Bacillus subtilis and Other Gram-Positive Bacteria

BIOCHEMISTRY, PHYSIOLOGY, AND MOLECULAR GENETICS
Bacillus subtilis
and Other Gram-Positive Bacteria
BIOCHEMISTRY, PHYSIOLOGY, AND MOLECULAR GENETICS

EDITOR IN CHIEF
Abraham L. Sonenshein
Department of Molecular Biology and Microbiology
Tufts University, Boston, Massachusetts

EDITORS
James A. Hoch
Division of Cellular Biology
Department of Molecular and Experimental Medicine
The Scripps Research Institute, La Jolla, California

Richard Losick
Department of Cellular and Developmental Biology
Harvard University, Cambridge, Massachusetts

AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, D.C.
CONTENTS

Contributors ........................................................... vii
Preface ................................................................. xi

I. GRAM-POSITIVE BACTERIA
2. Staphylococcus. Richard Novick ........................................ 17
3. Clostridium. Michael Young and Stewart T. Cole .................... 35
5. Lactococcus and Lactobacillus. Bruce M. Chassy and Cynthia M. Murphy .... 65
8. Bacillus anthracis. Curtis B. Thorne ................................ 113

II. METABOLISM AND ITS REGULATION
11. Carbohydrate Catabolism: Pathways, Enzymes, Genetic Regulation, and Evolution. Michel Steinmetz ......................... 157
12. Glycolysis. Peter Fortnagel ........................................... 171
13. The Krebs Citric Acid Cycle. Lars Hederstedt ..................... 181
17. Regulation of Phosphorus Metabolism. F. Marion Hulet .................. 229
19. Biosynthesis of Aromatic Amino Acids. Dennis Henner and Charles Yanofsky .... 269
20. Biosynthesis of Glutamine and Glutamate and the Assimilation of Ammonia. Harold J. Schreier ................. 281
22. Biosynthesis of the Branched-Chain Amino Acids. Pamela S. Fink .......... 307
24. De Novo Purine Nucleotide Synthesis. Howard Zalkin ............ 335
26. Purine and Pyrimidine Salvage Pathways. Per Nygaard ........... 359

III. CELL ENVELOPE
28. Biosynthesis and Function of Membrane Lipids. Diego de Mendoza, Roberto Grau, and John E. Cronan, Jr. .............. 411

IV. CHROMOSOME STRUCTURE
29. The Genetic Map of Bacillus subtilis. C. Anagnostopouloos, Patrick J. Piggott, and James A. Hoch ............. 425
30. Physical Map of the Bacillus subtilis 168 Chromosome. Mitsuhiro Itaya ........... 463
32. The Genetic Map of Bacillus megaterium. Patricia S. Vary ........ 475
33. The Genetic Map of Bacillus stearothermophilus NUB36. Neil E. Welker .......... 483
34. The Genetic Map of Staphylococcus aureus. Peter A. Pattee .............. 489
35. The Chromosome Map of \textit{Streptomyces coelicolor} A3(2). David A. Hopwood, Helen M. Kleser, and Tobias Kleser 497

V. CHROMOSOME REPLICATION, MODIFICATION, AND REPAIR
37. DNA Repair Systems. Ronald E. Yasbin, David Cheo, and David Bol 529
38. Restriction/Modification and Methylation Systems in \textit{Bacillus subtilis}, Related Species, and Their Phages. Thomas A. Trautner and Mario Noyer-Weidner 539

VI. GENETIC EXCHANGE AND GENETIC ENGINEERING
39. Genetic Exchange and Homologous Recombination. David Dubnau 555
40. Transposons and Their Applications. Philip Youngman 585
41. Conjugative Transposons. June R. Scott 597
42. Integrational Vectors for Genetic Manipulation in \textit{Bacillus subtilis}. Marta Perego 615
43. Plasmids. Laurent Janniere, Alexandra Gruss, and S. Dusko Ehrlich 625
44. Temperate Phage Vectors. J. Errington 645

VII. TRANSCRIPTION AND TRANSLATION MACHINERY
45. RNA Polymerase and Transcription Factors. Charles P. Moran, Jr. 653
46. Ribosomal Structure and Genetics. Tina M. Henkin 669
47. tRNA, tRNA Processing, and Aminoacyl-tRNA Synthetases. Christopher J. Green and Barbara S. Vold 683
49. Protein Secretion. Vasantha Nagarajan 713

VIII. POSTEXPONENTIAL-PHASE PHENOMENA
50. Two-Component Regulatory Systems. Tarek Msadek, Frank Kunst, and Georges Rapoport 729
51. spoO Genes, the Phosphorelay, and the Initiation of Sporulation. James A. Hoch 747
52. AbrB, a Transition State Regulator. Mark A. Strauch 757
54. Regulatory Proteins That Control Late-Growth Development. Issar Smith 785
55. Spore Structural Proteins. Peter Setlow 801

IX. BACTERIOPHAGES
56. SPO1 and Related Bacteriophages. Charles R. Stewart 813
57. Temperate Bacteriophages. Stanley A. Zahler 831
58. Replication and Transcription of Bacteriophage \(\phi29\) DNA. Margarita Salas and Fernando Rojo 843
59. Morphogenesis of Bacteriophage \(\phi29\). Dwight Anderson and Bernard Reilly 859

X. PRODUCTION OF COMMERCIAL PRODUCTS
60. Fermentation of \textit{Bacillus}. M. V. Arbige, B. A. Bulthuis, J. Schultz, and D. Crabb 871
61. Peptide Antibiotics. Peter Zuber, Michiko M. Nakano, and Mohamed A. Marahiel 897
62. Commercial Production of Extracellular Enzymes. Eugenio Ferrari, Alisha S. Jarmagin, and Brian F. Schmidt 917
63. Proteases. Janice Pero and Alan Sloma 939
64. Insecticidal Toxins. Arthur I. Aronson 953

Index 965
CONTRIBUTORS

C. Anagnostopoulos • Laboratoire de Génétique Microbienne, Institut National de la Recherche Agronomique, 78352 Jouy en Josas Cedex, France

Dwight Anderson • University of Minnesota, 18-246 Moos Tower, 515 Delaware Street, S.E., Minneapolis, Minnesota 55455

M. V. Arbige • Genencor International Inc., 180 Kimball Way, South San Francisco, California 94080

A. R. Archibald • Department of Microbiology, The Medical School, The University of Newcastle upon Tyne, Framlington Place, Newcastle upon Tyne NE2 4HH, United Kingdom

Arthur I. Aronson • Department of Biological Sciences, Purdue University, West Lafayette, Indiana 47907

Vasco Azevedo • Laboratoire de Génétique Microbienne, Institut National de la Recherche Agronomique, Domaine de Vilvert, 78352 Jouy en Josas Cedex, France

Simon Baumberg • Department of Genetics, University of Leeds, Leeds LS2 9JT, United Kingdom

David Bol • Department of Biological Sciences and The Program in Molecular and Cell Biology, University of Maryland Baltimore County, Baltimore, Maryland 21045

B. A. Bulthuis • Genencor International Inc., 180 Kimball Way, South San Francisco, California 94080

Michael G. Caparon • Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, Missouri 63110

Michael J. Chamberlin • Division of Biochemistry and Molecular Biology, University of California, Berkeley, California 94720

Glenn H. Chamblish • Department of Bacteriology, University of Wisconsin-Madison, Madison, Wisconsin 53706

Bruce M. Chassy • Department of Food Science, University of Illinois, ABL 103, 1302 W. Pennsylvania Avenue, Urbana, Illinois 61801

K. F. Chater • John Innes Institute, John Innes Centre, Norwich NR4 7UH, United Kingdom

David Cheo • Department of Biological Sciences and The Program in Molecular and Cell Biology, University of Maryland Baltimore County, Baltimore, Maryland 21045

Stewart T. Cole • Unité de Génétique Moléculaire Bactérienne, Institut Pasteur, 28 Rue du Docteur Roux, 75724 Paris Cedex 15, France

D. Crabb • Genencor International Inc., 180 Kimball Way, South San Francisco, California 94080

John E. Cronan, Jr. • Department of Microbiology and Department of Biochemistry, University of Illinois, Urbana, Illinois 61801

Diego de Mendoza • Departamento de Microbiologia, Facultad de Ciencias Bioquimicas y Farmaceuticas, Universidad Nacional de Rosario, Suipacha 531, 2000 Rosario, Argentina

David Dubnau • Department of Microbiology, Public Health Research Institute, 455 First Avenue, New York, New York 10016

S. Dusko Ehrlich • Laboratoire de Génétique Microbienne, Institut National de la Recherche Agronomique, Domaine de Vilvert, 78352 Jouy en Josas Cedex, France

J. Errington • Sir William Dunn School of Pathology, South Parks Road, Oxford OX1 3RE, United Kingdom

Matthew J. Fagan • Department of Biology, University of California at San Diego, La Jolla, California 92093-0116

Eugenio Ferrari • Genencor International Inc., 180 Kimball Way, South San Francisco, California 94080

Pamela S. Fink • Department of Microbiology and Immunology, Wright State University, Dayton, Ohio 45435

Susan H. Fisher • Department of Microbiology, Boston University School of Medicine, 80 East Concord Street, Boston, Massachusetts 02118

Peter Fortnagel • Abteilung für Mikrobiologie, Institut für Allgemeine Botanik, Universität Hamburg, Ohnhorststrasse 18, D-2000 Hamburg, Germany
Contributors

Roberto Grau • Departamento de Microbiologia, Facultad de Ciencias Bioquímicas y Farmaceuticas, Universidad Nacional de Rosario, Suipacha 531, 2000 Rosario, Argentina

Christopher J. Green • SRI International, 333 Ravenswood Avenue, Menlo Park, California 94025

Alexandra Gruss • Laboratoire de Génétique Microbienne, Institut National de la Recherche Agronomique, 78352 Jouy en Josas Cedex, France

I. C. Hancock • Department of Microbiology, The Medical School, The University of Newcastle upon Tyne, Framlington Place, Newcastle upon Tyne NE2 4HH, United Kingdom

C. R. Harwood • Department of Microbiology, The Medical School, The University of Newcastle upon Tyne, Framlington Place, Newcastle upon Tyne NE2 4HH, United Kingdom

Lars Hederstedt • Department of Microbiology, University of Lund, Sölvegatan 21, S-223 62 Lund, Sweden

Tina M. Henkin • Department of Biochemistry and Molecular Biology, Albany Medical College, Albany, New York 12208

Dennis Henner • Department of Cell Genetics, Genentech Inc., 460 Point San Bruno Boulevard, South San Francisco, California 94080

James A. Hoch • Division of Cellular Biology, Department of Molecular and Experimental Medicine, The Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, California 92037-1093

Christian Hoischen • Department of Biology, University of California at San Diego, La Jolla, California 92093-0116

David A. Hopwood • John Innes Institute, John Innes Centre, Norwich NR4 7UH, United Kingdom

F. Marion Hulett • Department of Biological Sciences, Laboratory for Molecular Biology, University of Illinois at Chicago, Chicago, Illinois 60680

Mitsuhiro Itaya • Mitsubishi Kasei Institute of Life Sciences, 11, Minamiooya, Machida-shi, Tokyo 194, Japan

Laurent Jannière • Laboratoire de Génétique Microbienne, Institut National de la Recherche Agronomique, 78352 Jouy en Josas Cedex, France

Alisha S. Jarnagin • Genencor International Inc., 180 Kimball Way, South San Francisco, California 94080

Helen M. Kieser • John Innes Institute, John Innes Centre, Norwich NR4 7UH, United Kingdom

Tobias Kieser • John Innes Institute, John Innes Centre, Norwich NR4 7UH, United Kingdom

Ursula Klingel • Department of Genetics, University of Leeds, Leeds LS2 9JT, United Kingdom

Frank Kunst • Unité de Biochimie Microbiennne, Centre National de la Recherche Scientifique, URA 1300, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris Cedex 15, France

