

Contents for Genetics

VOLUME 1

Contents for Genomics	xv
Contents for Proteomics	xxiii
Contents for Bioinformatics	xxxi
List of Contributors to Genetics	xxxix
Preface	xliv
1. Genetic Variation and Evolution	1
Introductory Review	
1. Population genomics: patterns of genetic variation within populations <i>Greg Gibson</i>	3
Specialist Reviews	
2. Modeling human genetic history <i>Lounès Chikhi and Mark A. Beaumont</i>	11
3. Homeobox gene repertoires: implications for the evolution of diversity <i>Claudia Kappen</i>	31
Short Specialist Reviews	
4. Studies of human genetic history using the Y chromosome <i>Mark A. Jobling</i>	52
5. Studies of human genetic history using mtDNA variation <i>Antonio Torroni and Chiara Rengo</i>	56
6. The genetic structure of human pathogens <i>Daniel J. Wilson and Daniel Falush</i>	60
7. Genetic signatures of natural selection <i>Carlos D. Bustamante and Molly Przeworski</i>	64
8. The role of gene regulation in evolution <i>Matthew V. Rockman</i>	71
9. Modeling protein evolution <i>David D. Pollock and Richard A. Goldstein</i>	75

Basic Techniques and Approaches

10. Measuring variation in natural populations: a primer 79
Henry Harpending

2. Cytogenetics 87

Introductory Reviews

11. Human cytogenetics and human chromosome abnormalities 89
Terry Hassold
12. The visualization of chromosomes 97
Stuart Schwartz

Specialist Reviews

13. Meiosis and meiotic errors 102
Hazel Baker, Maira Tankimanova and Maj Hultén
14. Acquired chromosome abnormalities: the cytogenetics of cancer 121
Susanne M. Gollin
15. Human X chromosome inactivation 134
Carolyn J. Brown and Samuel C. Chang

Short Specialist Reviews

16. Nondisjunction 151
Neil E. Lamb
17. Microdeletions 155
John A. Crolla
18. Mosaicism 161
Wendy P. Robinson
19. Uniparental disomy 166
Aaron P. Theisen and Lisa G. Shaffer
20. Cytogenetics of infertility 171
Maria Oliver-Bonet and Renée H. Martin
21. Preimplantation genetic diagnosis for chromosome abnormalities 176
Santiago Munné

Basic Techniques and Approaches

22. FISH 185
Mark J. Pettenati and P. Nagesh Rao
23. Comparative genomic hybridization 191
Brynn Levy
24. Cytogenetic analysis of lymphomas 200
Douglas E. Horsman
25. Human sperm–FISH for identifying potential paternal risk factors for chromosomally abnormal reproductive outcomes 210
Andrew J. Wyrobek, Francesco Marchetti and Thomas E. Schmid

Introductory Review

26. Imprinting and epigenetic inheritance in human disease 219
Constantin Polychronakos

Specialist Reviews

27. The histone code and epigenetic inheritance 226
Andrew R. Hoffman and Thanh H. Vu
28. Imprinting and epigenetics in mouse models and embryogenesis: understanding the requirement for both parental genomes 236
Melissa R. W. Mann
29. Imprinting in Prader–Willi and Angelman syndromes 245
Bernhard Horsthemke and Karin Buiting
30. Beckwith–Wiedemann syndrome 259
Benjamin Tycko and Marcel Mannens
31. Imprinting at the *GNAS* locus and endocrine disease 275
Akio Sakamoto, Jie Liu, Lee S. Weinstein and Min Chen

Short Specialist Reviews

32. DNA methylation in epigenetics, development, and imprinting 285
Hiroyuki Sasaki
33. Epigenetic reprogramming in germ cells and preimplantation embryos 292
Abraham L. Kierszenbaum
34. Epigenetics and imprint resetting in cloned animals 297
K. John McLaughlin, Satoshi Kurosaka and Sigrid Eckardt
35. Imprinted QTL in farm animals: a fortuity or a common phenomenon? 304
Martien A. M. Groenen
36. Variable expressivity and epigenetics 308
Emma Whitelaw and Marnie E. Blewitt
37. Evolution of genomic imprinting in mammals 315
Hamish G. Spencer
38. Rapidly evolving imprinted loci 320
Joomyeong Kim and Lisa Stubbs
39. Imprinting and behavior 325
Eric B. Keverne and James P. Curley
40. Spreading of X-chromosome inactivation 329
Jason O. Brant and Thomas P. Yang
41. Initiation of X-chromosome inactivation 336
Lygia V. Pereira and Raquel Stabellini
42. Mechanisms of epigenetic loss of chromosomes in insects 340
Clara Goday and Maria-Fernanda Ruiz

43. Epigenetic inheritance and RNAi at the centromere and heterochromatin 348
Beth A. Sullivan and Kristin S. Caruana Scott

Basic Techniques and Approaches

44. Techniques in genomic imprinting research 354
Todd A. Gray
45. Bioinformatics and the identification of imprinted genes in mammals 358
John M. Greally and Melissa J. Fazzari
46. UPD in human and mouse and role in identification of imprinted loci 363
Aaron P. Theisen and Lisa G. Shaffer

4. Gene Mapping 367

Introductory Reviews

47. Introduction to gene mapping: linkage at a crossroads 369
Nancy J. Cox
48. Parametric versus nonparametric and two-point versus multipoint: controversies in gene mapping 373
Joan E Bailey-Wilson

Specialist Reviews

49. Gene mapping, imprinting, and epigenetics 379
Konstantin Strauch
50. Gene mapping and the transition from STRPs to SNPs 389
Ellen M. Wijsman

Short Specialist Reviews

51. Choices in gene mapping: populations and family structures 399
Jeffrey R. O'Connell and Toni I. Pollin
52. Algorithmic improvements in gene mapping 403
Gonçalo R. Abecasis and Yu Zhao
53. Information content in gene mapping 409
Dan L. Nicolae
54. Sex-specific maps and consequences for linkage mapping 414
Daniel F. Gudbjartsson and Solveig K. Sieberts
55. Polymorphic inversions, deletions, and duplications in gene mapping 421
Susan L. Christian

