

## Contents

<b>ACKNOWLEDGEMENTS .....</b>	<b>XI</b>
<b>PREFACE .....</b>	<b>XIII</b>
<b>1. INSTALLATION OF DAMBE AND A QUICK START.....</b>	<b>1</b>
1. INSTALLATION.....	1
2. A JUMP START .....	2
<b>2. FILE CONVERSION.....</b>	<b>7</b>
1. A PLETHORA OF COMPUTER PROGRAMS .....	8
2. A PLETHORA OF SEQUENCE FORMATS .....	8
3. READSEQ.....	9
4. FILE CONVERSION USING DAMBE.....	10
4.1 <i>Convert all sequences from one format to another.....</i>	11
4.2 <i>Converting a subset of sequences.....</i>	12
4.3 <i>Output PHYLTEST files.....</i>	13
<b>3. PROCESSING GENBANK FILES.....</b>	<b>17</b>
1. GENBANK FILE FORMAT .....	18
2. READING GENBANK FILES WITH DAMBE.....	20
<b>4. ACCESSING GENBANK OR NETWORKED COMPUTERS .....</b>	<b>25</b>
1. INTRODUCTION.....	25
2. READING MOLECULAR SEQUENCES DIRECTLY FROM GENBANK.....	25
3. READING FROM AND WRITING TO ANOTHER NETWORKED COMPUTER .....	30

4. EXERCISE .....	32
<b>5. PAIR-WISE AND MULTIPLE SEQUENCE ALIGNMENT.....</b>	<b>33</b>
1. INTRODUCTION.....	33
<i>1.1 The dot-matrix approach.....</i>	<i>33</i>
<i>1.2 Similarity or distance method.....</i>	<i>36</i>
2. SEQUENCE ALIGNMENT USING DAMBE.....	37
<i>2.1 Align nucleotide or amino acid sequences .....</i>	<i>37</i>
<i>2.2 Align nucleotide sequences against amino acid sequences.....</i>	<i>38</i>
<b>6. FACTORS AFFECTING NUCLEOTIDE FREQUENCIES.....</b>	<b>41</b>
1. INTRODUCTION.....	41
<i>1.1 The frequency parameters.....</i>	<i>41</i>
<i>1.2 Factors that might change the frequency parameters.....</i>	<i>42</i>
<i>1.3 Frequency parameters and phylogenetic analyses.....</i>	<i>43</i>
2. COUNTING NUCLEOTIDE AND DINUCLEOTIDE FREQUENCIES.....	44
<b>7. CASE STUDY 1: ARTHROPOD PHYLOGENY.....</b>	<b>49</b>
1. INTRODUCTION.....	49
2. OBTAIN DATA FROM GENBANK.....	50
3. ALIGN THE SEQUENCES.....	53
4. DATA ANALYSIS .....	56
<b>8. FACTORS AFFECTING CODON FREQUENCIES.....</b>	<b>59</b>
1. INTRODUCTION.....	59
2. GENERATING CODON USAGE TABLE WITH DAMBE.....	60
3. DNA METHYLATION AND USAGE OF ARGININE CODONS.....	64
4. TRANSCRIPTION EFFICIENCY AND CODON USAGE BIAS .....	66
5. TRANSLATIONAL EFFICIENCY AND CODON USAGE BIAS .....	66
6. CODON FREQUENCY AND PEPTIDE LENGTH IN ANCIENT PROTEINS .....	68
<b>9. CASE STUDY 2: TRANSCRIPTION AND CODON USAGE BIAS.....</b>	<b>71</b>
1. INTRODUCTION.....	71
2. MAXIMIZING TRANSCRIPTIONAL EFFICIENCY.....	72
3. PREDICTIONS AND EMPIRICAL TESTS .....	75
4. AN ALTERNATIVE EXPLANATION.....	85
5. DISCUSSION.....	89
<b>10. CASE STUDY 3: TRANSLATION AND CODON USAGE BIAS.....</b>	<b>91</b>
1. INTRODUCTION.....	91
2. THE ELONGATION MODEL, ITS PREDICTIONS, AND EMPIRICAL TESTS .....	92
<i>2.1 Adaptation of Codon Usage to tRNA Content.....</i>	<i>94</i>
<i>2.2 Adaptation of tRNA to Codon Usage.....</i>	<i>98</i>