Mohamed A. Marahiel • FB Chemie, Philips-Universität Marburg, Marburg, Germany

Leticia Márquez-Magaña • Division of Biochemistry and Molecular Biology, University of California, Berkeley, California 94720

Charles P. Moran, Jr. • Department of Microbiology and Immunology, Emory University School of Medicine, Atlanta, Georgia 30322

Tarek Msadek • Unité de Biochimie Microbiennne, Centre National de la Recherche Scientifique, URA 1300, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris Cedex 15, France

Cynthia M. Murphy • Department of Food Science, University of Illinois, ABL 103, 1302 W. Pennsylvania Avenue, Urbana, Illinois 61801

Vasantha Nagarajan • Central Research and Development Division, E. I. du Pont de Nemours & Company, Wilmington, Delaware 19880-0228

Michiko M. Nakano • Department of Biochemistry and Molecular Biology, Louisiana State University Medical Center, 1501 Kings Highway, Shreveport, Louisiana 71130-3932
Richard Novick  •  Public Health Research Institute, 455 First Avenue, New York, New York 10016
Mario Noyer-Weidner  •  Max-Planck-Institut für Molekulare Genetik, Ihnestrassse 73, DW-1000 Berlin 33, Germany
Per Nygaard  •  Institute of Biological Chemistry B, University of Copenhagen, DK-1307 Copenhagen K, Denmark
George W. Ordal  •  Department of Biochemistry, College of Medicine, University of Illinois, Urbana, Illinois 61801
Peter A. Pattee  •  Department of Microbiology, Immunology and Preventive Medicine, 205 Science 1, Iowa State University, Ames, Iowa 50011
Henry Paulus  •  Department of Metabolic Regulation, Boston Biomedical Research Institute, 20 Stanford Street, Boston, Massachusetts 02114, and Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, Massachusetts 02115
Marta Perego  •  Istituto di Tecnica Farmaceutica, Università degli Studi di Parma, Via M. D'Azeglio 85, 43100 Parma, Italy, and Dipartimento di Genetica e Microbiologia, Università degli Studi di Pavia, Via Abbiategrasso 207, 27100 Pavia, Italy
John B. Perkins  •  OmniGene, Inc., 763D Concord Avenue, P.O. Box 9002, Cambridge, Massachusetts 02139-9002
Janice G. Pero  •  OmniGene, Inc., 763D Concord Avenue, P.O. Box 9002, Cambridge, Massachusetts 02139-9002
Patrick J. Piggot  •  Department of Microbiology and Immunology, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, Pennsylvania 19140-5196
Fergus G. Priest  •  Department of Biological Sciences, Heriot Watt University, Edinburgh EH14 4AS, Scotland
Cheryl L. Quinn  •  Molecular Immunology Group, Institute of Molecular Medicine, University of Oxford, John Radcliffe Hospital, Headington, Oxford OX3 9DU, England
Georges Rapoport  •  Unité de Biochimie Microbienne, Centre National de la Recherche Scientifique, URA 1300, Institut Pasteur, 2 rue du Docteur Roux, 75774 Paris Cedex 15, France
Bernard Reilly  •  University of Minnesota, 18-246 Moos Tower, 515 Delaware Street, S.E., Minneapolis, Minnesota 55455
Jonathan Reizer  •  Department of Biology, University of California at San Diego, La Jolla, California 92093-0116
Fernando Rojo  •  Centro de Biología Molecular (CSIC-UAM), Universidad Autónoma, Cantoblanco, 28049 Madrid, Spain
Milton H. Saier, Jr.  •  Department of Biology, University of California at San Diego, La Jolla, California 92093-0116
Margarita Salas  •  Centro de Biología Molecular (CSIC-UAM), Universidad Autónoma, Cantoblanco, 28049 Madrid, Spain
Richard M. Sayre  •  Nematology Laboratory, Agricultural Research Service, U.S. Department of Agriculture, 10300 Baltimore Avenue, Beltsville, Maryland 20705
Brian F. Schmidt  •  Genencor International Inc., 180 Kimball Way, South San Francisco, California 94080
Harold H. Schreier  •  Center of Marine Biotechnology, University of Maryland, 600 East Lombard Street, Baltimore, Maryland 21202, and Department of Biological Sciences, University of Maryland, Baltimore County, Baltimore, Maryland 21228
J. Schultz  •  Genencor International Inc., 180 Kimball Way, South San Francisco, California 94080
June R. Scott  •  Department of Microbiology and Immunology, Emory University Health Sciences Center, Atlanta, Georgia 30322
Pascale Serror  •  Laboratoire de Génétique Microbiennne, Institut National de la Recherche Agronomique, Domaine de Vilvert, 78352 Jouy en Josas Cedex, France
Peter Setlow  •  Department of Biochemistry, University of Connecticut Health Center, Farmington, Connecticut 06030-3305
Alan Sloma  •  Novo-Nordisk Biotech, Davis, California 95616
In the history of prokaryotic biology, only a few species have received highly intensive study. The rise to prominence of *Bacillus subtilis* as a subject of modern microbiological investigation can be traced to the success of John Spizizen, in the late 1950s, in demonstrating genetic transformation of a particular isolate of *B. subtilis* by purified DNA. Previously, transformation had been successful only with the pneumococcus. Using a mutant in tryptophan biosynthesis, isolated by Burkholder and Giles after heavy mutagenesis of the standard Yale University strain, Spizizen and Costa Anagnostopoulou determined the growth conditions that induce genetic competence, paving the way for all future studies in *B. subtilis* of gene structure, organization, and regulation and of the mechanisms of transformation and recombination. This highly transformable *trp* mutant, called strain 168, became the standard parental strain for most subsequent studies using either genetic or biochemical approaches.

With a few years after Spizizen's discovery, Pierre Schaeffer used the new technology to break open the study of microbial differentiation by integrating genetics, biochemistry, and morphology. The subsequent development of *B. subtilis* as a subject of intensive study was therefore dependent on and supported by the twin pillars of an all-important technological advance and the insight that bacterial differentiation was of enormous intrinsic interest and had become amenable to detailed analysis. At present, *Escherichia coli* and its closest relatives are the only prokaryotes as well understood as is *B. subtilis*.

The genus *Bacillus* incorporates many species of gram-positive, rod-shaped, aerobic, endospore-forming bacteria (see chapter 1). Most species normally inhabit the soil or rotting plant materials. Their usually strict aerobicism differentiates *Bacillus* species from *Clostridium* species, which are generally strict anaerobes. Except for *B. anthracis*, the *Bacillus* spp. are considered to be nonpathogenic or, at most, opportunistic pathogens for humans and animals. At least some species (e.g., *B. subtilis var. natto*) are sufficiently innocuous to be eaten in large quantities on a regular basis.

The division of the bacterial world according to the results of an early cytological reaction (the Gram stain) has proved to have a solid foundation in bacterial structure and evolution. It is the multilayered structure of the cell wall that allows gram-positive bacteria to retain a crystal violet-iodine precipitate when exposed to organic solvents. The outer membrane and thin cell wall of gram-negative bacteria are unable to protect the crystals. The significance of this division has been demonstrated by evolutionary studies of rRNA sequences, protein sequences, and DNA homologies. Even the molecular mass of the major RNA polymerase sigma factor seems to correlate strongly with Gram-staining properties. Moreover, the ability of plasmids to replicate and genes to be expressed in various host cells seems to be closely related to the Gram reaction. On the other hand, there are important exceptions to this rule, e.g., plasmids that replicate in both gram-positive and gram-negative bacteria and genes from a gram-positive bacterium that are more readily expressed in a gram-negative bacterium than they are in other gram-positive bacteria. Moreover, the special features associated with growth under particular environmental conditions, such as anaerobiosis, thermophily, and alkalophily, impose demands that cut across the gram-positive/gram-negative divide.

This book is meant to provide fundamental information about gram-positive bacteria; it is modeled on the two-volume set entitled *Escherichia coli and Salmonella typhimurium: Cellular and Molecular Biology* (American Society for Microbiology). These earlier volumes have proven to be an outstanding resource for the facts about bacterial physiology, genetics, biochemistry, and regulation. One could be led to believe that their regular updating would be a sufficient resource for understanding the entire bacterial world. We now know, however, that the *E. coli* paradigm is not always useful when applied to distantly related microbes. Thus, the interesting physiology of many gram-positive species, their role in pathogenesis, and their long and successful utilization in the fermentation industry make an up-to-date account of their special properties long overdue. It should be noted that several important phenomena, such as lysogeny, conjugative transposition, and alternative sigma factors for RNA polymerase, were discovered first in gram-positive bacteria. Some of these phenomena have been studied in these organisms at an unmatched level of detail. Moreover, the developmental biology and secondary metabolism of *Bacillus*, *Clostridium*, and *Streptomyces* have drawn researchers to study stationary-phase events in these bacteria for many decades, providing theoretical and experimental paradigms for all bacteria.

Diversity within a common framework is the hallmark of the bacterial world. Recent interest in understanding the detailed physiology of diverse bacteria has revealed similar but inexact counterparts to the genetic organization, metabolic pathways, and mechanisms of gene regulation found in *E. coli*. For instance, *E. coli* regulates expression of genes for
degradation of carbon and nitrogen sources by controlling the activities of positive regulatory proteins that stimulate transcription of large groups of genes. The evidence to date for gram-positive bacteria is that most carbon and nitrogen metabolism genes are controlled by negative regulatory proteins, and no evidence for very large regulons has been found. Moreover, in E. coli, the signal compound for carbon metabolism is cyclic AMP. In gram-positive bacteria, cyclic AMP is either absent or irrelevant to the regulation of carbon metabolism genes.

There are interesting nuances to this pattern of diversity. Some of the regulatory proteins active in gram-positive bacteria are clearly homologs of proteins found in all bacteria. They fall into various families of related proteins (e.g., the two-component systems, LysR family members, lac-gal repressor homologs, sigma factors, antitermination proteins, etc.). The E. coli glutamine synthetase and nitrogen metabolism regulon is controlled by a two-component system. In B. subtilis, two-component systems regulate stationary-phase gene expression, degradative enzyme synthesis, phosphorus metabolism, and genetic competence, but not nitrogen metabolism. Instead, the B. subtilis glutamine synthetase gene is regulated by a repressor homologous to the E. coli MerR repressor. (In Clostridium acetobutylicum, a third mechanism that may involve antisense RNA seems to be responsible for regulation of glutamine synthetase synthesis.) Similarly, in E. coli, a specific sigma factor, σ^54, recognizes promoter sites in the nitrogen metabolism regulon; the homologous protein in B. subtilis directs transcription of a carbon metabolism operon.

The predominant mechanisms of transcription attenuation in gram-positive and gram-negative bacteria also appear to be different. For many amino acid biosynthesis operons in E. coli and its relatives, the translatability of the RNA sequence upstream of the first structural gene of the operon determines whether transcription of the operon will continue or be aborted. That is, movement of ribosomes along the nascent mRNA is the determining factor. In the trp operon of B. subtilis, regulation by transcriptional attenuation also occurs, but in this case a specific protein acts as a termination factor when tryptophan is in sufficient supply. Terminator or antiterminator proteins are thought to regulate the B. subtilis purine biosynthesis, pyrimidine biosynthesis, levansucrase, and tyrosine tRNA synthetase transcription units as well.

The detailed mechanism of regulation of chemotaxis also differs in E. coli and B. subtilis. Both organisms use similar proteins to encode flagella, chemotactic receptors, switch functions, and the flagellar motor. In E. coli, the activity of the receptors (or methyl-accepting chemotaxis proteins) is modified by cycles of methylation and demethylation. The B. subtilis receptors, by contrast, maintain the same degree of methylation under all conditions, but exchange their methyl groups with an as yet unidentified regulator protein. This regulator seems to link the receptors to the flagellar motor. In addition, phosphorylation of a major regulatory protein, CheY, has opposite effects on the flagellar motor in the two organisms.