Basic Techniques and Approaches

56. Computation of LOD scores 426
Anthony L. Hinrichs and Brian K. Suarez

5. Complex Traits and Diseases

433

Introductory Review

57. Genetics of complex diseases: lessons from type 2 diabetes 435
Leif Groop and Peter Almgren

Specialist Reviews

58. Concept of complex trait genetics 444
Anne V. Buchanan and Kenneth M. Weiss
59. The common disease common variant concept 455
Deborah S. Cunninghame Graham and Timothy J. Vyse
60. Population selection in complex disease gene mapping 465
Leena Peltonen and Teppo Varilo

Short Specialist Reviews

61. Allergy and asthma 479
Miriam F. Moffatt and William O.C. Cookson
62. Inflammation and inflammatory bowel disease 485
Christopher G. Mathew
63. Hypertension genetics: under pressure 491
Anna F. Dominiczak, Fadi J. Charchar and Maciej Tomaszewski
64. Genetics of cognitive disorders 496
Brett S. Abrahams and Daniel H. Geschwind
65. Complexity of cancer as a genetic disease 508
Tea Vallenius and Tomi P. Mäkelä
66. The mitochondrial genome 512
Douglas C. Wallace

6. Genetic Medicine and Clinical Genetics

523

Introductory Reviews

67. Approach to rare monogenic and chromosomal disorders 525
Marc S. Williams
68. Approach to common chronic disorders of adulthood 535
Maren T. Scheuner

Specialist Reviews

69. Current approaches to prenatal screening and diagnosis 551
Paula C. Cospers
70. Advances in newborn screening for biochemical genetic disorders 558
Harvey L. Levy and Inderneel Sahai
71. Advances in cytogenetic diagnosis 578
Daynna J. Wolff
72. Current approaches to molecular diagnosis 594
O. Thomas Mueller

73. The clinical and economic implications of pharmacogenomics 625
David L. Veenstra

Short Specialist Reviews

74. Molecular dysmorphology 646
Leslie G. Biesecker
75. Changing paradigms of genetic counseling 650
Katherine A. Schneider and Vickie Venne
76. Ethical and legal issues in medical genetics 655
Mary Kay Pelias

Basic Techniques and Approaches

77. Mechanisms of inheritance 661
Arthur S. Aylsworth
78. Genetic family history, pedigree analysis, and risk assessment 670
Robin L. Bennett
79. The physical examination in clinical genetics 679
Marni J. Falk and Nathaniel H. Robin
80. Genetic testing and genotype–phenotype correlations 684
Elfride De Baere and Ludwine Messiaen
81. Genetic counseling process 689
Gretchen H. Schneider
82. Treatment of monogenic disorders 693
Joseph R. Biggio Jr and Maria Descartes
83. Carrier screening: a tutorial 699
Jean A. Amos and Wayne W. Grody
84. Prenatal aneuploidy screening 702
Katharine D. Wenstrom
85. Gene identification in common disorders: a tutorial 707
Jerome I. Rotter and Mark O. Goodarzi
86. Uses of databases 711
Roberta A. Pagon
87. The microdeletion syndromes 715
Elaine H. Zackai and Jodi D. Hoffman
88. Cancer genetics 718
*Anu B. Chittenden, Katherine A. Schneider, Kelly J. Branda and
Kristen M. Shannon*
89. Familial adenomatous polyposis 726
C. Sue Richards and Madhuri R. Hegde

7. Gene Therapy 737

Introductory Reviews

90. Gene therapy I: principles and clinical applications 739
J. Wesley Ulm

91. Gene therapy II: viral vectors and treatment modalities 747
J. Wesley Ulm

Specialist Reviews

92. Hematopoietic stem cell gene therapy 759
Adrian J. Thrasher and Fabio Candotti
93. Gene therapy in the central nervous system 771
Maria G. Castro, Pedro R. Lowenstein and Shyam Goverdhana
94. Cardiovascular gene therapy 780
Himadri Roy, Seppo Ylä-Herttuala and Shalini Bhardwaj

Short Specialist Reviews

95. Artificial self-assembling systems for gene therapy 793
Pierre Lehn
96. Adenovirus vectors 798
Monika Lusky
97. Adeno-associated viral vectors: depend(o)ble stability 806
Richard O. Snyder
98. Retro/lentiviral vectors 812
Andrew M. L. Lever and Douglas E. Brown
99. Immunity and tolerance induction in gene therapy 817
Jean Davoust, Nicolas Bertho, Carole Masurier and David Gross
100. Gene transfer vectors as medicinal products: risks and benefits 826
Christian J. Buchholz and Klaus Cichutek

Basic Techniques and Approaches

101. Gene transfer to skeletal muscle 831
Jeffrey S. Chamberlain
102. Gene transfer to the liver 836
Katherine Parker Ponder
103. Gene transfer to the skin 839
Flavia Spirito, Guerrino Meneguzzi and Laurent Gagnoux-Palacios
104. Control of transgene expression in mammalian cells 843
Beat P. Kramer and Martin Fussenegger

Contents for Genomics

VOLUME 3

1. Genome Sequencing 849

Introductory Reviews

1. Eukaryotic genomics 851
Mark D. Adams
2. Genome sequencing of microbial species 859
Claire M. Fraser and Jacques Ravel
3. Hierarchical, ordered mapped large insert clone shotgun sequencing 868
Bruce A. Roe

Specialist Reviews

4. Sequencing templates – shotgun clone isolation versus amplification approaches 873
Carl W. Fuller and Rebecca Deadman
5. Robotics and automation 882
Elaine R. Mardis

Short Specialist Reviews

6. Microelectrophoresis devices for DNA sequencing 888
Brian McKenna, Daniel J. Ehrlich, Elizabeth A. Gismondi, James H. Aborn, Roger Lam, Sameh A. El-Difrawy and Thomas O'Neil
7. Single molecule array-based sequencing 893
Simon T. Bennett and Tony J. Smith
8. Real-time DNA sequencing 899
Susan H. Hardin

2. Mapping 903

Introductory Reviews

9. Genome mapping overview 905
Michael Lovett and Wesley C. Warren
10. Linking DNA to production: the mapping of quantitative trait loci in livestock 911
Changxi Li, Christiane Hansen and Stephen S. Moore

