TABLE OF CONTENTS – Structure and Function of the Bacterial Genome

Preface

1 The Bacterial Genome – Where the Genes are 1

- 1.1 Genome Philosophy 1
- 1.2 The Bacterial Chromosome 4
- 1.3 Chromosome Replication: Initiation 6
- 1.4 Chromosome Replication: Elongation 11
- 1.5 Chromosome Replication: Termination 12
- 1.6 Replication Produces Physically Connected Products 13
- 1.7 Decatenating the Sister Chromosomes 13
- 1.8 Resolving Chromosome Dimers 14
- 1.9 Segregating the Products of Chromosome Replication 15
- 1.10 Polar Tethering of Chromosome Origins 20
- 1.11 Some Bacterial Chromosomes are Linear 20
- 1.12 Some Bacteria Have More than One Chromosome 21
- 1.13 Plasmids 22
- 1.14 Plasmid Replication 22
- 1.15 Plasmid Segregation 26
- 1.16 The Nucleoid 28
- 1.17 The Chromosome Has Looped Domains 29
- 1.18 The Macrodomain Structure of the Chromosome 29
- 1.19 The Chromosome Displays Spatial Arrangement Within the Cell 30
- 1.20 SeqA and Nucleoid Organisation 31

- 1.21 MukB, a Condensin-Like Protein 32
- 1.22 MatP, the matS Site and Ter Organisation 33
- 1.23 MaoP and the maoS Site 34
- 1.24 SImA and Nucleoid Occlusion 34
- 1.25 The Min System and Z Ring Localisation 34
- 1.26 DNA in the Bacterial Nucleoid 36
- 1.27 DNA Topology 36
- 1.28 DNA Topoisomerases: DNA Gyrase 38
- 1.29 DNA Topoisomerases: DNA Topoisomerase IV 40
- 1.30 DNA Topoisomerases: DNA Topoisomerase I 40
- 1.31 DNA Topoisomerases: DNA Topoisomerase III 41
- 1.32 DNA Replication and Transcription Alter Local DNA Topology 41
- 1.33 Transcription and Nucleoid Structure 41
- 1.34 Nucleoid-associated Proteins (NAPs) and Nucleoid Structure 43
- 1.35 DNA Bending Protein Integration Host Factor (IHF) 44
- 1.36 HU, a NAP with General DNA-binding Activity 46
- 1.37 The Very Versatile FIS Protein 47
- 1.38 FIS and the Early Exponential Phase of Growth 48
- 1.39 FIS and the Stringent Response 49
- 1.40 FIS and DNA Topology 49
- 1.41 Ferritin-Like Dps and the Curved-DNA-binding Protein CbpA 51
- 1.42 The H-NS Protein: A Silencer of Transcription 53
- 1.43 StpA: A Paralogue of H-NS 57
- 1.44 H-NS Orthologues Encoded by Plasmids and Phage 58
- 1.45 H-NSB/Hfp and H-NS2: H-NS Homologues of HGT Origin 58

- 1.46 A Truncated H-NS-Like Protein 59
- 1.47 Hha-like Proteins 59
- 1.48 Other H-NS Homologues: The Ler Protein from EPEC 60
- 1.49 H-NS Functional Homologues 62
- 1.50 H-NS Functional Homologues: Rok from Bacillus spp. 63
- 1.51 H-NS Functional Homologues: Lsr2 from Actinomycetes 63
- 1.52 H-NS Functional Homologues: MvaT from Pseudomonas spp. 63
- 1.53 The Leucine-responsive Regulatory Protein, LRP 64
- 1.54 Small, Acid-soluble Spore Proteins, SASPs 65

2 Conservation and Evolution of the Dynamic Genome 67

2.1 Disruptive Influences: Mutations 67

2.2 Repetitive Sequences in the Chromosome and Their Influence on Genetic Stability 69

- 2.3 Contingency Loci and the Generation of Microbial Variety 70
- 2.4 Rhs: Rearrangement Hotspots 71
- 2.5 REP Sequences 72
- 2.6 RIB/RIP, BIME-1, and BIME-2 Elements 73
- 2.7 ERIC Sequences 73
- 2.8 Repeat-Mediated Rearrangements: Mechanisms and Frequency 74
- 2.9 Site-specific Recombination and Phenotypic Variety 74
- 2.10 Site-Specific Recombination: Bacteriophage Lambda 75
- 2.11 The Lambda Lysis/Lysogeny Decision 76
- 2.12 Tyrosine Integrases 77
- 2.13 Serine Invertases 78
- 2.14 Large Serine Recombinases 79
- 2.15 Transposition and Transposable Elements 80