The ability of bacteria to find multiple ways to achieve the same end is also seen in the organization of biochemical pathways and the genes that encode the relevant enzymes. For example, the reactions catalyzed by anthranilate synthetase (the first step in tryptophan biosynthesis) and phosphonobutane synthetase are homologous. In E. coli and Serratia marcescens, the glutamine amidotransferase components of these enzyme complexes are encoded in separate genes in the trp and pab operons. In B. subtilis, however, a single gene, located in the pab operon, is used; the glutamine amidotransferase functions with both enzymes. For synthesis of threonine and methionine, B. subtilis and all other gram-positive bacteria use a single homoserine dehydrogenase. E. coli K-12 has two pathway-specific enzymes, each of which is a bifunctional aspartokinase-homoserine dehydrogenase. The gram-positives have, in these cases, opted to maximize efficient use of DNA; the gram-negatives achieve efficiency by maximizing the specificity of regulation. Gram-negative bacteria do not always choose pathway specificity over multifunctionality. B. subtilis has two carbamoylphosphate synthetases, whose synthesis or activity is regulated separately by arginine or uridine nucleotides, while E. coli has a single enzyme.

Such differences in metabolism or its regulation do not necessarily reflect overall evolutionary distances among species. In various bacteria, lysine is synthesized by the seven-step epimerase pathway, by the four-step dehydrogenase pathway, or by both pathways. The determining factor is whether meso-diaminopimelate is incorporated in the cell wall. This diversity does not correlate with the gram-positive/gram-negative dichotomy; even Bacillus species differ in this regard. A second point of divergence is the nature of the acyl blocking group used in lysine and methionine biosynthesis. E. coli uses succinylated intermediates, while B. subtilis uses acetylated intermediates. Most other gram-positive bacteria use acetyl blocking groups for methionine synthesis, but many use succinyl groups for the lysine pathway. This issue influences overall metabolism in a fundamental way, since the need to make succinyl coenzyme A (the succinyl donor) for amino acid biosynthesis forces some cells to express part of the Krebs cycle for that purpose only.

In summary, the contrasting themes of conservation and divergence, of homology and
diversity, will be found throughout this book whether stated explicitly or not. Realizing that
*B. subtilis* is no more perfect a paradigm for all gram-positives than is *E. coli* for all
microorganisms, we sought to include as much material as possible about other representa­
tives of the gram-positive world. In addition, we introduce the book with a series of
monographs designed to acquaint the reader with some of the special properties of various
gram-positive bacteria that make them particularly interesting subjects for investigation. We
feel that this aspect of our endeavor has not been fully realized, however. Even though it is true
that the breadth and depth of knowledge about *B. subtilis* cannot be matched for any other
gram-positive bacterium, our ability to provide a comprehensive treatment has been ham­
pered by the constraints of time, page allotment, and the sheer diversity of the gram-positive
world. Thus, we present the known facts about cell structure, intermediary metabolism,
synthesis of useful products, gene organization, and gene regulation for *B. subtilis* along with
substantial, but not exhaustive, information about other gram-positive bacteria. In some
cases, such as morphogenesis and transcriptional control of phage φ29, a particular system
has been presented in detail as a paradigm. In many cases, useful comparisons with
gram-negative bacteria, particularly *E. coli*, are drawn. We have purposely avoided detailed
discussions of important aspects of developmental biology, since this topic has been and will
be explored in considerable depth in other books.

Given the biological interest of gram-positive bacteria and the recent increase in available
information, it is not surprising that the American Society for Microbiology raised the
possibility of compiling this book as a companion to the *E. coli*-S. typhimurium "Bible." That
they did so is in great measure attributable to the efforts of our late colleague, Helen R.
Whiteley. Dr. Whiteley was a leader in molecular genetic analysis of *B. subtilis* transcription
and *B. thuringiensis* insect toxin gene structure and regulation. As the long-time head of the
ASM Publications Board, she was instrumental in assuring the quality of the Society's
journals and books and instigated a number of new projects, including the suggestion for a
book of this type.

It should be obvious that it would have been impossible to assemble this book without the
contributions of the many authors. We are extraordinarily grateful to them for their cheerful
participation, timely responses to deadlines, and assiduous incorporation of reviewers' com­
ments. We also offer special thanks to Patrick J. Piggot, who organized and edited the
series of chromosome maps. Many anonymous and unpaid reviewers helped us to assure the
factual accuracy and logical flow of the presentation. We hereby absolve them of any blame for
inaccuracies that remain.

Abraham L. Sonenshein
James A. Hoch
Richard M. Losick
teichuronic acids, 394

Cell wall assembly
incorporation into wall, 396, 397
linkage of, 395-396
structure and surface properties, 390

Anthranilate synthase, 273-274

Antibiotic resistance
clostridia, 36-37
heterologous expression, 706
ribosomal proteins, 673
Staphylococcus, 22, 27, 30
Staphylococcus aureus, 22

Antibiotics, 897-912

Actinomycetes, 908-910
Bacillus spp., 903-908
bacitracin, 904, 905-906
dipeptides and tripeptides, 907
gramicidin S and tyrocidine, 903-905
linear gramicidin, 906
lipopeptides, 906-907
mycobacillin, 907-908
permeases, 908
nonribosomal synthesis, 902-903
peptide synthetase gene family, 910-911
ribosomal synthesis, 897-902
Streptomyces genes of, 90-91
timing of, 88-90
TTA codons, 707

Anticapsin, 907

Anticodons, tRNAs, 687-688, 690

Antifolates, 369

Anticodons, tRNAs, 687-688, 690

Antiproters, solute:solute, 142-144

Antirepressor, translation of, 706

Antitermination, 662-663

L-arabinose operon, B. subtilis, 159, 167

Arginine
biosynthesis, 300-301
catabolism, 299
metabolism, 302-304
as nitrogen source, 222-224
in proline auxotrophy, 302
Arginine deiminase (ADI) pathway, 299
Arginine hydroxamate-resistant (Ahr) mutants, 302-304
Arogenate dehydrogenase, 278
Aromatic amino acid biosynthesis, 269-278

common aromatic pathway, 269-271
histidine, cross regulation by, 272
phenylalanine pathway, 271, 272
supraoperon organization, 277
tryptophan pathway, 272-277
anthranilate synthase, 273-274
comparison of organisms, 278
E. coli coding regions, 274-275
permeases, 278
regulation in B. subtilis, 275-277
Streptomyces spp., 88
supraoperon organization, 277
tyrosine pathway, 271-272
Aromatic amino acid permeases, 278
Arsenical resistance ATPase, 141
Arthrobacter, 137
Arthrobacter globiformis, 131
Arthrobacter pyridinolis, 142
Asparaginase, 283
Asparagine, as nitrogen source, 222
Asparagine synthetase, 281, 284-285
Aspartate
biosynthesis of, 262-263
as nitrogen source, 222
Aspartate aminotransferase, 262
Aspartate pathway, 237-238

aspartate biosynthesis, 262-263
aspartate semialdehyde dehydrogenase, 243
aspartokinases, 239-245
diaminopimelate-sensitive, 240
versus E. coli enzymes, 244-245
functional specialization of, 243-244
lysine-sensitive, 240-241
theonine-plus-lysine-sensitive, 241-243
diaminopimelate and lysine, 245-251
diaminopimelate decarboxylase, 251
diaminopimelate dehydrogenase, 246, 250
diaminopimelate terminal reactions, 250
dihydropicolinate reductase, 249
dihydropicolinate synthase, 247, 249
dipicolinate synthase, 246, 251
diahydrolipolactone synthase, 247, 249
dipicolinate synthase, 246, 251
functions, 237
gene organization, 256-262
diaminopimelate, 256-257, 258
lysine, 257-261
methionine, 262
threonine, 261-262
methionine, 255-256
phylotypic differences, 237-239
threonine, 251-255
homoserine dehydrogenase, 251-254
homoserine kinase and threonine synthase, 254-255
Aspartate semialdehyde dehydrogenase, 245, 257, 258, 261
Aspartate transcarbamylase (pyrB), 344-345, 348, 349, 352
Aspartokinase II, 257-258
Aspartokinase III, 261
Aspergillus niger amylases, 923
Aspergillus oryzae amylases, 922, 923, 924
ATP synthesis
from IMP, 363
respiratory chain adaptations in, 207
ATPases, 133-141
ABC-type, 138-140
A-type, 141
P-type, 135-136
F-type, 133-135
V-type, 136-138
Attenuation, 662-663, 706
Attractants, 770-772, 773
A-type ATPases, 141
AUG initiation codon, 706
Autolytic enzymes
cell wall, 399-401
motility functions and, 765, 767
Autonomously replicating sequences (ars), 515-516
Autophosphorylation, chemotaxis system and, 770, 777
Autoregulation, Streptomyces, 89, 90
AUX initiation codon, 702
Auxotrophic mutations, Tn9/7, 586, 587, 588, 589
Avermectin, 90
Azotobacter vinelandii, 186
ATPases, 136, 141
translational specificity, 699

Bacillopeptidase F, 941, 944

Bacillus
ammonia assimilation, 281
amyloses, 924
antibiotics produced by, 898, 899, 900, 903-908
ATPases, P-type, 134
cat gene expression, 705
common pathway to chorismate, 278
ecology, 11-13
glutamine synthesis, 283
purine degradation, 373
solute:cation symporters, 142
systematics, 3-14
classification, 7-8
ammonia assimilation, 282
amylases, 922, 923, 924
aspartate pathway
aspartate semialdehyde DH, 245
aspartokinase II, 243
diaminopimelate branch, 245, 247, 249
ATPases, F-type, 135
branched-chain amino acid synthesis, 310
response regulators, 740
ribonucleotide reduction, 366
respiratory chain terminal oxidases, 203
rRNA-16s-charging mechanism, 694
in sporulation, 685
vitamin B12 pathway, 329
xylose regulons, 163
Bacillus mycoides, 4
ecology, 12
phylogenetic relationships, rRNA sequence data, 669
taxonomy, 9-10
Bacillus natto, 787
Bacillus niger, 384, 385, 673, 899
Bacillus ohbensis, 924
Bacillus pallidus, 4, 13
Bacillus pasteurii, 3, 4
protein secretion, 714
aspartate pathway, diaminopimelate branch, 245, 247, 249
cell wall, 382
ecology, 13
Bacillus penetrans, see Pasteuria
Bacillus polymyxa, 4, 7, 11, 943
Bacteriophage 029, 843-853, 859-865

*Bacillus subtilis*
- amylase homologies, 923
- antibiotics, 898, 900
- chromosomal map, 463-470, 508, 509
gene transfer, interspecies, 11
genetic map, 425-426
physical map of 168 chromosome, 463-470
production strains, 918
as transconjugants, 592, 594, 606
translational species specificity, 699
yeast artificial chromosome, 473, 474

*Bacillus subtilis* group
- classification, 4, 5, 7-8
ecology, 12-13

*Bacillus subtilis* strain 168
- bacteriophages, defective, 837-838
- glutamate synthesis, 290
physical map of, 463-470
R/M systems, 539-540

