
CONTENTS

Foreword	xiii
Preface	xv
Contributors	xvii

1 BIOINFORMATICS AND THE INTERNET **1**

Andreas D. Baxevanis

Internet Basics	2
Connecting to the Internet	4
Electronic Mail	7
File Transfer Protocol	10
The World Wide Web	13
Internet Resources for Topics Presented in Chapter 1	16
References	17

2 THE NCBI DATA MODEL **19**

James M. Ostell, Sarah J. Wheelan, and Jonathan A. Kans

Introduction	19
PUBs: Publications or Perish	24
SEQ-Ids: What's in a Name?	28
BIOSEQs: Sequences	31
BIOSEQ-SETs: Collections of Sequences	34
SEQ-ANNOT: Annotating the Sequence	35
SEQ-DESCR: Describing the Sequence	40
Using the Model	41
Conclusions	43
References	43

3 THE GENBANK SEQUENCE DATABASE **45**

Ilana Karsch-Mizrachi and B. F. Francis Ouellette

Introduction	45
Primary and Secondary Databases	47
Format vs. Content: Computers vs. Humans	47
The Database	49

The GenBank Flatfile: A Dissection	49
Concluding Remarks	58
Internet Resources for Topics Presented in Chapter 3	58
References	59
Appendices	59
Appendix 3.1 Example of GenBank Flatfile Format	59
Appendix 3.2 Example of EMBL Flatfile Format	61
Appendix 3.3 Example of a Record in CON Division	63
4 SUBMITTING DNA SEQUENCES TO THE DATABASES	65
<i>Jonathan A. Kans and B. F. Francis Ouellette</i>	
Introduction	65
Why, Where, and What to Submit?	66
DNA/RNA	67
Population, Phylogenetic, and Mutation Studies	69
Protein-Only Submissions	69
How to Submit on the World Wide Web	70
How to Submit with Sequin	70
Updates	77
Consequences of the Data Model	77
EST/STS/GSS/HTG/SNP and Genome Centers	79
Concluding Remarks	79
Contact Points for Submission of Sequence Data to	
DDBJ/EMBL/GenBank	80
Internet Resources for Topics Presented in Chapter 4	80
References	81
5 STRUCTURE DATABASES	83
<i>Christopher W. V. Hogue</i>	
Introduction to Structures	83
PDB: Protein Data Bank at the Research Collaboratory for	
Structural Bioinformatics (RCSB)	87
MMDB: Molecular Modeling Database at NCBI	91
Structure File Formats	94
Visualizing Structural Information	95
Database Structure Viewers	100
Advanced Structure Modeling	103
Structure Similarity Searching	103
Internet Resources for Topics Presented in Chapter 5	106
Problem Set	107
References	107
6 GENOMIC MAPPING AND MAPPING DATABASES	111
<i>Peter S. White and Tara C. Matise</i>	
Interplay of Mapping and Sequencing	112
Genomic Map Elements	113

5.1	Types of Maps	115
5.2	Complexities and Pitfalls of Mapping	120
5.3	Data Repositories	122
5.4	Mapping Projects and Associated Resources	127
5.5	Practical Uses of Mapping Resources	142
	Internet Resources for Topics Presented in Chapter 6	146
	Problem Set	148
	References	149

7 INFORMATION RETRIEVAL FROM BIOLOGICAL DATABASES **155**

Andreas D. Baxevanis

	Integrated Information Retrieval: The Entrez System	156
	LocusLink	172
	Sequence Databases Beyond NCBI	178
	Medical Databases	181
	Internet Resources for Topics Presented in Chapter 7	183
	Problem Set	184
	References	185

8 SEQUENCE ALIGNMENT AND DATABASE SEARCHING **187**

Gregory D. Schuler

	Introduction	187
	The Evolutionary Basis of Sequence Alignment	188
	The Modular Nature of Proteins	190
	Optimal Alignment Methods	193
	Substitution Scores and Gap Penalties	195
	Statistical Significance of Alignments	198
	Database Similarity Searching	198
	FASTA	200
	BLAST	202
	Database Searching Artifacts	204
	Position-Specific Scoring Matrices	208
	Spliced Alignments	209
	Conclusions	210
	Internet Resources for Topics Presented in Chapter 8	212
	References	212

9 CREATION AND ANALYSIS OF PROTEIN MULTIPLE SEQUENCE ALIGNMENTS **215**

Geoffrey J. Barton

	Introduction	215
	What is a Multiple Alignment, and Why Do It?	216
	Structural Alignment or Evolutionary Alignment?	216
	How to Multiply Align Sequences	217

