis, 253–254
Postgaardi manager ensis, 217
Postwar bioprospecting, 441
Pradamycins, 340, 349
Pravastatin, 351, 368
Pressure-adapted bacteria, 154–159
Prianos, 185
Principles on Access and Benefit-Sharing for Participating Institutions, 435
Process innovation, 6
Process replacement, 5–6
Processing industries, 319–320
Prochlorococcus, 160
Prochlorococcus marinus, 218
Product improvement, 6
Prokaryotes, see also Bacteria
biogeography, 227–228, 230
genetic exchange, 35–36
recognition of new species, 36–37
species concept, 32–37
1,3-Propanediol, 3–4
Proportionate sampling, 73
Prorocentrum concavum, 183
Prorocentrum lima, 183
Protein(s)
consensus approach for stabilizing, 248
membrane, under pressure conditions, 155–157
microbial identification from protein analysis, 52–53
rational design, 248
Protein chips, 262
Protein engineering, rational, improving industrial enzymes, 381–383, 386
Proteinase, 382–383
Proteome, 260
databases, 262–266
Proteomic signature, 261–262
Proteomics, 241, 243, 249–250, 260–279
bacterial pathogenesis at proteome level, 268–273
development of therapeutic strategies, 273–275
microbial typing at proteome level, 267–268
Protists, 21–22
Protozoa, insect-associated, 193
Pseudoalteromonas, antifoulant production, 406–408
Pseudoalteromonas aurantia, 407
Pseudoalteromonas citrea, 407
Pseudoalteromonas haloplanktis, 408
Pseudoalteromonas luteoviolacea, 407
Pseudoalteromonas rubra, 407
Pseudoalteromonas tunica, 406–408
Pseudoalteromonas silicea, 406–407
Pseudobactin, 392
Pseudomassaria, 370–371
Pseudomonas, 205–206, 229, 391, 394–395
Pseudomonas aeruginosa, 46, 274, 296, 338, 345
Pseudomonas azotoformans, 141
Pseudomonas fluorescens, 95, 110, 246, 296, 337, 392
Pseudomonas fragi, 148
Pseudomonas isachenhowii, 296
Pseudomonas putida, 6, 233, 296, 392–393
Pseudomonas syxantha, 141
Pseudomurien, 291
Psychrobacter, 138, 148, 227
Psychrobacter glacincola, 141
Psychrobacter immobilis, 141, 148
Psychrobacter marincola, 141
Psychrobacter submarinus, 141
Psychroflexus torquis, 293
Psychrophiles, 147–148, 151–152
piezophilic, 155
Psychrotolerants, 147–148
Psyllids, 196–197
Puccinia melanocephala, 221
Punctuated equilibrium, 41
Pure culture, 80–81
Pyluteorin, 349
Pyripyprene A, 369–370
Pyrobaculum, 149
Pyrobaculum aerophilum, 149, 296
Pyrobaculum islandicum, 149
Pyrococcus, 148–149, 155, 228, 255
Pyrococcus abyssi, 155
Pyrococcus furiosus, 4, 149, 256, 305
Pyrococcus horikoshi, 305
Pyrococcus woesei, 151
Pyrodictium, 148–149, 228
Pyrodictium occultum, 149
Pyrolobus fumarii, 149
Pyrolysis mass spectrometry, 9, 54, 292
Pyrophosphate phosphohydrolase, 170
Pyrroline, 328, 349
Pythium, 207
Q
Quasi-option value, 474
Quinupristin, 348
R
Ractinomycins, 329
Raffaelea, 199
Ralstonia, 205
Ralstonia metallidurans, 246
**Ralstonia solanacearum**, 345
Random shotgun sequencing strategy, 250–251
Rapamycin, 300, 303, 306, 328, 344, 349, 351, 360–361
Rare species, 15, 219, 288, 442
Rarefaction analysis, 23, 72
Raromycin, 329
Ratjadon, 349
Real estate leases, 437
Real-time PCR, 52
Renewable raw materials, 3–4
Reporter genes, 94–95
Research collaborative agreements, INBio, 445–447
Resorcyclic acid lactones, 363
Resormycin, 349
Respiratory systems, pressure-regulated, 156
Resuscitation-promoting factor, 102–106
Revacryl 380 Tm, 408
Reverse dot blot hybridization, 51
Reverse transcription-PCR, 91
Rhizobacteria, 391–396
Rhizobia, 205–206
Rhizobium, 205, 295, 394