*Bacillus subtilis* (natto), 837

*Bacillus subtilis* subsp. *aizawai*, 943

*Bacillus subtilis* subsp. *niger*, 384, 385, 673, 899

*Bacillus subtilis* W23
- bacteriophages
defective, 837, 838

*SP16, 837*
cell wall, 386

*Bacillus thermocatenulatus*, 5, 13

*Bacillus thermocloacae*, 5, 8, 13

*Bacillus thermoglucosidasius*, 5, 8, 923, 924

*Bacillus thermodenitrificans*, 5, 13

*Bacillus thermoruber*, 940, 942, 943, 944

*Bacillus thermoproteolyticus*

*Bacillus thermoleovorans*, 5, 8, 13

*Bacillus thermoglucosidasius*, 5, 8, 923, 924

*Bacillus subtilis* (natto)
- plasmid pLS20, 120

*Bacillus subtilis* (natto), 787

*Bacillus subtilis* subsp. *niger*, 898, 904, 905-906

*Bacillus subtilis* strain 168
- genetic map, 479
- glutamate synthesis, 290, 292, 293
- nucleotide metabolism mutants, 369
- phage plasmid transduction, 119
- phylogenetic relationships, rRNA sequence data, 669
- plasmids, 119, 620, 630
- pyrimidine nucleoside metabolism and transport, 365
taxonomy, 9-10

transconjugants, 606

*Bacillus thuringiensis* subsp. *aizawai*, 957, 958, 959

*Bacillus thuringiensis* subsp. *berliner*, 958

*Bacillus thuringiensis* subsp. *israelensis*, 953, 956, 954, 960

*Bacillus thuringiensis* subsp. *kurstaki* HD1, 954, 955, 956, 958, 959, 960

*Bacillus* *tusciae*, 5, 13

Bacilysin, 989, 907

Bacitracin, 898, 904, 905-906

Bacteriocin, 70

Bacteriophage DNA, transformation process, 558

Bacteriophage expression vectors, 646-648, 649

Bacteriophage lambda
- $\phi 29$ connector, 865
- transposition of conjugative transposons, 604-605

Bacteriophage *611*, 50

Bacteriophage $\phi 29$, 843-853, 859-865
- morphogenesis, 859-865
- DNA-gp3 packaging, 862-865
- mutants, 862
- prohead assembly, determination of form, 861-862
- structure, 859-861

Bacteriophage replication, 843-849
transcription, 849-853

Bacteriophage $\phi 105$, 831-833
cloning vectors, 645-646
expression vectors, 646-648, 649

Bacteriophage *SPO1*
- cloning, 825
- concatemer resolution, 815-816
- DNA replication, 818-819
gene summary, 820-821
- hydroxymethyluracil effects, 815
- intron, 814-815
- maps, 819, 822-824
- recombination and mutagenesis, 825-826
- regulatory mechanisms, 816-817
- shutoff of host function, 817-818
- sigma cascade, 813
- structure and morphogenesis, 819, 822
- TFI, 814

Bacteriophage *SPO2*, 590, 833

Bacteriophage T4 lysozyme, 75

Bacteriophages
- *B. anthracis*, 117, 119-120
- binding site, 387
clostridia, 36
- methyltransferases, 539, 540, 543, 540-541
- R/M systems, 541-542, 543-546
- *Staphylococcus*, 30
- *Staphylococcus aureus*, 24-25
- *Streptomyces*, 84, 85-86
- transduction, 545
- transduction, specialized, 833, 837
- transformation process, 558

Bacteriophages, temperate, 831-838
defective phages, PBSX, PBSZ, 837-838
- group I $\phi 105$, 80, 810, and 84, 831-833
- group II *SPO2*, 833
- group III SPF, $\phi 3 T$, 811, SPR, Z, IG1, IG3, IG4 and H2, 833-837
- betacin production, 835
- DNA methyltransferases, 836-837
- host ranges and serology, 835
- immunity and chromosome attachment sites, 834-835
- isolation of, 834
- mutations, 835-836
- specialized transduction, 837
- thymidylate synthetase, 835
- group IV *SP16*, 837

*Bacteoides* pilins, 566, 567

Barnase, 716

Base excision repair, 530

Betacin, 835

Bialaphos, 89, 90

Bicarbonate, and *B. anthracis*, 116

Bidirectional replication, 509

*Biofilodermium*, 388

Blasticidin S gene, 618

Bid mutants, *Streptomyces*, 89, 90

Bluescript plasmid, 619

Bordetella pertussis, 729

Botulism toxin, 36, 39

Branched-chain amino acids, 307-315
- enzymes, 307-308
- pathways, 307
- regulation, 312-315

Branched-chain fatty acids, membrane biosynthesis, 414-415
- function of, 418-419

*Brevibacterium*, 385

common pathway to chorismate, 278
- purine degradation, 373
INDEX 971

ODHC, 188-189
PDHC, 183-186
Streptomyces, 88
succinate:menaquinone reductase, 189-192
succinate:thiokinase, 189
Citrobacter freundii, 598
Citrovorum, 302
Cloning vectors
Cloning efficiency, 620
Citrulline, 302
Citrulline, 302
Clostridium acidi-urici, 131, 699
Clostridium acetobutylicum, 35-44, 127
Clostridium butyricum, 35
Clostridium botulinum, 36, 39
Clostridium kluyveri, 36
Clostridium difficile, 43
Clostridium cellulovorans, 43
Clostridium cellulolyticum, 43
Clostridium bifermentans, 35
Clostridium barkeri, 35
Clostridium perfringens, 35-44
ilv and leu gene organization, 312
Clostridium sporogenes, 224, 310
Clostridium sporosarcina, 35, 36, 43
Clostridium symbiosum, 388
Clostridium tetani, 36, 39
Clostridium tetanomorphum, 699
Clostridium thermoaceticum
ATPases
F-type, 136
V-type, 137-138
evolution, 5
Clostridium thermocellum, 35-44, 43
cellulases, 930
genome size, 35
Clostridium thermohydrosulfuricum, 43-44, 922, 923, 924
Clostridium thermosaccharolyticum, 5, 922
Clostridium thermosulfurogenes, 922, 924, 925
Clostridium thermodenitrificans, 35, 36
Clustered genes, see Gene clusters
Coagulase, 20
Cobalamin, 329-330
Codon usage
Codon bias, 704
Codon usage
clostridia, 38
lactic acid bacteria, 73-74
non-AUG initiation codon, 701
Streptomyces, 87
translational control mechanisms, 703-704
Commercial products, see also Fermentation
cellulolytic enzymes, 925-931
production strains, 917-918
regulation of gene expression, 918-920
starch-degrading enzymes, 920-925
Common aromatic pathway, 269-271, 272, 278
Competence, 557
genetic properties, 562-568
comA, 571-572
comC, 564, 566, 574
comDE, 564, 574
comG, 564, 567, 574
comGOF family, 566
comJ, 562
comK, 563, 573
comL, 562
comM, 563
comP, 571-572
comQ, 571, 572
div-341 locus, 562-563
genetic map, 563
insertional mutagenesis with Tn917, 586, 587, 588, 589
nuclease, 562
and protein export systems, 565-568
transcriptional organization, 563-565
late growth development, 791
motility functions and, 765
regulation of, 568-577, 734-737
competence transcription factor, 574
mec loci, 573
regulatory cascade, 574-576
regulatory cascade function, 576-577
regulatory loci, 569-573
SOS system, 568-569
signal transduction, 737
transcription activators, 660
Competence transcription factor (CTF), 574
Complementation analysis, 648
Concatemers, SPO1, 815-816
Conjugation, 556, 605-606
counterselecting with, 592
plasmids, 638
Streptomyces spp., 83-84
Staphylococcus, 27
Corynebacterium, 278
Corynebacterium glutamicum, 84
Corynebacterium diphtheriae, 27
Corynebacterium, 27
Copper-heme proteins, terminal oxidases, 200-204
Control systems, 167
Conservation of genes, origin region, 512-514
Conjugative transposons, see Transposons, conjugative
Conjugative plasmids, 27, 556, Plasmids
see also Covalently closed circular transposon, 599, 600
Copper metabolism, regulation of, 740
Conjugation, 556, 605-606
Concatemers, SPO1, 815-816
Complementation analysis, 648
Competence transcription factor (CTF), 574
Cyclic-AMP (cAMP) receptor protein (CAP), 661
Cyanobacteria, 694
(CPT synthetase (pyrG), 346-347, 348, 349
Cyanobacteria, 694
Cyclic AMP
chemotaxis, 778
PTS and, 213
Cyclic-AMP (cAMP) receptor protein (CAP), 661
Cycloheximide reaction, 299
β-Cystathionase, 256
Cystathionine, 256
Cystathionine-δ-synthase, 256-257
Cysteine biosynthesis, 131
Cytochrome, heme formation, 200, 201
Cytochrome aα, 202, 204, 207
Cytochrome b, 556, 605-606
Cytochrome b-cytochrome c, complex, 204-205
Cytochrome c, 201, 204
Cytochrome cαα, 204, 207
Cytochrome d, 201
Cytochrome o, 202-203
dam methylation, 519
Damage-inducible loci, see din loci
deiA operon, 233
Decoyinine, 232, 369
Degradative enzymes (deg loci)
competition genes, 570-571, 573, 575, 576, 577
late-growth regulators, 786, 787-789, 791-792
motility functions, 779-780
phosphate and, 232
regulation of, 232, 734-737
signal transduction, 737
SOS system, 569
Deinococcus, 534
Deinococcus radiodurans, 534
Deinococcus, 534
Deinobacter, 534
Deletions
conjugative transposon excision and, 609
integration vector, 618
Streptomyces, 85, 501-502
replicating stability and, 638
Tn917 insertional mutations, 586
Delivery vectors, 590, 592, see also Vectors
Delta endotoxins, see Toxins
3-Deoxy-o-arabino-heptulosonate 7-phosphate (DAHP) synthetase, 269-271, 278
Deoxyribonucleotides, 361, 365-368
catabolism, 367-368
de novo synthesis, 365-366
dTTP formation, 346-347
salvage pathways, 366-367
utilization of preformed precursors, 366-367
Derepression, 662
meso-Diaminopimelate, 237-238
Diaminopimelate decarboxylase, 259
meso-Diaminopimelate dehydrogenase, 248, 249, 250
Diaminopimelate epimerase, 246, 250
Diaminopimelate synthesis, 245-251
Diaminopimelate-sensitive aspartokinase I, 240, 256-257
Dihydrolipoamide acetyltransferase, 182-183, 188, 189
Dihydrolipoamide succinyltransferase, 182-183, 188, 189
Dihydrodipicolinate synthase, 245, 246, 247
Dihydrodipicolinate reductase, 246, 249
Dihydrodipicolinate synthase, 245, 246, 247
Dihydrolipoamide acetyltransferase, see Pyruvate dehydrogenase multienzyme complex
Dihydrolipoamide succinyltransferase, 182-183, 188, 189
Dihydroorotase (pyrC), 345, 348, 352
Dihydroorotase dehydrogenase (pyrD), 345-346, 348, 352
7,8-Dihydroorotase, 328
din loci
competence and, 569
insertional mutagenesis with Tn917, 586, 587, 588, 589
regulatory regions, 574
Dipeptide permease (Dpp), 140
Dipeptide antibiotics, 907
Dipicolinic acid, 3, 238
Dipicolinic synthase, 246
Diplococcus glycinnophilus, 131
div-341 (secA) locus, 562-563
DNA, see also Genetic exchange
bacteriophage, 541-542
double-strand cleavage, 558
hydroxymethyluracil, 815
phage SPO1, 815
RTP recognition, 522
DNA binding
DnaA-binding sequence, 512
SPO1 TF1, 814
sporulation gene products, 753
DNA damage, see din loci; DNA repair
DNA integration, see also Integrational vectors
Campbell-type, 618
double-versus single-crossover events, 621
lactic acid bacteria, 76
DNA repair, 529-534
Chromosomal replication
see also DNA polymerases, Methyltransferases DNA methyltransferases, see 53, 54
INDEX 975

transformation pathway, 557-561
Genetic map, see Maps/mapping
Genomic library construction, 619-620
Germination of spores, see Spores, germination
Glucitol pathway, 557-561
Glucosidasases, 167