- 2.16 Pathways of Transposition 82
- 2.17 Peel-and-paste Transposition 85
- 2.18 Control of Transposition 88
- 2.19 Host Factors and Transposition 91
- 2.20 Integrative and Conjugative Elements (ICE) 91
- 2.21 Integrons 93
- 2.22 Introns 96
- 2.23 Horizontal Gene Transfer 96
- 2.24 Distinguishing Self from Non-self 99
- 2.25 Distinguishing Self and Non-self: CRISPR-Cas Systems 99
- 2.26 Distinguishing Self and Non-self: Argonaute Proteins 102
- 2.27 Distinguishing Self and Non-self: Restriction Enzymes/Methylases 103
- 2.28 Distinguishing Self and Non-self: BREX 103
- 2.29 Self-sacrifice and Other Behaviours Involving Toxin-antitoxin Systems 104
- 2.30 Conservative Forces: DNA Repair and Homologous Recombination 104
- 2.31 The RecA Protein 105
- 2.32 RecA, LexA, and the SOS Response 106
- 2.33 Holliday Junction Resolution 108
- 2.34 Mismatch Repair 109
- 2.35 Non-homologous End Joining 110

3 Gene Control: Transcription and Its Regulation 113

- 3.1 Transcription: More Than Just Transcribing Genetic Information 113
- 3.2 RNA Polymerase 113
- 3.3 The Core Enzyme 114
- 3.4 The Sigma Factors (and Anti-Sigma Factors) 116

- 3.5 Promoter Architecture 120
- 3.6 Stringently Regulated Promoters 120
- 3.7 Transcription Factors and RNA Polymerase 121
- 3.8 Transcription Initiation 124
- 3.9 Transcription Elongation 125
- 3.10 Transcription Termination: Intrinsic and Rho-Dependent Terminators 127
- 3.11 Rho and Imported Genes 128
- 3.12 Rho, R-Loops, and DNA Supercoiling 128
- 3.13 Rho and Antisense Transcripts 128
- 3.14 Anti-Termination: Insights from Phage Studies 129
- 3.15 Transcription Occurs in Bursts 129

4 Gene Control: Regulation at the RNA Level 133

- 4.1 Antisense Transcripts and Gene Regulation in cis 134
- 4.2 RNA that Regulates in trans 134
- 4.3 DsrA and the RpoS/H-NS Link 138
- 4.4 sRNA Turnover 140
- 4.5 DEAD-box Proteins 140
- 4.6 RNA Chaperone Proteins 141
- 4.7 StpA, H-NS, and RNA Binding 142
- 4.8 Degradation of mRNA 143
- 4.9 RNA Folding and Gene Regulation 144
- 4.10 Transcription Attenuation 145
- 4.11 Riboswitches 145
- 4.12 RNA as a Structural Component in the Nucleoid 146

5 Gene Control: Regulation at the Protein Level 149

- 5.1 Control Beyond DNA and RNA 149
- 5.2 Translation Machinery and Control: tRNA and rRNA 149
- 5.3 Translation Machinery and Control: The Ribosome 150
- 5.4 Translation Initiation 152
- 5.5 Translation Elongation 154
- 5.6 Elongation Factor P (EF-P) 155
- 5.7 Translation Termination 156
- 5.8 Protein Secretion 157
- 5.9 Protein Secretion: The Sec Pathway 157
- 5.10 The Twin Arginine Translocation (Tat) Pathway of Protein Secretion 159
- 5.11 Type 1 Secretion Systems (T1SS) 160
- 5.12 Type 2 Secretion Systems (T2SS) 161
- 5.13 Type 3 Secretion Systems (T3SS) 162
- 5.14 Type 4 Secretion Systems (T4SS) 164
- 5.15 Type 5 Secretion Systems (T5SS): The Autotransporters 165
- 5.16 Type 6 Secretion Systems (T6SS) 166
- 5.17 Protein Secretion in Gram-Positive Bacteria: SecA1, SecA2, and SrtA 167
- 5.18 Type 7 Secretion Systems (T7SS) 168
- 5.19 Protein Modification: Acetylation 168
- 5.20 Protein Modification: Glycosylation 169
- 5.21 Protein Modification: Phosphorylation 169
- 5.22 Protein Splicing 171
- 5.23 Small Proteins 172
- 5.24 Selenocysteine and Pyrrolysine: The 21st and 22nd Amino Acids 173