Rhizoctonia, 207
Rhizopogon, 207
Rhizosphere, 92, 95, 204, 391–396
Rhodobacter, 296
Rhodobacter sphaeroides, 46
Rhodococcus, 291–292
Rhodococcus koreensis, 299
Rhodococcus rhodochrous, 6, 102
Rhodopseudomonas palustris, 46
Rhopaloeides odorabile, 178–181, 187
Rhynchosporum nasuta, 217
Riboflavin, 5
Riboprinter, 52
Ribosequencing, 49–50
Ribotyping, 52
Rice paddy soil, 76, 82–83
Richness estimators, 23–24
Rifampin, 327, 337
Rifamycin, 326, 336, 341
Rigid (fixed) sampling, 73
RNA
environmental
dot blot hybridization and gene arrays, 92–93
evolutionary
extraction, 89
molecular analysis, 89–93
molecular fingerprinting, 91–92
PCR, cloning, and sequencing approach, 90–91
oligobacteria, 162
Roseobacter, 81–83
Royalties, 438, 452, 456
rpoB gene, 90
rRNA genes
genus-level biogeography, 228–229
microbial identification, 49–51, 54
oligobacteria, 163
16S or small-subunit, 21–25, 33–35, 42, 75–76, 80–81, 90, 289–290
soil microbes, 112–113
sponge-associated microbes, 179–180
taxonomic significance, 289–290, 299
Rubber, 441
Russula, 207
Rustmicin, 340, 348
S
Saccharomyces cerevisiae, 154, 157, 166, 284, 286
Saccharopolyspora erythraea, 102, 337
Saccharothrix, 66
Safe minimum standards approach, 470
Saintpaulia, 440–442
Salinibacter ruber, 83
Salmonella enterica, 271–272, 297–298, 305
Salterns, 82, 150
Sampling effort, 73
Sampling strategy, 72–73
Sand layers, deep terrestrial, 124
Sanglifehrins, 361–362
Sapropels, 122–123
Sarcina ventriculi, 147
Sarkomycin, 329
Schizochytrium, 293
Sea ice, 130, 227
Search strategy, 3, 306, 375–376
Seawater, see Marine environment
Seed banks, 464
Selenium, reduction by sulfate-reducing bacteria, 173
Self-assembly, 322
Serratia ficaria, 92
Service industries, 319–320
“Sex ratio Spiroplasma,” 195
Sherlock Microbial Identification System, 53, 55
Shewanella, 155, 292–293, 306
Shewanella benthica, 155
Shewanella violacia, 155, 157
Shinkwrap license, 437
SibopManus, 69–71
Siderophores, 392–393
Sigma 54, pressure-regulated, 157
Silicification, 322
Similarity species concept, 32
Simocyclinones, 332–333
Simonsiella, 44
Simvastatin, 368
Sinefungin, 349
Single-strand conformation polymorphism, 91
Sinorhizobium, 205
Site-directed mutagenesis, 384
Skaermania, 292
Slime molds, 63
Snowball Earth Hypothesis, 132
Soda lakes, 217–219
Sodalis glossinidius, 196–197
Sodium/proton antiporter, 382
Soil
DNA extraction, 88–89
saline, 150
Soil microbes
  functional diversity, 113
  history of soil biology, 109-111
  linking phylogeny and function, 113-115
  metagenomic libraries, 109-119
  biological insights from, 115-117
  challenges and limitations, 115
  experimental strategy, 113-114
  future, 117
  metagenomics as experimental strategy, 113-114
Soil structure, 110-111
Solfataras, 146-149
Sorangicin, 349
Sorangium cellulosum, 349, 364-365
Sordarin, 340, 349
Spatial variability, microbial population, 72
Speciation, 40-48
  animals and plants, 40-41
  bacterial, see Bacterial speciation
Species
  common, 15
  definition, 23
  rare, 15, 219, 288, 442
  unit of biodiversity, 15
Species 2000, 16, 19
Species accumulation curves, 17, 72-73, 76
Species concept, 13, 19, 29-39, 290
  bacteria, 41-42
  phyllospecies, 42-43
  eukaryotic microbes, 31-32
  formulation, 30-31
  prokaryotes, 32-37
  polyphasic approach, 35
uncultured bacteria, 36
Species genome, 20, 36
Species inventories, 15-16
Species redundancy, 415, 417
Species richness, 15, 415