Tools to Assist the Analysis of Multiple Alignments	222
Collections of Multiple Alignments	227
Internet Resources for Topics Presented in Chapter 9	228
Problem Set	229
References	230
10 PREDICTIVE METHODS USING DNA SEQUENCES	233
<i>Andreas D. Baxevanis</i>	
GRAIL	235
FGENEH/FGENES	236
MZEF	238
GENSCAN	240
PROCRUSTES	241
How Well Do the Methods Work?	246
Strategies and Considerations	248
Internet Resources for Topics Presented in Chapter 10	250
Problem Set	251
References	251
11 PREDICTIVE METHODS USING PROTEIN SEQUENCES	253
<i>Sharmila Banerjee-Basu and Andreas D. Baxevanis</i>	
Protein Identity Based on Composition	254
Physical Properties Based on Sequence	257
Motifs and Patterns	259
Secondary Structure and Folding Classes	263
Specialized Structures or Features	269
Tertiary Structure	274
Internet Resources for Topics Presented in Chapter 11	277
Problem Set	278
References	279
12 EXPRESSED SEQUENCE TAGS (ESTs)	283
<i>Tyra G. Wolfsberg and David Landsman</i>	
What is an EST?	284
EST Clustering	288
TIGR Gene Indices	293
STACK	293
ESTs and Gene Discovery	294
The Human Gene Map	294
Gene Prediction in Genomic DNA	295
ESTs and Sequence Polymorphisms	296
Assessing Levels of Gene Expression Using ESTs	296
Internet Resources for Topics Presented in Chapter 12	298
Problem Set	298
References	299

13	SEQUENCE ASSEMBLY AND FINISHING METHODS	303
	<i>Rodger Staden, David P. Judge, and James K. Bonfield</i>	
	The Use of Base Cell Accuracy Estimates or Confidence Values	305
	The Requirements for Assembly Software	306
	Global Assembly	306
	File Formats	307
	Preparing Readings for Assembly	308
	Introduction to Gap4	311
	The Contig Selector	311
	The Contig Comparator	312
	The Template Display	313
	The Consistency Display	316
	The Contig Editor	316
	The Contig Joining Editor	319
	Disassembling Readings	319
	Experiment Suggestion and Automation	319
	Concluding Remarks	321
	Internet Resources for Topics Presented in Chapter 13	321
	Problem Set	322
	References	322
14	PHYLOGENETIC ANALYSIS	323
	<i>Fiona S. L. Brinkman and Detlef D. Leipe</i>	
	Fundamental Elements of Phylogenetic Models	325
	Tree Interpretation—The Importance of Identifying Paralogs and Orthologs	327
	Phylogenetic Data Analysis: The Four Steps	327
	Alignment: Building the Data Model	329
	Alignment: Extraction of a Phylogenetic Data Set	333
	Determining the Substitution Model	335
	Tree-Building Methods	340
	Distance, Parsimony, and Maximum Likelihood: What's the Difference?	345
	Tree Evaluation	346
	Phylogenetics Software	348
	Internet-Accessible Phylogenetic Analysis Software	354
	Some Simple Practical Considerations	356
	Internet Resources for Topics Presented in Chapter 14	356
	References	357
15	COMPARATIVE GENOME ANALYSIS	359
	<i>Michael Y. Galperin and Eugene V. Koonin</i>	
	Progress in Genome Sequencing	360
	Genome Analysis and Annotation	366
	Application of Comparative Genomics—Reconstruction of Metabolic Pathways	382
	Avoiding Common Problems in Genome Annotation	385

Conclusions	387
Internet Resources for Topics Presented in Chapter 15	387
Problems for Additional Study	389
References	390
16 LARGE-SCALE GENOME ANALYSIS	393
<i>Paul S. Meltzer</i>	
Introduction	393
Technologies for Large-Scale Gene Expression	394
Computational Tools for Expression Analysis	399
Hierarchical Clustering	407
Prospects for the Future	409
Internet Resources for Topics Presented in Chapter 16	410
References	410
17 USING PERL TO FACILITATE BIOLOGICAL ANALYSIS	413
<i>Lincoln D. Stein</i>	
Getting Started	414
How Scripts Work	416
Strings, Numbers, and Variables	417
Arithmetic	418
Variable Interpolation	419
Basic Input and Output	420
Filehandles	422
Making Decisions	424
Conditional Blocks	427
What is Truth?	430
Loops	430
Combining Loops with Input	432
Standard Input and Output	433
Finding the Length of a Sequence File	435
Pattern Matching	436
Extracting Patterns	440
Arrays	441
Arrays and Lists	444
Split and Join	444
Hashes	445
A Real-World Example	446
Where to Go From Here	449
Internet Resources for Topics Presented in Chapter 17	449
Suggested Reading	449
Glossary	451
Index	457