6 Gene Control and Bacterial Physiology 175

- 6.1 The Bacterial Growth Cycle 175
- 6.2 Physiology Changes Throughout the Growth Cycle 176
- 6.3 Generating Physiological Variety from Genetic Homogeneity 178
- 6.4 Bacterial Economics Some Basic Principles 179
- 6.5 Carbon Sources and Metabolism 180
- 6.6 Gene Control and Carbon Source Utilisation 183
- 6.7 Anaerobic Respiration 183
- 6.8 ArcA, Mobile Genetic Elements, and HGT 184
- 6.9 Stress and Stress Survival in Bacterial Life 185
- 6.10 Oxygen Stress 185
- 6.11 Iron Starvation 186
- 6.12 Siderophores and Iron Capture 188
- 6.13 TonB-Dependent Transporters 188
- 6.14 Gene Regulation and Iron Transport 190
- 6.15 Iron Storage and Homeostasis 191
- 6.16 Osmotic Stress and Water Relations in Bacteria 191
- 6.17 Signal Molecules and Stress 193
- 6.18 The Stringent Response 194
- 6.19 Regulation of the Acid Stress Response 196
- 6.20 Alkaline pH Stress Response 200
- 6.21 Motility and Chemotaxis 201
- 6.22 Quorum Sensing 203
- 6.23 Biofilms 205
- 6.24 'Cheating' as a Lifestyle Strategy 206
- 6.25 Thermal Regulation 207

- 6.26 Epigenomics and Phasevarions 209
- 6.27 Some Unifying Themes 210

7 Gene Control: Global Regulation by H-NS 211

- 7.1 H-NS is a Global Regulator 211
- 7.2 H-NS and Foreign DNA 211
- 7.3 H-NS and Xenogenic Silencing: Three Case Studies 212
- 7.4 The H-NS Virulence Regulon in Vibrio cholerae 212
- 7.5 HGT in V. cholerae: The CTX Phage and the VPI1 Island 213
- 7.6 The ToxRS, ToxT, TcpPH Regulatory Network 215
- 7.7 Control by VpsR, VpsT, and HapR 215
- 7.8 Quorum Sensing and Cholera 217
- 7.9 Chitin and HGT 217
- 7.10 The H-NS Virulence Regulon in Shigella flexneri 219
- 7.11 Shigella Infection 221
- 7.12 The VirF AraC-Like Transcription Factor 222
- 7.13 VirB: A Recruit from a Plasmid-Partitioning System 222
- 7.14 The Shigella Virulence Plasmid 223
- 7.15 The Salmonella H-NS Virulence Gene Regulon 223
- 7.16 Salmonella's Pathogenicity Islands (SPI) 224
- 7.17 SlyA, PhoP/Q, and SPI Gene Expression 227
- 7.18 Gene Control in SPI1 and SPI2 227

8 An Integrated View of Genome Structure and Function 231

- 8.1 Networks versus Hierarchies 231
- 8.2 Regulons, Stimulons, and Heterarchies/Netarchies 232
- 8.3 Transcription Burstiness and Regulatory Noise 233

- 8.4 The Significance of Gene Position 234
- 8.5 Messenger RNA May Not Be Free to Diffuse Far in Bacteria 236
- 8.6 RNA Polymerase Activity and Genome Organisation 237
- 8.7 Gene–Gene Interactions in the Folded Chromosome 239
- 8.8 DNA Supercoiling as a Global Regulator 240
- 8.9 Modelling the Nucleoid 243
- 8.10 Synthetic Biology 243

References 247

Index 379.