Specialist Reviews

11. Mapping complex disease phenotypes 916
David A. Collier
12. Haplotype mapping 936
Alexandre Montpetit, Fanny Chagnon and Thomas J. Hudson
13. YAC-STS content mapping 947
Claudia Gosele, Heike Zimdahl and Norbert Hubner
14. The construction and use of radiation hybrid maps in genomic research 958
André Eggen and Mathieu Gautier
15. Linkage mapping 971
Marie-Pierre Dubé and Mark E. Samuels

Short Specialist Reviews

16. Microarray comparative genome hybridization 989
Martin Krzywinski and Robert A. Holt
17. Linkage disequilibrium and whole-genome association studies 997
Angela R. Brooks-Wilson and Karen L. Novik
18. Fingerprint mapping 1002
Jacqueline E. Schein and Martin I. Krzywinski
19. Restriction fragment fingerprinting software 1013
Carol A. Soderlund
20. Synteny mapping 1017
Simon G. Gregory
21. Hitchhiking mapping 1021
Christian Schlötterer
22. The Happy mapping approach 1025
Francis Galibert

3. The Human Genome 1031

Introductory Reviews

23. The technology tour de force of the Human Genome Project 1033
Elaine R. Mardis
24. The Human Genome Project 1038
Tim Hubbard

Specialist Reviews

25. Genome assembly 1047
Asif T. Chinwalla, John W. Wallis, LaDeana W. Hillier, Michael C. Wendl and Shiaw-Pyng Yang

26. Segmental duplications and the human genome 1058
Evan E. Eichler and Rhea U. Vallente
27. Noncoding RNAs in mammals 1076
David A. Hume and Timothy Ravasi
- Short Specialist Reviews**
28. The distribution of genes in human genome 1088
Giorgio Bernardi
29. Pseudogenes 1096
David Torrents
30. Alternative splicing: conservation and function 1101
Evgenia V. Kriventseva and Mikhail S. Gelfand
31. Overlapping genes in the human genome 1105
Izabela Makalowska
32. Comparisons with primate genomes 1109
Mariano Rocchi and Nicoletta Archidiacono
33. Transcriptional promoters 1114
Wyeth W. Wasserman
34. Human microRNAs 1119
Sam Griffiths-Jones
35. Endogenous retroviruses 1125
Jens Mayer

4. Model Organisms: Functional and Comparative Genomics 1129

Introductory Reviews

36. Genome archaeology 1131
Samuel Aparicio
37. Functional analysis of genes 1135
Carol Bult and Rick Woychik

Specialist Reviews

38. Mouse models 1142
Michelle E. Goldsworthy and Roger D. Cox
39. The rat as a model physiological system 1154
Dominique Gauguier
40. Farm animals 1171
Leif Andersson
41. Mouse mutagenesis and gene function 1184
Ralf Kühn and Wolfgang Wurst
42. Systematic mutagenesis of nonmammalian model species 1201
David Sattelle and Marcel van den Heuvel

Short Specialist Reviews

43. Functional genomics in *Saccharomyces cerevisiae* 1217
Kara Dolinski and Olga Troyanskaya
44. The *C. elegans* genome 1224
Jonathan Hodgkin
45. The *Drosophila* genome(s) 1226
Casey M. Bergman and Steven Russell
46. The Fugu and Zebrafish genomes 1230
Greg Elgar
47. The mouse genome sequence 1235
Ian J. Jackson
48. Comparative sequencing of vertebrate genomes 1239
Eric D. Green and Matthew E. Portnoy

VOLUME 4

5. Bacteria and Other Pathogens 1249

Introductory Reviews

49. Bacterial pathogens of man 1251
Julian Parkhill
50. Eukaryotic parasite genome projects 1256
Neil Hall

Specialist Reviews

51. Genomics of enterobacteriaceae 1261
Jeremy D. Glasner and Nicole T. Perna
52. Genomics of the *Mycobacterium tuberculosis* complex and *Mycobacterium leprae* 1273
Roland Brosch and Stephen V. Gordon
53. The Mycoplasmas – a congruent path toward minimal life functions 1289
Leka Papazisi and Scott N. Peterson
54. The nuclear genome of apicomplexan parasites 1303
Elizabeth T. Brooke-Powell, James W. Ajioka and Kiew-Lian Wan
55. Reverse vaccinology: a critical analysis 1320
Guido Grandi

Short Specialist Reviews

56. The staphylococci 1331
Steven R. Gill
57. Genome-wide analysis of group A *Streptococcus* 1336
James M. Musser and Nicole M. Green
58. *Yersinia* 1342
Nicholas R. Thomson

59. Chlamydiae 1351
Timothy D. Read
60. Spirochete genomes 1356
George Weinstock
61. Comparative genomics of the ϵ -proteobacterial human pathogens
Helicobacter pylori and *Campylobacter jejuni* 1359
Nick Dorrell and Brendan Wren
62. The neisserial genomes: what they reveal about the diversity and
behavior of these species 1364
Lori A. S. Snyder and Nigel J. Saunders
63. Kinetoplastid genomics 1369
Christiane Hertz-Fowler and Chris Peacock
64. The organelles of apicomplexan parasites 1377
Elizabeth T. Brooke-Powell, James W. Ajioka and Kiew-Lian Wan
65. Environmental shotgun sequencing 1386
Gene W. Tyson and Philip Hugenholtz
66. Methods for detecting horizontal transfer of genes 1392
Jeffrey G. Lawrence

6. SNPs/Haplotypes 1397

Introductory Reviews

67. History of genetic mapping 1399
Newton E. Morton
68. Normal DNA sequence variations in humans 1405
Kenneth K. Kidd

Specialist Reviews

69. Reliability and utility of single nucleotide polymorphisms for
genetic association studies 1416
C. Leigh Pearce and Joel N. Hirschhorn
70. Pharmacogenetics and the future of medicine 1431
Alun D. McCarthy, James L. Kennedy and Lefkos T. Middleton
71. SNPs and human history 1449
Jeffrey D. Wall