Glutamate
ylase, 557-561
synthesis of, 289-284
ammonia assimilation, 281-283, 284-285
GluC, 159, 167
Glutaminase, 293
GOGAT, 160-161, 164, 167
Glutamyl-tRNA synthetase, 694
Glutaryl polypeptide, 113-114
Glutaryl-tRNA synthetase, 694
Glutaminase, 214
Glyceroldehyde-3-phosphate dehydrogenase, 173, 176
Glycerol metabolism
B. subtilis, 160-161, 164, 167
catabolite repression, 215
and competence genes, 577
transport, 141-142, 173, 175
Glycerol auxotrophs, membrane lipid synthesis for, 416
Glycerol kinase, 173, 175
Glycerol-3-phosphate dehydrogenase, 173, 175-176
Glycine biosynthesis, 131
Glycolipids, membrane, see Membrane lipids
Glycolysis, 127, 171-192
B. subtilis, 158
enzymes, 171-178
Glyoxylate cycle, 127
GMF reductase pathway, 364
OGAT, 281
nitrogen sources and, 292
properties, 289-291
species distribution, 290
Gramicidin, 91, 899
biosynthesis, 903-905
linear, 906
Gramicidin S synthetase, 903-905, 910
Group A streptococci, 54, 390
Growth stages and conditions
and antibiotic production, 88-89
and growth and production kinetics, 874-885
postexponential phase phenomena, see AbrB; Late
growth development; Sporulation/sporulation genes
starvation, purine and pyrimidine metabolism in, 352-
353, 361, 370-371
stationary-phase cultures, 672
GsiA operon, 233
Guanine nucleotides and nucleosides, see also Purine sal-
vage and interconversion

Hemolysins, S. aureus, 21-22
Heterologous gene expression
antibiotic resistance, 706
barrier to, 706
lactic acid bacteria, 75-76
Hexokinase, 173
Hexosamines, 159
Hexose monophosphate pathway, Streptomyces, 88
High-molecular-weight (HMW) linear multimeric ssDNA
rolling-circle replication and, 626-627
replication and, 632-633
Hill number, 874
Histidine, 272
as nitrogen source, 225-226
synthesis of, 129-130, 364
overlap of aromatic AA operons, 277
Streptomyces spp., 88
Histidine tRNA, 689
Homocysteine, 256
Homologous recombination
genetics of, 561-562
lactic acid bacteria, 75, 76
phage derivatives, 648
Homoserine acetyltransferase, 255-256, 262
Homoserine dehydrogenase, 261, 262
Homoserine kinase, 254-255, 261
Homoserine transacytetyase, 262
Hook and basal body (HBB), 770
Horizontal gene transfer, 11, 278
phage derivatives, 648
Homoserine acetyltransferase, 255-256, 262
Homoserine dehydrogenase, 261, 262
Homoserine kinase, 254-255, 261
Homoserine transacytetyase, 262
Hook and basal body (HBB), 770
Horizontal gene transfer, 11, 278
phage derivatives, 648
Homoserine acetyltransferase, 255-256, 262
Homoserine dehydrogenase, 261, 262
Homoserine kinase, 254-255, 261
Homoserine transacytetyase, 262
Hook and basal body (HBB), 770
Horizontal gene transfer, 11, 278
carbohydrate enzymes, 166-167
clostridia, 44-45
ribosomal protein genes, 673
hpr locus, 146, 790-791
H2 phage, 833-837
Human protease E, 944
kun, 215, 217, 225, 281
Hydrolases, Staphylococcus, 20
Hydroxymethyluracil, 813, 815
Hydroxystreptomycin, 90
IG1 phage, 833-837
IG3 phage, 833-837
IG4 phage, 833-837

Haemophilus influenzae
competence, 557
lateral gene transfer, 11
transport systems, 140
hag, 659, 765, 788
Haldane equation, 874
Halobacterium, 137
Halobacterium halobium, 776
Harford-Dedonder map, 508, 509
Helicobacter pylori, 626
Heme proteins, terminal oxidases, 200-204
Hemicellulose, clostridia utilization, 43
Hemolysins, S. aureus, 21-22
Heterologous gene expression
antibiotic resistance, 706
barrier to, 706
lactic acid bacteria, 75-76
Hexitol, 158
Hexokinase, 173
Hexosamines, 159
Hexose monophosphate pathway, Streptomyces, 88
High-molecular-weight (HMW) linear multimeric ssDNA
rolling-circle replication and, 626-627
replication and, 632-633
Hill number, 874
Histidine, 272
as nitrogen source, 225-226
synthesis of, 129-130, 364
overlap of aromatic AA operons, 277
Streptomyces spp., 88
Histidine tRNA, 689
Homocysteine, 256
Homologous recombination
genetics of, 561-562
lactic acid bacteria, 75, 76
phage derivatives, 648
Homoserine acetyltransferase, 255-256, 262
Homoserine dehydrogenase, 261, 262
Homoserine kinase, 254-255, 261
Homoserine transacyetylase, 262
Hook and basal body (HBB), 770
Horizontal gene transfer, 11, 278
carbohydrate enzymes, 166-167
clostridia, 44-45
ribosomal protein genes, 673
hpr locus, 146, 790-791
H2 phage, 833-837
Human protease E, 944
kun, 215, 217, 225, 281
Hydrolases, Staphylococcus, 20
Hydroxymethyluracil, 813, 815
Hydroxystreptomycin, 90
IG1 phage, 833-837
IG3 phage, 833-837
IG4 phage, 833-837
**Klebsiella**, 567

**Klebsiella aerogenes**
- amyloses, 922
- asparagine synthetase, 294-295
- chemostat cultures of, 878
- nac gene, 292
- nitrogen sources, amino acids, 221, 222, 224, 225, 226

**Klebsiella pneumoniae**, 68, 875
- amyloses, 924
- permease homologies, 144
- PTS homology, 148
- pullulanase secretion, 565-566
- regulatory systems, 733
- sucrose pathways, 161

Koch’s hypothesis of surface stress, 397, 399
Krebs citric acid cycle (CAC), see Citric acid cycle

**L forms**, *Bacillus* spp., 390
*lac* operon
- lactic acid bacteria, 67-68

*S. aureus*, 27
- β-Lactam biosynthesis, *Streptomyces* spp., 91
- Lactamases, 75, 76, 139, 661-662
- *S. aureus*, 27
- *Streptomyces*, 87
- Lactase (ebgA) gene, 159
- Lactic acid bacteria, 65-76
- biochemistry, 66-70
- exoproteins, 70
- lactose metabolism, 66-68
- peptidases and amino acid transport, 69-70
- proteinases, 68-69
- genetic manipulation, 74-76
- genetics, 70-74
- and human health, 66
- metabolism, 66
- morphology, 65
- phylogeny, 65-66
- taxonomy, 65

*Lactobacillus*, 5, 299, see also Lactic acid bacteria
- arginine deiminase (ADI) pathway, 299
- cell wall, 385, 394
- purine-pyrimidine pathways, 353, 359, 365, 366, 367
- rRNA sequences, 670
- transport mechanisms, solute:cation symporters, 142

*Lactobacillus acidophilus*, 66, 69, 70, 72
- dTMP biosynthesis, 366
- thymidine kinase, 367
- tRNA 20S-charging mechanism, 694
- *Lactobacillus amylovorus*, 70
- *Lactobacillus arabinosus*, 295
- *Lactobacillus bulgaricus*, 73
- non-PTS-dependent lactose-galactose systems in, 165
- permease homologies, 144
- PTS permease, 148
- tRNA genes, 691
- *Lactobacillus casei*, 73, 74, 76, 278
- ATPases, F-type, 136
- deoxyribonucleoside catabolism, 367
- *lac* operon, 165
- lactose metabolism, 66, 67
- non-PTS-dependent lactose-galactose systems in, 165
- nucleotide metabolism, 366, 369
- promoters, 72
- proteinase, 69
- PTS permease, 148
- *Lactobacillus catenaformis*, 70
- *Lactobacillus confusus*, 66, 70, 72, 73
- *Lactobacillus curvatus*, 654
- *Lactobacillus delbrueckii*, 69, 691
- *Lactobacillus delbrueckii* subsp. bulgaricus, 68, 69
- *Lactobacillus helveticus*
- carbohydrate catabolism, 164, 166
- deoxyribonucleoside salvage, 367
- *Lactobacillus hilgardii*, 626
- *Lactobacillus leichmannii*, 299
- deoxyribonucleoside salvage, 367
- ribonucleotide reduction, 366
- thymidine kinase, 367
- thymine metabolism, 366
- *Lactobacillus pentosus*, 76
- *Lactobacillus plantarum*, 70, 73
- heterologous gene expression, 75, 76
- insertional mutagenesis, 591
- plasmids, rolling-circle, 626
- *Lactobacillus viridescens*, 66
- Lactococcin A, 70
- *Lactococcus*, 53, see also Lactic acid bacteria
- deoxyribonucleoside catabolism, 367
- proteinases, 946-947
- tRNA operons, 673
- solute:solute antiporters, 142-143
Lactococcus lactis
amino acid transport and peptidases, 69
antibiotics, 900
codon usage, 73
conjugative transposition, 604
Dorinao gene expression, 75
histidine biosynthesis, 130
lac operon, 165
lactose metabolism, 66, 67
plasmids
nonmobilizable, 638
rolling-circle, 626
replicating, 630
proteinases, 68-69
proteins, secreted, 70
PrtM protein, 719
S tetrahydromimide metabolism, 359, 365
ribosomal binding sites, 73, 74
ribosomal protein genes, 674
as transconjugants, 599
translation, initiation of, 73
transport mechanisms
glycerol facilitators, 141
solute:solute antiporters, 142-143
Lactococcus lactis subsp. cremoris, 65, 66, 69
Lactococcus lactis subsp. lactis, 65, 69, 70, 71, 73
Lactose metabolism, 165
catabolite repression, 216
lactic acid bacteria, 66-68
S. aureus, 27
Lactose transporter, membrane construction, 417
Lactose-galactose system, 165
Lantibiotics, 897-902
L-lysine synthesis, 661
diaminopimelate decarboxylase, 251
diaminopimelate dehydrogenase, 246, 250
diaminopimelate terminal reactions, 250
dihydropicolinate reductase, 249
dihydropicolinate synthase, 247, 249
dipicolinate synthase, 246, 251
phylogenetic differences in, 237-238
Lysine-sensitive aspartokinase, 240-241, 259
Lysin, cell wall autolysis, 399-400, 401
LysR family, 661

M protein, 55-59, 390
Macrolides, 90
Malate dehydrogenase, 182, 183, 192
Mannokinase, 173, 174-175
> Mannose, B. subtilis utilization, 159
Mannose-6-phosphate isomerase, 173, 175
Maps/mapping
B. megaterium, 475-479
B. stearothermophilus NUB36, 483-487, 672
B. subtilis
competence genes, 563, 571-572
Tn917 insertions, 587
B. subtilis 168 chromosome, 425-446, 463-470, 508, 509, 540,
cloning, 470
construction of, 463-465
designation of genes, 467-469
features of, 465-467
genic markers, 441-445
genome size, 469-470
integration vector applications, 618
Methanobacterium thermoautotrophicum, 483
motility and chemotaxis functions, 768
origin of replication region, 513
pT181, 25
ribosomal genes, 672
rRNA and tRNA operons on, 686
Harford-Dedonder, 508, 509
S. aureus, 489-493
S. coelicolor A3(2) chromosome, 497-502
SP01 genome, 819, 822-825
tRNA genes, 686-687, 690
Marker frequency analysis, 507-508
Material balance equations, 877
Mating pair, transconjugants, 606
mec loci, 568, 573, 575
Medium-independent expression of competence, 573
Melanin, 740
Membrane, 3
and initiation, 517-518
pro peptide and, 716
respiratory chain, see Respiratory chain
Membrane lipids
cis and trans lipid biosynthesis, 411-412
cis lipid composition, 411
diversification of pathway, 414-415
fatty acid biosynthesis, 413
diacyl fatty acid composition, 412-413
generic approaches, 415-419
branched-chain fatty acid function, 418-419
coupling of fatty acid and phospholipid syntheses, 416-417
fatty acid synthesis mutations, 416
glycerol auxotrophs, 416
phospholipid synthesis and insertion into membrane, 417
unsaturated fatty acid function, 419
unsaturated fatty acid synthesis, temperature regulation of, 417-418
overall pathway: acyl carrier proteins, 413-414
and protein secretion, 720
Menaquinones, 3, 205-207
Mesosome structure, 557
Metabolic control theory (MCT), 883
Metabolic pathways, see also Citric acid cycle
carbon utilization, 127, 128
nitrogen utilization, 128-131
orphan, 129-131
Metabolic state, and competence, 557
Metalloproteases, 942, 943-944, 947
Methylation, see also Insertional mutagenesis
cjugative transposons, 607-609
gene-directed, 619
phage SP01, 825-826
Mycobericillin, 907-908
Mycobericillus, 84
arginine decarboxylase, 299
cell wall, 383, 388
mobile elements, 86
thymine-pyrimidine degradation, 373
purine-pyrimidine requirements, 359
rRNA sequences, 670
mRNA, 691
Mycobericillus leprae, 359
Mycobericillus phlei, 136
Mycoberit, 690
ATPases, ABC-type, 138-140
deoxyribonucleoside catabolism, 367
purine-pyrimidine requirements, 359
ribosomal-protein profiles, 670
rRNA sequences, 670
Mycoberit capricolum
CAU anticodon in, 687
dnaA gene and DnaA box regions, 514
ribosomal protein genes, 674
tRNA gene clusters, 690
Mycoberit gallisepticum, 136
Mycoberit hyorhinis, 138
Mycoberit mycoides
plasmids, rolling-circle, 626
tRNA gene clusters, 690
myo-Inositol, B. subtilis, 159
Mycoberit xanthus, 140