  effect of human activities, 421-422
  estimation, 23-24
  global, 219
scale effects, 72
  supersaturated coexistence, 71-72
Specific affinity theory, 163-167
Spectinomycin, 337, 341, 344
Spergualin, 361
Spher obs assay, 348
Sphingofungin, 349
Sphingomonas, 137, 141
Sphingomonas alaskensis, 75, 82, 85, 166
Spinosyn, 351
Spirastrella spinispirulifera, 183
Spirochetes, insect-associated, 194
Spirulina, 147
Sponge(s), 177-190, 322
  anatomy and physiology, 177
  aquaculture, 187
Sponge 01IND 35, 180-181, 185-186
Sponge 01IND 52, 185-186
Sponge-associated microbes, 177-190
  diversity, 179-181
  manzamine-containing sponges, 185-186
  microbiology, 177-179
  natural products from, 181-185
Spongia, 183
Spongiostatins, 183
Sporormiella intermedia, 368
Spray-ionization mass spectrometry, 54, 292, 333
Squalestatins, 368-369
Stable isotope technique, linking microbial community
  structure with function, 93-94
Stachybotrys, 369
Staphylococcus, 185, 291
Staphylococcus agalactiae, 256
Staphylococcus aureus, 225, 256, 296-297, 306
  drug-induced gene expression, 275
  drug-resistant, 338-339
Staphylococcus carnosus, 296
Staphylococcus epidermidis, 256
Staphylococcus pneumoniae, 256
Staphylothermus, 149
Stated preference techniques, 475
Statins, 330-331, 356, 368
Stauroporine, 366
Stellata, 184
Stephanodiscus niagarae, 220
Stigmastellin, 349
Strain development, 285-286
Strain discrimination, 9
Strain typing, at proteome level, 267-268
Stramenopiles, 61
Streptococcus equisimilis, 274
Streptococcus pneumoniae, 225, 253
drug-resistant, 274, 338
Streptococcus pyogenes, 273
Streptogramins, 336
Streptomycetes, 246, 305, 340-342, 361-362, 366
  antitumor agents, 363
  sponge-associated, 182
taxonomy, 291
“Streptomycetes aerouvifer,” 295
Streptomycetes albidoflavineger, 303
Streptomycetes antibioticus, 325, 332, 344, 349
Streptomycetes amylolius, 367-368
Streptomycetes argillaceus, 349
Streptomycetes asiaticus, 300
Streptomycetes auranticolor, 303
Streptomycetes aureofaciens, 326, 337
Streptomycetes avermitilis, 246, 299-300, 332, 344
Streptomycetes caespitosus, 349
Streptomycetes cangkringensis, 300
Streptomycetes cinnamonensis, 337
Streptomycetes clavuligerus, 337
Streptomycetes coelicolor, 46, 103, 246, 253, 296,
  299-300, 306, 344
Streptomycetes coeruloreubides, 330
Streptomycetes cyaneus, 364-365
Streptomycetes diastaticus, 330
Streptomyces erythraea, 326
Streptomyces felleus, 326
Streptomyces fradiae, 327, 337
Streptomyces galilaeus, 330, 349
Streptomyces garyphalus, 326
"Streptomyces geldamyceticus," 300, 303
Streptomyces griseiniger, 303
Streptomyces griseolosporeus, 295, 341
Streptomyces griseus, 337, 344
Streptomyces hygroscopicus, 300, 303, 328, 344, 360-361
Streptomyces indonesiensis, 300
Streptomyces javensis, 300
Streptomyces kanamycetus, 337
Streptomyces lavendulae, 186-187, 326
Streptomyces lincolnensis, 337
Streptomyces lividans, 306
Streptomyces malaysiensis, 300
Streptomyces mediterranei, 337
Streptomyces melanosporofaciens, 300
Streptomyces niveus, 295, 326
Streptomyces noursei, 328, 337
Streptomyces orchidaceus, 326, 337
Streptomyces orientalis, 337
Streptomyces parvulus, 349
Streptomyces peucetius, 349
Streptomyces phaeogriseichromogenes, 303
Streptomyces phaeoluteichromogenes, 303
Streptomyces phaeoluteigriseus, 303
Streptomyces pristinaespiralis, 337
Streptomyces rhizosphaericus, 300
Streptomyces rimosus, 326, 337