Short Specialist Reviews

72. Evolutionary modeling in haplotype analysis 1457
Peter Donnelly
73. Creating LD maps of the genome 1461
Andrew Collins and Sarah Ennis

74. Finding and using haplotype blocks in candidate gene association studies <i>Daniel O. Stram</i>	1467
75. Avoiding stratification in association studies <i>Bernie Devlin and Kathryn Roeder</i>	1478
76. Mapping by admixture linkage disequilibrium (MALD) <i>Michael William Smith</i>	1486
77. Genotyping technology: the present and the future <i>Pui-Yan Kwok and Ting-Fung Chan</i>	1493
7. ESTs: Cancer Genes and the Anatomy Project	1499
Introductory Reviews	
78. What is an EST? <i>Andrey Ptitsyn and Winston A. Hide</i>	1501
79. Technologies for systematic analysis of eukaryotic transcriptomes <i>Robert L. Strausberg</i>	1504
Specialist Reviews	
80. EST resources, clone sets, and databases <i>Janet F. Kelso</i>	1515
81. Using ESTs for genome annotation – predicting the transcriptome <i>Eduardo Eyras</i>	1524
82. Using ORESTES ESTs to mine gene cancer expression data <i>Pedro A.F. Galante, Rodrigo Soares and Sandro J. de Souza</i>	1534
83. Proteome knowledge bases in the context of cancer <i>Djamel Medjahed and Peter A. Lemkin</i>	1542
Short Specialist Reviews	
84. Disease gene candidacy and ESTs <i>Mark I. McCarthy</i>	1567
85. The role of nonsense-mediated decay in physiological and pathological processes <i>Andreas E. Kulozik, Gabriele Neu-Yilik, Jill A. Holbrook and Matthias W. Hentze</i>	1571
86. Pilot gene discovery in plasmodial pathogens <i>Jane M. Carlton</i>	1579
Basic Techniques and Approaches	
87. Manufacturing EST libraries <i>Marcelo B. Soares and Maria F. Bonaldo</i>	1584
88. EST clustering: a short tutorial <i>Winston A. Hide</i>	1590

89. Using UniGene, STACK, and TIGR indices 1594
Alan G. Christoffels

8. Expression Profiling 1601

Introductory Review

90. Microarrays: an overview 1603
Jörg D. Hoheisel

Specialist Reviews

91. Creating and hybridizing spotted DNA arrays 1608
Ivana V. Yang

92. Using oligonucleotide arrays 1616
Eric P. Hoffman and Lindsay W. Mitchell

93. Microarray CGH 1631
Denis A. Smirnov and Vivian G. Cheung

94. Expression and localization of proteins in mammalian cells 1643
Jennifer L. Stow and Rohan D. Teasdale

95. Integrating genotypic, molecular profiling, and clinical data to elucidate common human diseases 1660
Alan Sachs and Eric E. Schadt

96. The promise of gene signatures in cancer diagnosis and prognosis 1679
Alice Y. Lee, Jimmy C. Sung and Timothy J. Yeatman

Short Specialist Reviews

97. Seven years of yeast microarray analysis 1688
Gavin Sherlock and Paul T. Spellman

98. Bacterial genome organization: comparative expression profiling, operons, regulons, and beyond 1696
Scott N. Peterson

99. Genomic analysis of host pathogen interactions 1707
Catherine V. Gale and Paul Kellam

100. Protein microarrays as an emerging tool for proteomics 1714
Ji Qiu and Sam Hanash

101. Tissue microarrays 1725
Guido Sauter, Martina Mirlacher and Ronald Simon

Basic Techniques and Approaches

102. The use of external controls in microarray experiments 1731
Dik van Leenen, Frank C.P. Holstege and Joop M.L.M. van Helvoort

103. SAGE 1737
Seth Blackshaw

104. Sample preparation for MALDI and electrospray 1850
J. J. van der Vliet and M. Snel

Contents for Proteomics

VOLUME 5

- 1. Core Methodologies** 1743
- Introductory Review**
1. Core methodologies 1745
Gerard Cagney
- Specialist Reviews**
2. Sample preparation for proteomics 1749
Thierry Rabilloud
3. Tandem mass spectrometry database searching 1756
Daniel B. Martin, Jimmy K. Eng and Ruedi Aebersold
4. Interpreting tandem mass spectra of peptides 1765
Richard S. Johnson
5. FT-ICR 1778
Mark P. Barrow, Peter J. Derrick and William I. Burkitt
6. Laser-based microdissection approaches and applications 1787
Rosamonde E. Banks
- Short Specialist Reviews**
7. Time-of-flight mass spectrometry 1799
Robert J. Cotter
8. Quadrupole mass analyzers: theoretical and practical considerations 1809
Frank A. Kero, Randall E. Pedder and Richard A. Yost
9. Quadrupole ion traps and a new era of evolution 1818
Jae C. Schwartz
10. Hybrid MS 1826
J. I. Langridge and R. H. Bateman
11. Nano-MALDI and Nano-ESI MS 1831
Gyorgy Marko-Varga, Johan Nilsson and Thomas Laurell
12. Protein fingerprinting 1836
David Fenyo
13. Multidimensional liquid chromatography tandem mass spectrometry for biological discovery 1844
Claire M. Delahunty and John R. Yates III
- Basic Techniques and Approaches**
14. Sample preparation for MALDI and electrospray 1850
J. I. Langridge and M. Snel

15. Handling membrane proteins 1857
Richard J. Simpson and Robert J. A. Goode
16. Improvement of sequence coverage in peptide mass fingerprinting 1862
Karin Hjernø and Peter Roepstorff
17. Tutorial on tandem mass spectrometry database searching 1868
Jimmy K. Eng
18. Techniques for ion dissociation (fragmentation) and scanning in MS/MS 1875
Jack Throck Watson and O. David Sparkman
19. Making nanocolumns and tips 1882
Claire Delahunty and John R. Yates III

2. Expression Proteomics 1887

Introductory Reviews

20. Separation-dependent approaches for protein expression profiling 1889
Michael J. Dunn and Stephen R. Pennington
21. Separation-independent approaches for protein expression profiling 1893
Rosalind E. Jenkins and Stephen R. Pennington