NADH dehydrogenase, 205
Natural competence, 557
ndk gene, 349
Neisseria gonorrhoeae, 300, 557, 567
Neisseria meningitidis, 140
Neisseria pilus, 566, 567
Neupullulanase, 925
Neurospora crassa
ATPases, V-type, 135
iron usage, 704
mitochondrial membrane protein, 185
TrpG domain, 273
Neutral protease B, 942
Neutral proteases, 940-941, 942
lactic acid bacteria expression, 75, 76
late growth development, 790
pro peptide, 716
regulation of, 945-946
Sen and, 785
Nick errors, RCR plasmids, 628
Nisin, 899, 901

Monod-type equations, 874-875, 882
Moraxella pilus, 566, 567
Morphological coupling, 91
Motility and chemotaxis
genes and mutations affecting, 765-769
hpr and, 790
mechanisms of, 769-773
molecular mechanisms of signaling, 773-776
protein functional characteristics, 776-778
regulation of gene expression, 738, 778-780
Tn917 insertions, 589-590
Movable genetic elements, see Transposons
Mpr protease, 941

Nitrogen fixation, 12
Nitrogen regulation
catabolic pathway, 283
Tn917-lac insertions, 587, 588, 589, 590
Nitrogen sources, see also Ammonia assimilation
amino acid utilization, 221-226
ammonium ion, 221
and catabolic pathway regulation, 283
and GOGAT levels, 282
nitrate, 226
peptides, 226
urea, 226
Nitrogen utilization, metabolic pathways, 127-131
Nocardia
antibiotics, 899
cell wall, 383
common pathway to chorismate, 278
Nocardia lactamdurans, 910
Non-AUG initiation codon, 703-704
Nucleoside diphosphokinase, 349
Nuclease, competence, 562
Nucleosides and nucleotides, 349, 370
see also Nucleotide excision repair, 529-530
Paracoccus denitrificans, 201
Nucleoside phosphorylation, 90
Peptidases, lactic acid bacteria, 68-69
Peptococcus aerogenes,
Phages, see Bacteriophages; specific phages
PhDC, see Pyruvate dehydrogenase multienzyme complex
Phenylalanine, as nitrogen source, 226
Peptidoglycan, 3, 381-383
Phosphoglycerate mutase, 173, 177
Phosphoglucomutase, 171-173
Phospho/β-galactosidases, 167
Pli operon, 789-790
Panctamycin, 707
Pantotena, 221
Pasteuria, 101-110
Pathways, B. subtilis, 157-164, 165-166
PBSX, 837-838
PBSZ, 837-838
PDHC, see Pyruvate dehydrogenase multienzyme complex
Penicillinase
antirepressor gene, 706
membrane-bound lipid-modified, 721
Penicillin-binding proteins (PBPs), 392
Penicillium chrysogenum, 910
Perfringolysin, 39
Perfringolysin, 39
Permease
amino acid, aromatic, 278
antitermination, 663
Peptidoglycan, 3, 381-383
Peptidoglycan, 3, 381-383
Phages, see Bacteriophages; specific phages
PhDC, see 2-Oxooacid dehydrogenase multienzyme complex
Phenylalanine, as nitrogen source, 226
Peptidoglycan, 3, 381-383
Phosphoglycerate mutase, 173, 177
Phosphoglucomutase, 171-173
Phospho/β-glucosidases, 167
Pli operon, 789-790
Panctamycin, 707
Pantotena, 221
Pasteuria, 101-110
Pathways, B. subtilis, 157-164, 165-166
PBSX, 837-838
PBSZ, 837-838
PDHC, see Pyruvate dehydrogenase multienzyme complex
Penicillinase
antirepressor gene, 706
membrane-bound lipid-modified, 721
Penicillin-binding proteins (PBPs), 392
Penicillium chrysogenum, 910
Perfringolysin, 39
two-component regulatory systems, 729-734
Phosphotransferase systems (PTS), 145-148, 165
and adenyl cyclase, 213
B. subtilis, 157-159, 161
gluconate permease sequence similarities, 142
lac-PTS, 66-67
sucrose regulon homologies, 163
Photobacterium phosphoreum, 691
Photoproduct, spore, 805
Photoreactivation, 529
Phylogenetic relationships, see also Evolutionary relationships
aspartate pathway, 237-239
Bacillus species, 6
lactic acid bacteria, 65-66
rRNA sequence data, 669, 700
Physical map, see Maps/mapping
Pigmentation, regulation of, 740
Pili, 568
Pilin, 566-568, 569
Pirt equation, 876, 877
Plasmids, 585, 625-638, see also Integrational vectors
B. anthracis, 113, 116-119, 120
B. subtilis oriC, 516-517
B. thuringiensis strains, 953-961
Clostridia, 35-37
conjugative, see Conjugative plasmids
lactic acid bacteria, 68-69, 75
phage SPO1, 825
rolling-circle replicating, 629-629
classes of, 625
cloning vectors and transposon delivery system, 628-629
copy number control, 627, 630
replication, 625-627
stability, 627-629
selection for Tn917 insertions into, 590
Staphylococcus, 23-24, 27-30
Streptococcus, 53-54
Streptomyces, 83-84, 85
θ replicating, 629-638
classes of, 629-631
conjugational transfer, 638
copy control, 633-635
nick errors, 628
replication of, 631-633
ssDNA and stimulation of recombination, 628
stability, 635, 637-638
Tn917 analysis, 591-592
Tn917 insertion delivery vectors, 590, 610-611
transformation process, 545, 558
translational coupling, 706
transposon vectors, 585, 592
Polyamines, 299, 302
Polymyxin, 906
Polysaccharide A, 18
Polysaccharide utilization, clostridia, 42-44
Portable gene fusions, 648
Postexponential growth phase, see also Late growth development
gene expression, 577-578
pyrimidine biosynthesis, 352
Postreplication repair, 531
Posttranscriptional mode of induction, 705
Posttranscriptional processing, phage SPO1, 817
Posttranslational regulation
amino acid metabolism, 88
histidase, 88
ppGpp, 89
Prephenate dehydratase pathway, 278
P-RNA, 691-693
Pro peptide, 716-717
Proline, 88
chemotaxis and transport, 772
genes and regulation, 299, 302, 304-305
as nitrogen source, 224
in proline auxotrophy, 302
Promoters
B. thuringiensis, 960
sigma subunit of RNA polymerase and, 653-656
rRNA gene, 689-690
Pronase, 947
Prophage, 544
defective, 837, 838
λ, 604
of PBSX, 837-838
φ105, 833
reporter gene constructs, 648
Prophage transformation, 646
Propionibacteria, cell walls, 388
Propionigenium modestum, 136
Protease E, 944
Proteases, 672, 939-947
AbR, 791
commercial production, 886-889, 920
collection of, 943-944
construction of strains with reduced levels of, 946
extracellular, 939-942, see also Extracellular proteases
intracellular, 942-943
lactic acid bacteria, 68-69, 946-947
late growth development, 790
pro peptide, 716
protein secretion, 719-720
regulation of, 944-947
Sen and, 785
signal sequence mutants, 715, 716
Streptococcus pyogenes, 947
Streptomyces, 947
Protein A, 19, 55
Protein kinases, 729-730, see also Regulatory systems, two-component
antibiotic gene regulation, 89
in chemotaxis, 774
phosphorelay genes, 749-751
Protein secretion, 713-722
alternative pathway, 721
biochemistry of, 719-720
chaperonins, 721
com gene similarities, 565-568
E. coli comparisons, 721-722
genes, secretory, 717-719
genetic methods, 719
lactic acid bacteria, 70
lipoproteins, 721
mature protein sequence role, 717
physiology, 720-721
pro peptide, 716-717
signal peptides, 713-715
signal sequence mutants, 715-716
Streptomyces, 87
vectors, 647-648, 649, 717
Proteinases, see Proteases
Proteins
cell wall, 388
membrane insertion of, 417
regulatory, see Late growth development
ribosomal, see Ribosomal proteins
Proton motive force (PMF)-driven proton symport, 142
Proton symporters, 142
Protoplast fusion, 556-557
Protoplast transformation, 84
Protoxin genes, see Toxins, insecticidal
PRPP synthetase, 347, 349
prs, 349, 718-719
PS3, 135, 201
Pseudomonas, 567


Pseudomonas aeruginosa, 566
Pseudomonas amylo bacter, 922, 924
Pseudomonas atlantica, 86
Pseudomonas fluorescens, 692, 699
Pseudomonas putida, 512, 514, 593
Pseudomonas saccharophila, 921, 922
Pseudomonas stutzeri, 921, 922

Purine analogs, 368-369
Purine metabolism
degradation, 373
deoxynucleotide synthesis, de novo, 365-366
excretion of compounds, 369-370
mutants defective in, 368-370
in starving cells, 370-371

Purine salvage and interconversion, 359-364
adenine and guanine compound interconversion, 363-364
adenine deaminase pathway, 364
ATP and GTP formation from IMP, 363
deoxynucleotide metabolism, 365-368
GMP reductase pathway, 364
in growth cells, 370
histidine pathway, 364
metabolism of bases, 360-362
metabolism of deoxynucleotides, 365-368
metabolism of nucleosides, 362-363
transport of bases and nucleosides, 360
utilization of bases and nucleosides, 359-360
Purple bacteria group, RNase P, 691
put pathway, 281
Putrescine, 299
Pyrimidine analogs, 369
Pyrimidine metabolism
deoxynucleotide synthesis, de novo, 365-366
excretion of compounds, 369-370
mutants defective in, 368-370
in starving cells, 370-371

Pyrimidine salvage pathways
degradation pathways, 373
deoxynucleoside catabolism, 367-368
deoxynucleotide synthesis, 366-367
in growth cells, 370
mutants, 368-370
physiological function of, 370-373
in starving cells, 370-371
utilization of bases and nucleosides, 364-365

Pyrimidine synthesis, 343-355
allosteric regulation, 347-348
comparisons of species, 353-355
genetics, 348-350
pathways and enzymes, 343-347
accessory enzymes, 346-347
aspartate transcarbamylase, 344-345
carbamylphosphate synthetases, 343
dihydroorotase, 345
dihydroorotic dehydrogenase, 345-346
OMP decarboxylase, 346
orotate phosphoribosyltransferase, 346
UMP biosynthesis, 343
regulation of gene expression, 350-352
starvation and, 352-353
Pyruvate carboxylase, 173, 178, 262
Pyruvate dehydrogenase multienzyme complex, 173, 177-
178, 183-186, 307
Pyruvate kinase, 173, 177
Quinate, 271
Quinone, 205-207