Streptomyces sparsogenes, 303
Streptomyces spectabilis, 337
Streptomyces spheroides, 295, 326, 337
Streptomyces tendae, 328
Streptomyces toxytricini, 370-371
Streptomyces tsukubaensis, 360-361
Streptomyces venezuelae, 326, 337
Streptomyces verticillus, 329, 349
Streptomyces violaceoruber clade, 303-304, 306, Color Plate 9
Streptomyces violaceusniger clade, 300-303, 306
Streptomyces viridochromogenes, 325, 337
Streptomyces viridofaciens, 337
Streptomycin, 300, 306, 326, 336-337, 341, 344
Subsurface environment, 120-129
Subtilisin, 386
Sulfate-reducing bacteria, 69, 94, 169-176, 297
dissimilatory sulfate reduction, 169-171, 297
fermentation of inorganic sulfur compounds, 171
fermentation of organic substrates, 171
metal reduction, 173
reduction of elemental sulfur, nitrate, and oxygen, 172-173
Sulfide-producing bacteria, 124, 170
Sulfite oxidase, 296-297
Sulfite reductase, 297
Sulfolobus, 146-147, 149
Sulfolobus acidocaldarius, 147
Sulfolobus brierley, 147
Sulfolobus "islandicus," 228-229
Sulfolobus metallicus, 147
Sulfolobus solfataricus, 149, 255
Sulfur, elemental, reduction by sulfate-reducing bacteria, 172
Supercooled clouds, 137
Supersaturated coexistence, 71-72
Suppressive subtractive hybridization, 255-256
Sustainable industry, 5
Swinholide A, 182-183
Symbionts, 21, 76
of insects, 191-203
of marine invertebrates, 186-187
of plants, 204-210
of sponges, 177-190
Sympatric speciation, 41
Synechococcus, 160, 296
Synechocystis, 46, 263
Synercid, 337, 348
Syringomycin, 349
Syringopeptin, 349
T
TA, 343
Tacrolimus, see FK506
Taq polymerase, 450-451, 454
Taxic diversity, 15
Taxols, 350, 364
Taxomyces andreanae, 205
Taxon, 30
Taxonomic databases, 75
Taxonomy
α-taxonomy, 19
β-taxonomy, 19
biodiversity estimates from, 17
genes and, 291-298
history, 289
importance, 19
modern era, 289-291
morphologically based, 289
phylogeny-based, 289-290
as roadmap to genes, 239-240, 288-313
role in bioprospecting, 288-313
Taxonomy Workbench, 244
Taxon-to-taxon ratios, 16
Taxus, 349
Technological innovation, recovery of microorganisms, 74–75
Technology transfer, 429, 431–432, 438, 446–447, 449
Tedania ignis, 182
Teleostatin, 367–368
Temperature gradient gel electrophoresis, 91–92
Temporal variability, microbial population, 72
Tenipocide, 349
Tensin, 349
Tephritids, 193
Terminal restriction fragment analysis, 91
Termites, 192–194, 196, 198–200
Termitomyces, 199
Terpenoids, 341
Terragine, 115–117
Tethya aurantia, 322
Tetracenomycins, 327
Tetracyclines, 326, 336–337
Thauera, 94
Thelephora, 207
Theonella swinhoei, 179, 181–183
Theopalauamide, 182–183
Thermoalkaliphiles, 147
Tbermoanaerobacter, 149
Thermoanaerobacter ethanolicus, 149
Thermobispora, 299
Thermococcus, 148–149, 155, 228
Thermococcus acidaminivorans, 147
Thermococcus aggregans, 149
Thermococcus alcaliphilus, 147
Thermococcus peptonophilus, 155
Thermodesulfobacterium, 170
Thermofilum, 149
Thermomicrospira, 217
Thermomonospora chromogena, 299
Thermophiles, piezophilic, 155
Thermoplasma, 146
Thermoplasma acidophilum, 147
Thermoproteus, 149
Thermoproteus tenax, 146, 149
Thermotoga, 148–149
Thermotoga maritima, 149, 151, 253–256, 298
Thermotoga neapolitana, 4, 149
Thermus, 83, 149
Thermus aquaticus, 149
Thermus thermophilus, 296
Thienamycin, 327
Thiobacillus caldus, 147
Thiobacillus ferrooxidans, 147
Thraustochytrium, 293
Time-series description, discovery of new species, 16
TNP-470, 364
Toxoplasma, 345