Specialist Reviews

22. Two-dimensional gel electrophoresis 1903
Angelika Görg, Michael J. Dunn and Walter Weiss
23. ICAT and other labeling strategies for semiquantitative LC-based expression profiling 1916
Connie Byrne and Gerard Cagney
24. Protein arrays 1926
Derek Murphy and Dolores J. Cahill

Short Specialist Reviews

25. 2D DIGE 1938
Kathryn S. Lilley
26. Image analysis 1945
Andrew W. Dowsey, Guang-Zhong Yang and Michael J. Dunn
27. Detecting protein posttranslational modifications using small molecule probes and multiwavelength imaging devices 1952
Wayne F. Patton
28. Real-time measurements of protein dynamics 1955
Caoimhín G. Concannon, Heiko Duessmann and Jochen H. M. Prehn

Basic Techniques and Approaches

29. Two-dimensional gel electrophoresis (2-DE) 1960
Emma McGregor and Michael J. Dunn

30. 2-D Difference Gel Electrophoresis – an accurate quantitative method for protein analysis 1966
Edward Hawkins and Stephen O. David
31. MS-based methods for identification of 2-DE-resolved proteins 1970
Achim Treumann and Christopher Gerner
32. Arraying proteins and antibodies 1975
David S. Wilson and Steffen Nock
33. Basic techniques for the use of reverse phase protein microarrays for signal pathway profiling 1979
Emanuel F. Petricoin III, Julia Wulfkuhle, Lance A. Liotta, Valerie S. Calvert and Virginia Espina

3. Mapping of Biochemical Networks 1987

Introductory Reviews

34. Protein interactions in cellular signaling 1989
Tony Pawson
35. Structural biology of protein complexes 1994
Gabriel Waksman

Specialist Reviews

36. Biochemistry of protein complexes 1999
Bertrand Séraphin
37. Inferring gene function and biochemical networks from protein interactions 2008
Stephen W. Michnick
38. The *C. elegans* interactome project 2020
David E. Hill, Marc Vidal and Michael E. Cusick
39. The yeast interactome 2033
Andrei Grigoriev and Peter Uetz

Short Specialist Reviews

40. Human signaling pathways analyzed by protein interaction mapping 2052
Frédéric Colland and Pierre Legrain
41. Investigating protein–protein interactions in multisubunit proteins: the case of eukaryotic RNA polymerases 2057
Benjamin Guglielmi, Cécile Zaros, Michel Werner and Pierre Thuriaux
42. Membrane-anchored protein complexes 2063
Igor Stagljar
43. Energy transfer–based approaches to study G protein–coupled receptor dimerization and activation 2074
Michel Bouvier, Ralf Jockers and Stefano Marullo

44. Protein interaction databases 2079
Henning Hermjakob and Rolf Apweiler
45. Computational methods for the prediction of protein interaction partners 2089
Alfonso Valencia and David Juan
46. Functional classification of proteins based on protein interaction data 2095
Anais Baudot, Bernard Jacq and Christine Brun

Basic Techniques and Approaches

47. Bioluminescence resonance energy transfer 2102
Ralf Jockers and Stefano Marullo

4. Functional Proteomics 2109

Introductory Review

48. Probing cellular function with bioluminescence imaging 2111
Gabriela da Silva Xavier, Guy A. Rutter, John W. Hanrahan, Kathryn J. Mitchell and Takashi Tsuboi

Specialist Reviews

49. Small molecule fluorescent probes for protein labeling and their application to cell-based imaging (including FLAsH etc.) 2122
Tony Cass
50. Using photoactivatable GFPs to study protein dynamics and function 2129
Dmitry M. Chudakov and Konstantin A. Lukyanov
51. FRET-based reporters for intracellular enzyme activity 2138
Moritoshi Sato and Yoshio Umezawa

Short Specialist Reviews

52. High content screening 2147
D. Lansing Taylor and Kenneth A. Giuliano
53. Photobleaching (FRAP/FLIP) and dynamic imaging 2150
George Banting
54. Probing protein function in cells using CALI 2155
Daniel G. Jay and Thomas J. Diefenbach
55. Imaging protein function using fluorescence lifetime imaging microscopy (FLIM) 2162
Daniel Zicha and Yan Gu
56. Elucidating protein dynamics and function using fluorescence correlation spectroscopy (FCS) 2170
Petra Schwille
57. Quantum dots for multiparameter measurements 2174
Marcel P. Bruchez

Basic Techniques and Approaches

58. Immunofluorescent labeling and fluorescent dyes 2180
David J. Stephens, Krysten J. Palmer and Peter Watson
59. Quantitative image analysis and the Open Microscopy Environment 2187
Andrea Falconi, Chris Allan, Jason R. Swedlow and Jean-Marie Burel
60. siRNA approaches in cell biology 2194
Alexandra Gampel and Harry Mellor

VOLUME 6

5. Proteome Diversity 2201

Introductory Reviews

61. Posttranslational modification of proteins 2203
Martin R. Larsen and Ole N. Jensen
62. Glycosylation 2211
Richard D. Cummings

Specialist Reviews

63. Protein phosphorylation analysis by mass spectrometry 2223
Hanno Steen and Judith A. Jebanathirajah
64. Structure/function of *N*-glycans 2242
Miriam V. Dwek and Susan Brooks
65. Structure/function of *O*-glycans 2252
Anthony P. Corfield
66. GPI anchors 2264
Nigel M. Hooper

Short Specialist Reviews

67. Posttranslational cleavage of cell-surface receptors 2275
Hsi-Hsien Lin, John Davies, Martin Stacey and Siamon Gordon
68. S-nitrosylation and thiolation 2281
Solomon H. Snyder and Yunfei Huang
69. Glycosylation in bacteria: that, what, how, why, now what? 2287
Ben J. Appelmelk, Christina M. J. E. Vandenbroucke-Grauls and Wilbert Bitter
70. *O*-glycan processing 2292
Anthony P. Corfield
71. *O*-Mannosylation 2298
Tamao Endo
72. *O*-linked *N*-acetylglucosamine (*O*-GlcNAc) 2303
Gerald W. Hart and Stephen A. Whelan