2.3	<i>Evolution of tRNA in Response to Amino Acid Usage</i> .....	99
2.4	<i>Translational Efficiency and Translational Accuracy</i> .....	102
3.	DISCUSSION.....	103
3.1	<i>Validity of the Model</i> .....	103
3.2	<i>Translational Efficiency and Accuracy on Codon Usage Bias</i> .....	104
3.3	<i>How Optimized Are the Translational Machinery?</i> .....	105
11.	<b>EVOLUTION OF AMINO ACID USAGE</b> .....	<b>107</b>
1.	INTRODUCTION.....	107
2.	AMINO ACID USAGE BIAS.....	109
12.	<b>PATTERN OF NUCLEOTIDE SUBSTITUTIONS</b> .....	<b>115</b>
1.	INTRODUCTION.....	115
2.	USE DAMBE TO DOCUMENT EMPIRICAL SUBSTITUTION PATTERNS .....	118
2.1	<i>Simple output</i> .....	118
2.2	<i>Detailed Output</i> .....	119
13.	<b>PREAMBLE TO THE PATTERN OF CODON SUBSTITUTION</b> .....	<b>125</b>
1.	INTRODUCTION.....	125
2.	DEFAULT SUBSTITUTION PATTERNS WITH NO SELECTION .....	126
14.	<b>FACTORS AFFECTING CODON SUBSTITUTIONS</b> .....	<b>131</b>
1.	INTRODUCTION.....	131
1.1	<i>The Rate of Codon Substitutions and its Determinants</i> .....	131
1.2	<i>Models of Codon Substitution</i> .....	132
1.3	<i>The Expected Pattern of Nonsynonymous Codon Substitutions</i> .....	134
2.	CODON COMPARISON WITH DAMBE .....	136
2.1	<i>Tracing evolutionary history</i> .....	136
2.2	<i>Summary of codon substitution pattern</i> .....	140
2.3	<i>Single-step Nonsynonymous Codon Substitutions</i> .....	142
15.	<b>CASE STUDY 4: TRANSITION BIAS</b> .....	<b>147</b>
1.	INTRODUCTION.....	147
2.	GET SEQUENCE DATA .....	151
3.	DATA ANALYSIS .....	152
3.1	<i>Phylogeny reconstruction</i> .....	152
3.2	<i>Pair-wise comparisons between neighboring nodes</i> .....	157
4.	RESULTS.....	160
5.	DISCUSSION.....	162
16.	<b>SUBSTITUTION PATTERN IN AMINO ACID SEQUENCES</b> .....	<b>165</b>
1.	SUBSTITUTION PATTERN FROM SEQUENCES IN RST FORMAT.....	165
2.	SUBSTITUTION PATTERN FROM ALL PAIR-WISE COMPARISONS.....	169

17.	A STATISTICAL DIGRESSION.....	171
1.	INTRODUCTION.....	171
2.	TWO DISCRETE PROBABILITY DISTRIBUTIONS.....	172
2.1	<i>The Binomial Distribution and the Goodness-of-fit test</i> .....	172
2.2	<i>The Multinomial Distribution</i> .....	174
3.	THE SIMPLEST PRESENTATION OF THE MAXIMUM LIKELIHOOD METHOD..	175
4.	BIAS IN THE MAXIMUM LIKELIHOOD METHOD .....	177
5.	EXERCISE.....	178
18.	THEORETICAL BACKGROUND OF GENETIC DISTANCES .....	179
1.	INTRODUCTION.....	179
2.	GENETIC DISTANCES FROM NUCLEOTIDE SEQUENCES .....	180
2.1	<i>JC69 and TN84 distances</i> .....	181
2.2	<i>Kimura's two parameter distance</i> .....	183
2.3	<i>F84 distance</i> .....	184
2.4	<i>TN93 distance</i> .....	185
2.5	<i>Lake's paralinear distance</i> .....	186
3.	DISTANCES BASED ON CODON SEQUENCES .....	187
3.1	<i>The empirical counting approach</i> .....	188
3.2	<i>Codon-based maximum likelihood method</i> .....	190
4.	DISTANCES BASED ON AMINO ACID SEQUENCES .....	192
5.	GENETIC DISTANCES FROM ALLELE FREQUENCIES .....	193
5.1	<i>Net's genetic distance</i> :.....	194
5.2	<i>Cavalli-Sforza's chord measure</i> .....	195
5.3	<i>Reynolds, Weir, and Cockerham's genetic distance</i> .....	196
19.	MOLECULAR PHYLOGENETICS: CONCEPTS AND PRACTICE	197
1.	THE MOLECULAR CLOCK AND ITS CALIBRATION.....	198
1.1	<i>Calibrating a molecular clock</i> .....	200
1.2	<i>Complications in calibrating a molecular clock</i> .....	201
2.	COMMON APPROACHES IN MOLECULAR PHYLOGENETICS .....	204
2.1	<i>Distance methods</i> .....	204
2.2	<i>Maximum parsimony method</i> .....	214
2.3	<i>Maximum likelihood method</i> .....	216
2.4	<i>Reconstructing Ancestral Sequences</i> .....	221
3.	EXERCISE .....	224
20.	TESTING THE MOLECULAR CLOCK HYPOTHESIS.....	225
1.	THE T-TEST.....	226
2.	THE LIKELIHOOD RATIO TEST .....	227
3.	TEST THE MOLECULAR CLOCK HYPOTHESIS.....	230
21.	TESTING PHYLOGENETIC HYPOTHESES.....	233

1.	BASIC STATISTICAL CONCEPTS .....	234
2.	TESTING PHYLOGENETIC HYPOTHESES WITH THE DISTANCE METHOD ..	236
2.1	<i>The Rationale</i> .....	236
2.2	<i>Test alternative phylogenetic hypotheses with the distance method.</i> ..	238
3.	TESTING PHYLOGENETIC HYPOTHESES WITH THE PARSIMONY METHOD ..	241
4.	TESTING PHYLOGENETIC HYPOTHESES WITH THE LIKELIHOOD METHOD..	243
5.	RESAMPLING METHODS .....	247
6.	EXERCISE.....	248
<b>22.</b>	<b>FITTING PROBABILITY DISTRIBUTIONS .....</b>	<b>249</b>
1.	INTRODUCTION.....	249
1.1	<i>The Poisson distribution</i> .....	250
1.2	<i>The negative binomial distribution</i> .....	252
1.3	<i>The gamma distribution</i> .....	254
1.4	<i>Some general guidelinesfor fitting statistical distributions</i> .....	257
2.	FITTING DISCRETE DISTRIBUTIONS WITH DAMBE.....	258
3.	ESTIMATINGTHESHAPEPARAMETEROFTHEGAMMADISTRIBUTION ..	261
4.	EXERCISE.....	263
<b>LITERATURE CITED.....</b>		<b>265</b>
<b>INDEX .....</b>		<b>275</b>