Radiococcus, 534
recA, 557, 574
recM, 561
Recombination
homologous, 561-562
phage SP01, 825-826
RCR plasmids, 628
recA and, 557, 574
Staphylococcus, 27

Regulatory systems, two-component
chemotaxis, 738, see also Motility and chemotaxis
competence, 734-737
copper metabolism and melanin in S. lividans, 740
domain structure and phosphorylation, 729-734
exoprotein synthesis in S. aureus, 739
phosphate assimilation, 738
signal transduction, 738-739
sporulation, 737-738, 747-753
unknown function, 738, 740
vancomycin resistance in E. faecium, 739-740
Regulons and operons in B. subtilis, 159-164
Reinitiated chromosomes, 508-509
Repellants, 772-773
Replication terminator protein, 520-522
Respiratory chains, 199-208
alkaliphilic bacilli, 207
cytochromes other than terminal oxidases, 204-205
energetics, 199-200
menaquinone, 205-207
prosthetic groups, heme formation, 200, 201
during sporulation, 207-208
terminal oxidases, 200-204
Response regulators, late growth functions, 785
Restriction maps
motility and chemotaxis functions, 768
SP01 genome, 819
Restriction/modification systems, 539-549
and DNA processing following uptake, 542-546
gene arrangements, comparison of, 548-549
nomenclature, 539-541, 539
phage interactions, 541-542
sequence comparisons, 546-548
Streptomyces spp., 83, 84
Rhizobiales, glutamine synthetase, 283
Rhizobium leguminosarum, 140
Rhizobium melliloti, 733
acyl carrier proteins, 413
ATPases, P-type, 134-135
Rhizocincins, 899, 907
p6, p10, and p14 phages, 831-833
p11 phage, 833-837
Rhodobacter capsulatus, 145, 146
Rhodobacter sphaeroides, 413
Riboflavin, 319-324
biosynthetic enzymes and intermediates, 319-321
commercial production, 324-325
genetics, 321-322
structure and regulation of rib operon, 322-324
Ribonucleoside metabolism, 359-360, see also Nucleosides;
Purine metabolism; Pyrimidine metabolism
Ribonucleosides, see Nucleosides
Ribosomal proteins, 670, 671
gen characterization, 673-675
gen regulation, 675-676
Ribosomal RNA (rRNA)
Bacillus classification, 5
evolutionary relationships, see Evolutionary relationships;
Phylogenetic relationships
Shine-Dalgarno sequence complementarity, 700, 702
in sporulation, 685
Ribosomal RNA operons, tRNA genes, 686
Ribosome binding site (RBS), 699-700, 702
Saccharomyces carlsbergensis, 164
Saccharomyces carlsbergensis, 164
Saccharomyces cerevisiae, 301
codon usage, 704
fumarase, 192
invertase, 163
mitochondrial inner membrane protease 1, 718
peptide synthetase enzymes, 911
pyrimidine biosynthesis in, 354
threonine synthases, 254
Saccharopolyspora erythraea, 84, 85
acyl carrier proteins, 413
antibiotic genes, 90
Salmonella, sigma factor, 659
Salmonella typhimurium, 92, 140, 145, 199, 396, 718
adenine conversion, 364
AmiB homologies, 139
ATPases, 135
branched-chain amino acid biosynthetic pathway, 307
dTMP biosynthesis, 366
glycolysis, 171
histidine biosynthesis, 130
HPr proteins, 146
interspecific gene exchange, 11
motility and chemotaxis, 770
nitrogen sources, amino acids, 221
OppA, 138, 140
peptide transport systems, 139
purines and pyrimidines, 353-354, 362, 365
put expression, 224
regulatory systems, 729, 730, 733
rRNA operon, 686
sucrose pathways, 161
threonine deaminase, 310
transport mechanisms, 135, 138, 139, 140
tryptophan pathway gene organization, 274
vitamin B12 synthesis, 329-330
xylose regulons, 163
Sarcina albida, 131
SASP-specific protease, 943
secA, 562-563, 718, 719
Secondary structure effects, 702-703
cat genes regulation, 705
RBS, 704
translational control, 702, 706
Secretion, see Extracellular proteases; Extracellular proteins;
Protein secretion
secY, 718
Segregational stability
RCR plasmids, 627-628
replicating plasmids, 635
Sen, 785, 786, 787
Sensory transduction, 773-774, 775-776,
see also Motility and chemotaxis
Septal cleavage, 401
Sequential feedback inhibition, 278
Serine biosynthesis, 131
Serine proteases, 939, 943, see also Subtilisin
amino acid sequences, 944
intracellular, 942
lactic acid bacteria, 68-69
Streptomyces, 947
Serratia marcescens, 274, 278
Shigella sonnei, 626
Shikimate pathway, 269-271, 272, 278
Shikimate kinase, 269, 270
Signal peptides, 713-715
Signal peptides, 713-715
lactic acid bacteria, 70
N-terminal, 721
signal sequence mutants, 715-716, 719
Signal transduction, 577-578, 738-739
chemotaxis proteins, 774-775
competence, 576-577
degrative enzyme regulation, 736
sporulation phosphorelay, 747-753
transcription activators, 660
Signaling proteins, homologies of structure and function, 773-776
chemotaxis proteins, 774-775
regulation of competence, 734
regulation of proteases, 944, 945
represors in, 662
signal transduction, 737
signal transduction system, 750
transition state regulation, 757-763

Single-stranded DNA
high-molecular-weight (HMW) linear multimeric ssDNA
rolling-circle replication and, 626-627
replication and, 632-633
repair system signal, 568
and stimulation of recombination, 628
Site-specific recombination, Staphylococcus, 27
S-layer proteins, 388
Small, acid-soluble spore proteins (SASP), 805-807
Solute efflux, 144-145
Solutexation symporters, 142
Solute:solute antiporters, 142-144
SOS system, 531-533, 568-569
SPR phage, 833-837
Stall sequence, 705
Staphylococcus, 385
ATPases, A-type, 141
cat gene expression, 705
common pathway to chorismate, 278
sigma factors, 663
solute-solute symporters, 142
Staphylococcus aureus, 19, 165, 385
antibiotic resistance plasmid pE194, 704
ATPases
A-type, 141
P-type, 134, 135
autolysin, 401
bacilysin activity, 907
bacteriophages, 24-25
bacteriocin processing, 213-217
cell wall, 382, 383, 385, 387, 396, 482
chromosomal antigens, 18-20
DNA repair, 534
development and biotyping, 18
dextran synthesis regulation, 739
dehydogenase, 131
degradative enzyme regulation, 736
dipicolinate and, 238
dipicolinate synthase, 735
DNA synthesis, 568-569
DNA repair system signal, 568
and stimulation of recombination, 628
DNA repair system signal, 568
and stimulation of recombination, 628
epidemiology and biotyping, 18
exopolysaccharides, 21
extracellular proteins, 20-21
fitness, 27
histidine biosynthesis, 130
histidine biosynthesis, 130
HPr proteins, 146
ivh and leu gene organization, 311
lac operon, 165
lactamase, 139
morphology, 17
pathogenicity, 18-21
plasmids, 23-24, 626, 630
protein A of, 55
protein secretion, 714, 715
PTS, 145
PTS permease, 148
regulation of gene expression, 27, 30
regulatory systems, 730, 732
sigma factors, 663