Basic Techniques and Approaches

73. Protein phosphorylation analysis – a primer 2308
Hanno Steen and Judith A. Jebaranathirajah
74. Glycoproteomics 2317
Miriam V. Dwek and Philippa Mills
75. Mass spectrometry 2322
David J. Harvey
76. Analysis of N- and O-linked glycans of glycoproteins 2332
Catherine M. Radcliffe, Louise Royle, Pauline M. Rudd, Raymond A. Dwek, Sviatlana A. Astrautsova and Tony H. Merry
77. Glycosylphosphatidylinositol anchors – a structural perspective 2344
Angela Mehlert

6. Proteome Families 2349

Introductory Review

78. Classification of proteins into families 2351
Nicola J. Mulder and Rolf Apweiler

Specialist Reviews

79. Metalloproteins 2359
Kirill Degtyarenko
80. Peptidases, families, and clans 2387
Alan J. Barrett and Neil D. Rawlings
81. Transporter protein families 2399
Ian T. Paulsen and Qinghu Ren
82. Structure comparison and protein structure classifications 2412
Christine Orengo, Christopher Bennett and Oliver Redfern

Short Specialist Reviews

83. InterPro 2435
Nicola J. Mulder
84. Functionally and structurally relevant residues in PROSITE motif descriptors 2439
Amos Bairoch, Christian J. A. Sigrist, Edouard De Castro, Nicolas Hulo, Petra S. Langendijk-Genevaux and Virginie Le Saux
85. The PRINTS protein fingerprint database: functional and evolutionary applications 2445
Alexander L. Mitchell, Anna Gaulton, Georgina Moulton, Neil Maudling, Paul M. Bradley and Teresa K. Attwood
86. Pfam: the protein families database 2451
Robert D. Finn
87. The PIR SuperFamily (PIRSF) classification system 2456
Anastasia N. Nikolskaya, Cathy H. Wu, Raja Mazumder and Winona C. Barker

88. Equivalog protein families in the TIGRFAMs database 2462
Daniel H. Haft and Jeremy D. Selengut
89. The CATH domain structure database 2465
Christine Orengo, Christopher Bennett and Frances Pearl
90. COGs: an evolutionary classification of genes and proteins from sequenced genomes 2474
Eugene V. Koonin

Basic Techniques and Approaches

91. Classification of proteins by sequence signatures 2479
Kay Hofmann
92. Classification of proteins by clustering techniques 2485
Evgenia V. Kriventseva
93. Getting the most out of protein family classification resources 2492
Nicola J. Mulder

7. Structural Proteomics 2501

Introductory Reviews

94. What use is a protein structure? 2503
Simon E. V. Phillips
95. History and future of X-ray structure determination 2509
Caitriona Dennis and Joachim Jaeger

Specialist Reviews

96. Fundamentals of protein structure and function 2514
David R. Westhead, James R. Bradford and Jennifer A. Siepen
97. Structural genomics – expanding protein structural universe 2529
Andrzej Joachimiak
98. Target selection for structural genomics 2552
Dmitrij Frishman

Short Specialist Reviews

99. Large complexes by X-ray methods 2565
Poul Nissen
100. Large complexes and molecular machines by electron microscopy 2572
H. Engelhardt and J. M. Plitzko
101. The importance of protein structural dynamics and the contribution of NMR spectroscopy 2578
Arnout P. Kalverda, Gary S. Thompson and W. Bruce Turnbull
102. New approaches to bridging the timescale gap in the computer simulation of biomolecular processes 2583
Chandra S. Verma and Leo S. D. Caves
103. Modeling membrane protein structures 2588
Mark S.P. Sansom and Yalini Arinaminpathy

Basic Techniques and Approaches

104. X-ray crystallography 2593
Susan Firbank
105. NMR 2600
C. Jeremy Craven
106. Electron microscopy as a tool for 3D structure determination in molecular structural biology 2607
Neil A. Ranson

8. Systems Biology 2613

Introductory Review

107. Integrative approaches to biology in the twenty-first century 2615
Marvin Cassman

Specialist Reviews

108. Functional networks in mammalian cells 2621
Ravi Iyengar and Yuguang Xiong
109. Analyzing and reconstructing gene regulatory networks 2632
Aaron Kershenbaum, Gustavo Stolovitzky and J. Jeremy Rice
110. Reverse engineering gene regulatory networks 2643
James J. Collins, Michael E. Driscoll, Michael J. Thompson and Timothy S. Gardner
111. Functional inference from probabilistic protein interaction networks 2661
Joel S. Bader
112. Constraint-based modeling of metabolomic systems 2672
Daniel A. Beard and Hong Qian
113. Metabolic dynamics in cells viewed as multilayered, distributed, mass-energy-information networks 2683
Miguel A. Aon and Sonia Cortassa
114. A complex systems approach to understand how cells control their shape and make cell fate decisions 2699
Donald E. Ingber and Sui Huang
115. Systems biology of the heart 2713
Denis Noble
116. Integrative modeling of the pancreatic β -cell 2721
Arthur Sherman and Richard Bertram

Short Specialist Review

117. EGFR network 2733
Stanislav Y. Shvartsman

Basic Techniques and Approaches

118. Data collection and analysis in systems biology 2736
Trey Ideker

Contents for Bioinformatics

VOLUME 7

1. Genome Assembly and Sequencing 2745

Introductory Review

1. Contig mapping and analysis 2747
Asim Siddiqui and Steven Jones

Specialist Reviews

2. Algorithmic challenges in mammalian whole-genome assembly 2756
Serafim Batzoglou
3. Genome signals and assembly 2765
Marek Kimmel

Short Specialist Reviews

4. Microbial sequence assembly 2775
George Weinstock
5. Comparative analysis for mapping and sequence assembly 2777
Aleksandar Milosavljevic
6. Statistical signals 2782
Andrew J. Gentles and Samuel Karlin
7. Errors in sequence assembly and corrections 2788
Björn Andersson and Martti T. Tammi

Basic Techniques and Approaches

8. Genome maps and their use in sequence assembly 2793
Paul H. Dear
9. Repeatfinding 2799
Richard Sucgang
10. Graphs and metrics 2805
Andreas Dress
11. Algorithms for sequence errors 2808
Björn Andersson and Martti T. Tammi
12. Polymorphism and sequence assembly 2815
Brinda K. Rana, Douglas W. Smith and Nicholas J. Schork