Toxoplasma gondii, 356, 359–360, 429, 441–442
Topotecan, 349–350
Toxicogenomics, 245
ToxR-ToxS proteins, 156–157
Transcript profiling, 246
Transcriptional regulation, piezophiles, 157–158
Transcriptome, 260
Transcriptomics, 241, 243
Transglutaminase, 377
Transporters, oligobacteria, 162–167
Translational organisms, 163
Travel behavior, 475
Trembya princeps, 196–197
Treponema, 194
Treponema pallidum, 244
Tributyltin-based paints, 405
Trichoderma, 207–208, 345, 378, 391
plant growth-promoting agents, 394–395, Color Plates 10 and 11
Trichoderma harzianum, 208, 394–395, Color Plates 10 and 11
Trichoderma polysporum, 8–9, 328
Trichomonas, 58
Trichomonas vaginalis, 63, 298
Trichostatin A, 341
Trisporic acids, 392
Triionate pathway, 170
Tryprostatin, 341
Tryptophan uptake, pressure-sensitive, 157
Trytide, 196–197
Tsukamurella, 292
Tubercidin, 349
Turbochrysins, 115–117, 346
Two-component regulatory system, pressure-regulated, 157
Two-dimensional gel electrophoresis, monitoring protein synthesis, 261–262, 267
Tylosin, 337
Tyropeptins, 368
Tyrothricin, 337
U
Ubiquitous dispersal, free-living microbes, 213–214, 216–224
UCN-01, 366–367
Ultramicrobacteria, 85
Ulva reticulata, 407
Unculturability/uncultured microbes, 22–25, 74–76
antifoulant production, 409
classification, 36
culture-independent microbiology, 88–89
genomics, 250, 256–257
industrial enzyme production, 377, 380–382
metagenomics approach, 109–119
resuscitation, 100–108
soil, 109–119
Uranium, reduction by sulfate-reducing bacteria, 173
Uraochimycins, 182
Uronema, 219
Usmic acid, 207
V
Vaccine development, 246, 273–274
Valinomycin, 341, 344
Vancomycin, 336–337
Vancomycin resistance, 338–339
*Verrucomicrobia*, 82–83, 133
Vertical gene transfer, 32
*Verticillium balanoides*, 366
Viability, 100
  oligobacteria, 163
“Viable but nonculturable,” 88, 288
*Vibrio*, 182, 407
*Vibrio anguillarum*, 408
*Vibrio cholerae*, 293–295, 298
*Vibrio parahaemolyticus*, 166, 408
*Vibrio psychrothermus*, 148
*Vibrio splendidus*, 408
Vinblastine, 349, 441
Vincristine, 349, 441
Vinorelbine, 349
Violacein, 115–117
Violaceol I, 346
Virginiamycin, 337
Virtual whole-cell models, 247
Virulence, investigations at proteome level, 268–273
Vicosinamide, 349
Volcanic eruptions, 221
W
Wastewater treatment, 397–404, 422
  nitrogen removal, 398–399
  phosphorus removal, 400–402
Water, transport of microbes, 220–221
Water molds, 61
Weevils, 196
Well-being, equation of, 470–472
Western Australian Department of Conservation and Land Management, 437
Whiteflies, 196–197
Whole-genome sequencing, see Genome sequencing
Wigglesworthia glossinidia, 196–197
Willingness to pay, 470–471, 473
Wind, transport of microbes, 220–221
Wolbachia, 195
Wolbachia pipientis, 195
WORLDMAP project, 16
Wortmannin, 366
X
Xanthomonas, 345
Xenical, 351
Xenobiotics, 397
*Xestospongia*, 185
XR774, 362–363
XR842, 364–365
Xylaria, 345
Xylella fastidiosa, 162, 263, 345
Y
Yellowstone National Park
  hot pools, 84
  *Taq* polymerase, 450–451, 454
Yellowstone National Park Microbial Database and Map Server, 214, 232–236, Color Plates 3 through 7
Yellowstone-Diversa CRADA, 429–430, 450–457
  benefit distribution, 455–456
  effect on conservation, 454–455
  legal challenges, 452–453
  sustainable use of biotic resources, 455
*Yersinia enterocolitica*, 148, 271
*Yersinia pestis*, 298
Yew tree, 349–350
Z
Zaragozic acids, 368–369
Zeatin, 392
Zygomycetes, 62–63