Sporulation-related mutations
insertional mutagenesis with Tn917, 586, 587
for industrial fermentation, 886
Stall sequence, 705
Staphylococcus, 385
ATPases, A-type, 141
cat gene expression, 705
common pathway to chorismate, 278
sigma factors, 663
solute-solute symporters, 142
Staphylococcus aureus, 19, 165, 385
antibiotic resistance plasmid pE194, 704
transposons, 25-27, 592
Staphylococcus carnosus, 146, 158
Staphylococcus epidermidis, 18, 23
antibiotics, 898, 899, 900, 901, 902
plasmids, 626
Staphylococcus gallinarum, antibiotics, 900
Staphylococcus hyicus, 17
Staphylococcus intermedius, 17
Staphylococcus lactis cell wall, 382
Staphylococcus saprophyticus cell wall, 385
Staphylococcus xylosus, 141, 163
Staphylokinase, 20
Starch, Clostridia, 43-44
Starch-degrading enzymes, 920-925, see also a-Amylase; Amylases
Stationary-phase cultures, 672
Streptococci, cariogenic, 164-165
Streptococcus ATases
A-type, 141
ABC-type, 138-140
cell wall, 387
common pathway to chorismate, 278
disease, 54
gene transfer in, 53-54
glyceraldehyde-3-phosphate dehydrogenase, 176
group A, 54, 390
group N, 66
nucleoside deoxyriboyltransferases, 367
pyrimidine biosynthesis, 353
sigma factors, 663
translational species specificity, 699
Streptococcus acidominimus, 66
Streptococcus agalactiae, 54, 66, 626, 629
Streptococcus bovis, 295
Streptococcus cremoris, 946-947
Streptococcus dysgalactiae, 66
Streptococcus equinus, 629
Streptococcus faecalis, 25, 299
arginase, 223, 299, 304
branched-chain, 310
common pathway to chorismate, 278
glutamine, 283
histidine, 225
nitrogen sources, 223, 225
proline, 299, 304-305
ammonia assimilation, 281
antibiotics, 898, 899, 900, 908-910
cellular differentiation, 163, 164, 166, 167
catabolite repression, 214
cellulases, 930
extracellular enzymes, 87
gene duplication, 92
gene expression, 86-87
molecular manipulation, 83-84
genome, 84-86
ferredoxin, 921
heterologous gene expression, 76
lac operon, 68
lactose permease, 143-144
nomenclature, 65
non-PTS-dependent lactose-galactose systems in, 165
phylogeny, 66
PTS permease, 148
ribosome binding sites, 74
Streptococcus thermophilus vectors, 75
Streptococcus zymogenes, 402
Streptomyces, 164
amino acids
arginine, 223, 299, 304
branched-chain, 310
common pathway to chorismate, 278
glutamine, 283
histidine, 225
nitrogen sources, amino acids, 226
proteases, 947
arginase genes and regulation, 304
as transposon, 597
antibiotics, 898, 899, 900, 901, 902
plasmids, 626
Streptomyces antibioticus, 898, 899, 909
Streptomyces aureofaciens, 706
Streptomyces avermitilis, 90
Streptomyces cacaoi, 947
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
Streptomyces clavuligerus, 85
nitrogen sources  
arginine, 223  
histidine, 225  
proline genes and regulation, 304  
**Streptomyces coelicolor**, 83  
amino acid metabolism, 88  
ammonia assimilation, 283  
antibiotic genes, 90  
arginine genes and regulation, 304  
carbohydrate catabolism, 164, 167  
catabolite repression, 214  
chromosome, 84-85  
chromosome map, 497  
glutamate synthesis, 290, 294  
glycerol transport, 175  
glycerol utilization, 160  
histidine biosynthesis, 130  
insertional mutagenesis, 592  
metabolic switching, 89  
mobile elements, 86  
nitrogen sources  
arginine, 223  
histidine, 225  
origin of replication, 85  
plasmid integration, 85  
proline genes and regulation, 304, 305  
RNA polymerase subunits, 654  
rRNA operons, 673  
transport mechanisms, glycerol facilitators, 141  
TTA codon, 92  
**Streptomyces coelicolor A3, 84**  
**Streptomyces fradiae**, 84  
antibiotic genes, 90  
glutamate synthesis, 290, 294  
translation in, 706  
transposons, 86, 592  
**Streptomyces glaucescens, 90, 501, 947**  
**Streptomyces griseofuscus, 84**  
**Streptomyces griseus, 88**  
A-factor, 90  
alkaline phosphatase, 230  
antibiotics, 90, 898, 899, 908  
arginine genes and regulation, 304  
arginine metabolism, 299  
nitrogen sources  
arginine, 223  
histidine, 225, 226  
nucleic acid metabolism, 372  
protease regulation, 947  
TTA codon, 92  
**Streptomyces hygroscopicus**  
amylases, 923, 924  
antibiotics, 90, 898, 909-910  
regulatory systems, 733  
**Streptomyces lavendulae**, 706, 790  
**Streptomyces lixoides**, 824  
**Streptomyces lugdunensis**, 237  
**Streptomyces lividans**, 84, 706  
antibiotic production, 909  
ATPases, F-type, 136  
carbohydrate catabolism, 164  
IS493, 593  
mobile elements, 86  
nitrogen sources, arginine, 223  
origin of replication, 85  
pigmentation, 740  
plasmids, 85, 626  
protease, 947  
regulatory systems, 730, 732, 740  
rresistance to translational inhibitors, 707  
**Streptomyces noursei**, 290  
**Streptomyces plicatus**, 707  
**Streptomyces peucetius**, 140  
**Streptomyces picicatii**, 214  
**Streptomyces reiculi**, 930  
**Streptomyces rimosus**, 84  
**Streptomyces rubiginosus**, 163  
**Streptomyces venezuelae**, 84, 290  
**Streptomyces violaceoruber**, 90  
**Streptomyces virginiiae**, 90  
**Streptomyces viridochromogenes**, 909-910  
**Streptomycin genes**, 90  
Stress regulons, 778  
Stringent response, 706, 725-726, 735, 736, 876  
Subtilin, 899, 900  
Subtilisin, 350, 399-940  
amino acid sequences, 944  
fermentor production, 886-889  
gene expression, 918-920  
pro peptide, 716  
production strains of **Bacillus**, 918  
regulation of, 944-945  
sequence homologies, 943  
Succinate dehydrogenase, 205  
Succinate thiokinase, 182, 183, 189  
Succinate:menaquinone reductase, 182, 183, 189-192  
Sucrose metabolism  
**B. subtilis**, 159, 161-163  
cariogenic streptococci, 164-165  
Sucrose operons, 167  
Sugars, see also Carbohydrate catabolism; Catabolite repression, carbon source-mediated  
as attractants, 772  
transport systems  
ABC-type ATPases, 138  
PfT, 145-148  
**Sulfobolus**, 137  
**Sulfobolus acidocaldarius**  
ATPases, V-type, 135, 137  
terminal oxidases, 203  
**Sulfolobus solfataricus**, 262  
Supraoperon organization, 277  
Surface properties, 390  
Surfactin, 572-573, 575, 576, 577, 734, 735, 899, 906-907  
Switch proteins, 778  
Symptors, solute:cation, 142  
**Synechoxystis**, tRNA 4th-charging mechanism, 694  
Tagatose-phosphate pathway, 165-166  
Teichoic acid, 232  
**Bacillus**, 384  
bacteriophage binding, 387  
biosynthesis of, 393-394  
carbon sources, 127  
linkage of, 395  
and protein secretion, 720  
synthesis of, 396  
Teichoic acid glycosyltransferase, 173  
Teichuronic acid biosynthesis, 394  
Temperate phage vectors, 645-649  
cloning, 645-646  
expression, 646-648, 649  
methyltransferases, 540-541  
**Streptomyces**, 84  
Temperature, membrane lipid composition, 411, 412-413, 417-418  
Temperature-sensitive vectors  
RCR plasmids, 628  
transposon-carrying, 585, 592, 593  
TenA-TenI operon, 786, 788  
terC, 509  
deleted, 523-524  
location of, 522  
model for fork arrest and fusion at, 522
polarity of action of, 524
relocation of, 524
Terminal oxidases, 200-204
Terminal protein (TP), φ28, 843-844, 847
Terminal redundancy, SPO1, 823-824
Termination of transcription, see Transcription, termination of
Terminus of replication, 509, 519-525
Tetanus toxin, 39
Tetrahydrodipicolinate acetyltransferase, 246, 250
TF1, 814
Thermoactinomyces, 3, 5
Thermobacillus, 7
Thermomonospora curvata, 923
Thermomonospora fusca, 930
Thermophilic Bacillus, 262
classification, 4-5
glutamate synthesis, 290
phylogenetic relationships, 6
Thermophilic Clostridia, 42, 43
Thermus aquaticus, 547
Thermus thermophilus ATPases, V-type, 137
mobile elements, 86
terminal oxidases, 201, 203
Threonine synthase, 254-255
Threonine synthesis, 251-255
homoserine dehydrogenase, 251-254
homoserine kinase and threonine synthase, 254-255
Threonine-plus-lysine-sensitive aspartokinases, 241-243, 261
Threonyl-tRNA synthetase, 694
Thymidine kinase, 367
Thymidylate synthases, 366, 835
Toxins, 38
B. anthracis, 114-116
clostridial, 35-36, 39
insecticidal
bacilli producing, 853
genetic engineering of protoxin genes, 960-961
mode of action, 957-958
plasmids, protoxin genes on, 953-955
regions required for toxicity and specificity, 958-959
regulation of protoxin synthesis, 959-960
stability and persistence of B. thuringiensis, 960
structural features of B. thuringiensis protoxins, 955-957
Staphylococcus, 20
Transcription, see also RNA polymerase; Sigma factors
clostridia, 38
gene fusion constructions, 620-622
lactic acid bacteria, 70-72
repressors, 661-662
Streptomyces spp., 87-88
termination of
codon usage, 683-684
Streptomyces genes, 87
trp, 706
Transcription activators
agr, Staphylococcus, 30
phosphorylated, 659-661
Transcription factors, see also Sigma factors
comp petition (CTF), 574
Transcriptional attenuation, 350-351
Transcriptional control
clostridia, 38
phosphorelay, 752-753
Transcriptional mapping
SPO1 genome, 822-825
tRNA genes, 686-687, 690
Transducing phages, 648
Transduction, 543, 545
B. anthracis, 119-120
group III phages, 837
φ105, 833
plasmids, 119
specialized, 833, 837
Streptomyces, 27
transposon-carrying vectors, 593
Transfection, 545
cloning in φ105, 645-646
phage derivatives, 648
restriction sensitivity, 546
Streptomyces, 84
transformation process, 558
Transformation, 545
B. anthracis, 120
B. subtilis orIC plasmids, 516-517
Bacillus species, 10-11
lactic acid bacteria, 74-75
restriction sensitivity, 546
ribosomal protein genes, 673
R/M and, 543, 545
Streptomyces, 27
transposon-carrying vectors, 593
Transformation pathway
classification by donor DNA, 557-558
stages of, 557-561
binding, 558
fragmentation, 558-559
integration and resolution, 560-561
uptake, 559-560
Transition state regulators, 757-763
Translation, 699-707
antibiotics affecting, 673
in actinomycetes, 706-707
control mechanisms, 703-706
initiation of, 700-703
in vitro, 672, 707
lactic acid bacteria, 73
species specificity, 699-700, 703
Streptomyces spp., 87
Translation factors, ribosomal gene, 675
Translation inhibitors, resistance to, 706-707
Translational coupling, 90, 335, 706
Transport mechanisms, 133-148
amino acid, aromatic, 278
ATPases, 133-141
ABC-type, 138-140
A-type, 141
F-type, 135-136
P-type, 133-135
V-type, 136-138
diaminopimelate, 250
facilitators, 141-145
glycerol importers, 141-142
solute efflux porters, 144-145
solute:cation symporters, 142
solute:solute antiporters, 142-144
glycerol kinase, 175
membrane construction, 417
phosphotransferase system, 145-148
enzyme I complex, 145-146
enzyme II complex, 148
HPr system, 146-147
purine, 360
Transport mutagenesis, B. anthracis, 118, 120
Transposons, 592
B. anthracis, 118, 120
B. thuringiensis, 960
clostridia, 36
conjugative, 556, 597-612
conjugation, 605-606
definitions, 597-598
excision and conjugation, 606-607
host range, 599-598
mechanism of transposition, 599-605
as mutagens, 607-609
as shuttles, 609-611
Streptococcus, 53
mini-Tn10 derivative, 592
plasmid delivery systems, 628-629
Staphylococcus, 25-27
Streptomyces, 84, 86
Transposons, Tn9/6, 592, 597, 598, see also Transposons, conjugative
Transposons, Tn9/7, 118, 585-593
insertion into plasmids, selection for, 590
insertional mutagenesis in B. subtilis, 585-590
auxotrophic mutations, 586, 587
catalog of insertions, 588-589
chemotaxis-related mutations, 589-590
competence mutations, 586, 587, 589
genetic map of insertions, 587
nitrogen regulation, 590
phenotypically cryptic mutations, 585-586, 587
sporulation mutations, 586, 587
miscellaneous gram-positive bacteria, 590-591
Trehalose, 159
Treponema denticola plasmids, 626
Trichoderma reesei, 930
Triose-phosphate isomerase, 173, 175
Tripeptide antibiotics, 907
Tripeptide permease (Tpp), 140
tRNAs, see also Translation
aminoacyl-tRNA synthetases, 693-694
genesis, 672
evolution of gene cluster, 691-692
organization in B. subtilis, 686-687
nucleosides, 684
processing, 692-693
promoters, 689-691
species of, 683-684
and sporulation, 685-686
Trypsin, 947
Tryptophan, UGA termination codon, 683
Tryptophan pathway, 272-277
anthranilate synthase, 273-274
attenuation, 662
common aromatic pathway, 269-271
comparison with other organisms, 278
E. coli coding regions, 274-275
permeases, 278
regulation in B. subtilis, 275-277
Streptomyces spp., 88
supraoperon organization, 277
trp operon, translational control, 706
TSST-1 element, 27
TTA codon, 87, 89, 90, 707
Two-component system, see Regulatory systems, two-component
Tylosin, 90
Tyrocidine, 900, 903-905
Tyrosine pathway, 271-272
common aromatic pathway, 269-271
comparison with other organisms, 278
permeases, 278
supraoperon organization, 277
Tyrosyl-tRNA synthetase, 694
UDP-glucose-pyrophosphorylase, 173
UGA codon, 683-684
Ultraviolet (UV) irradiation
sensitivity of B. thuringiensis cells, 960
spore photoproduct, 805
Undecylprodigiosin, 88, 90
Uoopers, glycerol, 141-142
Uracil, 361
Uracil phosphoribosyltransferase, 349
Urea, as nitrogen source, 226
Urease, 283
Uridine, 361
Uridine monophosphate, 343, 346
Vaccines, anthrax, 120
Valine
as nitrogen source, 226
synthesis of, see Branched-chain amino acids
Vancomycin, 900
Vancomycin resistance, 739-740
Vectors, see also Integrational vectors; Plasmids; specific bacteriophages
clostridia, 36-37
insertion of cloned DNA into Tn916, 610-611
lactic acid bacteria, 75-76
Vibrio alginolyticus, 161
Vibrio cholerae, 733
Vibrio fischeri, 733
Vibrio harveyi, 87
Vibrioaceae tRNA genes, 691
Virulence, 390, see also Toxins
Bacillus anthracis, 113-114
clostridia, 35-36, 38
M protein, 54-59
Vitamin B₂, 319-325
Vitamin B₅, 325-327
Vitamin B₁₂, 329-330, 367
Vitamin H, 325-327
Vpr protease, 942
V-type ATPases, 136-138
Xanthine, see Purine salvage and interconversion
Xanthomonas, 567
Xylanases, Streptomyces, 87
Xylose, 164
B. subtilis, 159
catabolite repression, 215, 217
Yeast, see also Saccharomyces cerevisiae
codon usage, 704
mitochondrial inner membrane protease I, 718
tRNA Won-charging mechanism, 694
Yeast artificial chromosomes (YACs), 473, 474
Z phage, 833-837
Zygotic induction, 607