2. Gene Finding and Gene Structure 2825

Introductory Reviews

13. Prokaryotic gene identification *in silico* 2827
Mark Borodovsky and Rajeev Azad

14. Eukaryotic gene finding <i>Roderic Guigó</i>	2833
Specialist Reviews	
15. Spliced alignment <i>Xiaoqiu Huang</i>	2841
16. Searching for genes and biologically related signals in DNA sequences <i>Mihaela Pertea</i>	2849
17. Pair hidden Markov models <i>Lior Pachter, Marina Alexandersson and Nicolas Bray</i>	2858
18. Information theory as a model of genomic sequences <i>Chengpeng Bi and Peter K. Rogan</i>	2869
Short Specialist Reviews	
19. Promoter prediction <i>Thomas Werner and Vladimir B. Bajic</i>	2881
20. Operon finding in bacteria <i>Maria D. Ermolaeva</i>	2886
21. Gene structure prediction in plant genomes <i>Volker Brendel</i>	2891
22. Eukaryotic regulatory sequences <i>Edgar Wingender and Mathias Krull</i>	2895
23. Alternative splicing in humans <i>Inna Dubchak and John G. Conboy</i>	2899
24. Exonic splicing enhancers and exonic splicing silencers <i>Stephen M. Mount</i>	2903
25. Gene finding using multiple related species: a classification approach <i>Manolis Kellis</i>	2908
Basic Techniques and Approaches	
26. Dynamic programming for gene finders <i>William H. Majoros</i>	2916
27. Gene structure prediction by genomic sequence alignment <i>Burkhard Morgenstern</i>	2920
28. Computational motif discovery <i>Martin Tompa</i>	2924
3. Protein Function and Annotation	2929
Introductory Review	
29. <i>In silico</i> approaches to functional analysis of proteins <i>L. Aravind</i>	2931

Specialist Reviews

30. Contextual inference of protein function 2943
Aswin Sai Narain Seshasayee and M. Madan Babu
31. Protein domains in eukaryotic signal transduction systems 2959
Kay Hofmann

Short Specialist Reviews

32. Sequence complexity of proteins and its significance in annotation 2970
Birgit Eisenhaber and Frank Eisenhaber
33. Protein repeats 2975
Carolina Perez-Iratxeta and Miguel A. Andrade
34. Large-scale protein annotation 2978
Sarah K. Kummerfeld
35. Measuring evolutionary constraints as protein properties reflecting underlying mechanisms 2984
Andrew F. Neuwald and Jun S. Liu
36. Large-scale, classification-driven, rule-based functional annotation of proteins 2993
C. R. Vinayaka, Cathy H. Wu and Darren A. Natale

Basic Techniques and Approaches

37. Signal peptides and protein localization prediction 3005
Henrik Nielsen
38. Transmembrane topology prediction 3011
Erik Sonnhammer and Lukas Käll
39. IMPALA/RPS-BLAST/PSI-BLAST in protein sequence analysis 3017
Yuri I. Wolf

4. Comparative Analysis and Phylogeny 3025

Introductory Reviews

40. The domains of life and their evolutionary implications 3027
Carl R. Woese
41. Phylogenetic profiling 3037
David Eisenberg, Matteo Pellegrini, Sorel T. Fitz-Gibbon and Todd O. Yeates

Specialist Reviews

42. Reconstructing vertebrate phylogenetic trees 3047
Alan Filipinski and Sudhir Kumar
43. Evolution of regulatory networks 3057
Amelie Veron and Erich Bornberg-Bauer

Short Specialist Reviews

44. Phylogenomic approaches to bacterial phylogeny 3074
Vincent Daubin

45. Phylogenomics for studies of microbial evolution 3080
Hans-Henrik Fuxelius and Siv G. E. Andersson
46. Mapping mutations on phylogenies 3084
Rasmus Nielsen
47. Phylogenetic analysis of BLAST results 3093
Fiona S. L. Brinkman
48. Connecting genes by comparative genomics 3097
Itai Yanai
49. Chromosome phylogeny 3102
Guillaume Bourque

5. Computational Methods for High-throughput Genetic Analysis: Expression Profiling 3109

Introductory Reviews

50. Integrating statistical approaches in experimental design and data analysis 3111
Ernst Wit and Raya Khanin
51. Mass spectrometry and computational proteomics 3117
Knut Reinert and Vineet Bafna

Specialist Reviews

52. Experimental design 3127
Kevin K. Dobbin and Richard M. Simon
53. Statistical methods for gene expression analysis 3136
Russ D. Wolfinger, Shibing Deng, Tzu-Ming Chu and Young K. Truong
54. Algorithms for gene expression analysis 3148
Aedín C. Culhane and Alvis Brazma
55. Differential expression with the Bioconductor Project 3159
Anja von Heydebreck, Robert Gentleman and Wolfgang Huber
56. Mass spectrometric data mining for protein sequences 3173
Christian Cole, Patrick J. Lester and Simon J. Hubbard

Short Specialist Reviews

57. Low-level analysis of oligonucleotide expression arrays 3187
Cheng Li, Wing Hung Wong and Xuemin Fang
58. CGH data analysis 3193
Adam A. Margolin, Barbara L. Weber and Joel Greshock
59. A comparison of existing tools for ontological analysis of gene expression data 3201
Purvesh Khatri and Sorin Draghici
60. Extracting networks from expression data 3224
Eleftherios T. Papoutsakis and Vassily Hatzimanikatis

61. Data standardization and the HUPO proteomics standards initiative 3229
Chris Taylor, Henning Hermjakob, Rolf Apweiler, Sandra Orchard and Weimin Zhu

Basic Techniques and Approaches

62. Large error models for microarray intensities 3234
Anja von Heydebreck, Martin Vingron and Wolfgang Huber
63. Relevance networks 3239
Atul J. Butte

6. Methods for Structure Analysis and Prediction 3243

Introductory Review

64. Protein structure analysis and prediction 3245
William R. Taylor

Specialist Reviews

65. Analysis and prediction of membrane protein structure 3252
Janet M. Thornton, Linda Partridge and Tina A. Eyre
66. *Ab initio* structure prediction 3264
David Baker and William R. Taylor
67. Score functions for structure prediction 3272
Richard A. Goldstein
68. Protein domains 3283
Jaap Heringa
69. Complexity in biological structures and systems 3298
Arthur M. Lesk
70. Modeling by homology 3321
Kenji Mizuguchi

Short Specialist Reviews

71. The Protein Data Bank (PDB) and the Worldwide PDB 3335
<http://www.wwpdb.org>
Haruki Nakamura, Helen Berman and Kim Henrick
72. Threading for protein-fold recognition 3340
Kuang Lin
73. CASP 3343
Krzysztof Fidelis
74. Molecular simulations in structure prediction 3346
Franca Fraternali and Jens Kleinjung
75. Protein structure comparison 3353
Liisa Holm
76. Secondary structure prediction 3358
Ching Wai Tan and David T. Jones

77. DNA/protein modeling 3363
Richard Lavery
78. Modeling tertiary structure of RNA 3368
Benoît Masquida and Eric Westhof

VOLUME 8

7. Structuring and Integrating Data 3373

Introductory Review

79. Introduction to ontologies in biomedicine: from powertools to assistants 3375
Russ B. Altman

Specialist Reviews

80. Ontologies for the life sciences 3380
Barry Smith and Steffen Schulze-Kremer
81. Unified Medical Language System and associated vocabularies 3400
Christopher G. Chute
82. The Gene Ontology project 3409
Amelia Ireland, Jane Lomax, Jennifer I. Clark and Midori A. Harris
83. Ontologies for information retrieval 3419
William Richard Hersh
84. Ontologies for natural language processing 3428
Yves A. Lussier
85. TAMBIS: transparent access to multiple bioinformatics services 3445
Andy Brass, Carole Goble, Gary Ng, Martin Peim, Norman W. Paton, Patricia Baker, Robert Stevens and Sean Bechhofer

Short Specialist Reviews

86. Automatic concept identification in biomedical literature 3454
William H. Majoros
87. Merging and comparing ontologies 3458
Natalya F. Noy
88. Bioinformatics pathway representations, databases, and algorithms 3462
Peter D. Karp
89. Proteomics data representation and management 3470
Andrew Jones, Norman W. Paton and Stephen G. Oliver
90. Ontologies for three-dimensional molecular structure 3474
Helen M. Berman and John Westbrook

Basic Techniques and Approaches

91. Frame-based systems: Protégé 3481
Iwei Yeh

92. Description logics: OWL and DAML + OIL 3485
Carole A. Goble, Ian Horrocks, Phillip Lord and Robert D. Stevens

8. Modern Programming Paradigms in Biology 3489

Introductory Reviews

93. Detecting protein homology using NCBI tools 3491
Scott D. McGinnis and Wayne T. Matten
94. Integrated bioinformatics software at NCBI 3500
Fabrizio Ferre

Specialist Reviews

95. Bioconductor: software and development strategies for statistical genomics 3510
Robert Gentleman and Vincent Carey
96. RNA secondary structure prediction 3523
David H. Mathews and Michael Zuker
97. Ensembl and UniProt (Swiss-Prot) 3536
David Jackson and Reinhard Schneider
98. Hidden Markov models and neural networks 3546
Pierre Baldi and Stefan C. Kremer
99. Threading algorithms 3555
Jadwiga Bienkowska and Rick Lathrop

Short Specialist Reviews

100. Acedb genome database 3569
Edward Griffiths and Richard Durbin
101. Design of KEGG and GO 3572
Minoru Kanehisa
102. Simulation of biochemical networks 3577
Andrzej M. Kierzek
103. Using the Python programming language for bioinformatics 3585
Michel F. Sanner
104. Perl in bioinformatics 3594
Michael Gribskov, R. Hannes Niedner and T. Murlidharan Nair
105. The MATLAB bioinformatics toolbox 3603
Lucio Cetto and Robert Henson
106. Gibbs sampling and bioinformatics 3613
Xiaole Shirley Liu
107. Applications of RNA minimum free energy computations 3617
Peter Clote

Basic Techniques and Approaches

108. Cluster architecture 3623
Chris Dagdigan

109.	Relational databases in bioinformatics <i>Hans-Peter Kriegel, Peer Kröger and Stefan Schönauer</i>	3628
110.	Support vector machine software <i>William Stafford Noble</i>	3632
111.	Brief Python tutorial for bioinformatics <i>Michael Poidinger</i>	3638
112.	A brief Perl tutorial for bioinformatics <i>Michael J. Moorhouse</i>	3648
113.	Ontologies for the life sciences <i>Harry Smith and Stefan Schulz-Kriem</i>	3653
114.	United Medical Language System <i>Christopher C. Chute</i>	3657
115.	The Gene Cloning <i>David Jackson and Johanna Schuster</i>	3661
116.	Evolutionary models and neural networks <i>Freyr Balin and Stefan C. Krause</i>	3665
117.	Threading algorithms <i>Johanna Blencowe and Rick Lathrop</i>	3669
118.	Ontology for natural language processing <i>Wes A. Lester</i>	3673
119.	Accdb genome database <i>Andy Brass, Gail Cottle, Gurr Ag, Martin, Elizabeth, and Paul</i>	3677
120.	Design of KEGG <i>Yoon, Patricia Baker, Robert Stevens and</i>	3681
121.	Simulation of biological networks <i>Andrey M. Kozlov</i>	3685
122.	Using the Python programming language for bioinformatics <i>Michael F. Sanner</i>	3689
123.	Perl in bioinformatics <i>Michael Chalkley, K. Winters, and</i>	3693
124.	The MATLAB bioinformatics toolbox <i>Peter D. Karp</i>	3697
125.	Gene and Robert Herson <i>Andrew Jones and Norman W. Paton</i>	3701
126.	Gene samples and annotations <i>Stuart Zentgraf</i>	3705
127.	Applications of KMA <i>Peter Chute</i>	3709
128.	Basic Techniques and Algorithms <i>Christoph Dargatzis</i>	3713