

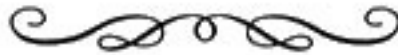
*You know how it is.
You pick up a book, flip to the dedication & find that, once again,
the author has dedicated a book to someone else & not to you.*

Not this time.

Because we haven't yet met/have only a glancing acquaintance/are just crazy about each other/haven't seen each other in much too long/are in some way related/will never meet, but will, I trust, despite that, always think fondly of each other....

This one's for you.

for the explorer inside all of us



courtesy of Neil Gaiman

To the gentle reader. If when reading, you find a mistake or significant omission, please let us know. In the life of the mind, there is no more valuable friend or ally than the engaged & critical reader.

- M.K. but I am sure someone has already captured the sentiment.

Acknowledgements 7

Preface: A biofundamentalist's approach to teaching & learning biology 8

How biology differs from physics and chemistry 9

Your background and our (Socratic) teaching approach 11

PART I - Foundations 14

Chapter 1: Understanding (biological) science & thinking scientifically 15

The interconnectedness (self-consistency) of science 17

Models, hypotheses, and theories 18

Knowing what you know: constructing models, answers, explanations & critiques 19

Science is social 21

Teaching and learning science 22

Understanding scientific ideas 23

Distinguishing the scientific from the trans-scientific 24

Chapter 2: Life and its origins 26

What is life, exactly? 27

The cell theory and the continuity of life 29

The organization of organisms 30

Spontaneous generation and the origin of life 31

The death of vitalism 34

Thinking about life's origins 35

Experimental studies on the origins of life 35

Mapping the history of life on earth 37

Fossil evidence for the history of life on earth 38

Life's impact on the earth 40

Chapter 3: Evolutionary mechanisms and the diversity of life 43

Organizing organisms, hierarchically 45

Natural and un-natural groups 47

Evolution: making theoretic sense of Linnaean classification 47

Fossils and family relationships: introducing cladistics (briefly) 48

Evolution theory's core concepts 50

So what do we mean by genetic factors? 51

Limits on populations 52

The conceptual leap made by Darwin and Wallace 54

Mutations and the origins of genotype-based variation 55

Genotype-phenotype relationships: discrete and continuous traits 57

Variation, selection, and speciation 59

Types of (simple) selection 60

Considering stochastic processes 63

Population size, founder effects and population bottlenecks 65

A reflection on the complexity of phenotypic traits 71

Gene linkage: one more complication 72

Speciation & extinction 74

Mechanisms of speciation 76

Signs of evolution: homology and convergence 80

Homologies provide evidence for a common ancestor 84

Anti-evolution arguments 84

Chapter 4: Social evolution and sexual selection 86

Selecting social (cooperative) traits 88

Community behaviors & quorum sensing 89

Active (altruistic) cell death and survivors 91

Inclusive fitness, kin and group selection, and social evolution 92

Group selection 94

Defense against social cheaters 95

Driving the evolutionary appearance of multicellular organisms 97

Origins and implications of sexual reproduction 98

Sexual dimorphism	99
Sexual selection	102
Curbing runaway selection	106
Chapter 5: Molecular interactions, thermodynamics & reaction coupling	108
A very little thermodynamics	108
Thinking entropically (and thermodynamically)	111
Reaction rates	113
Coupling reactions	115
Inter- and Intra-molecular interactions	117
Covalent bonds	118
Bond stability and thermal motion (a non-biological moment)	119
Bond polarity, inter- and intramolecular interactions	122
The implications of bond polarity	122
Interacting with water	124
Turning to entropy	125
Chapter 6: Membrane boundaries and capturing energy	127
Defining the cell's boundary	127
The origin of biological membranes	130
Transport across membranes	131
Channels and carriers	134
Generating gradients: using coupled reactions and pumps	136
Simple Phototrophs	137
Chemo-osmosis (an overview)	140
Oxygenic photosynthesis	140
Chemotrophs	142
Using the energy stored in membrane gradients	144
Osmosis and living with and without a cell wall	145
An evolutionary scenario for the origin of eukaryotic cells	146
Making a complete eukaryote	147
Chapter 7: The molecular nature of the heredity material	151
Discovering how nucleic acids store genetic information	153
Locating hereditary material within the cell	155
Identifying DNA as the genetic material	156
Unraveling Nucleic Acid Structure	158
DNA, sequences & information	161
Discovering RNA: structure and some functions	162
DNA replication	163
Replication machines	166
Accuracy and error in DNA synthesis	167
Further replication complexities in eukaryotes: telomeres	168
Topoisomerases	169
Mutations, deletions, duplications & repair	170
A step back before going forward: what, exactly, is a gene anyway?	171
Alleles, their origins and their impact on evolution	173
DNA repeat diseases and genetic anticipation	175
Chapter 8: Peptide bonds, polypeptides, proteins, and molecular machines	177
Specifying a polypeptide's sequence	179
Protein synthesis: transcription (DNA to RNA)	181
Ribosomes	184
The translation (polypeptide synthesis) cycle	185
Effects of point mutations on polypeptides and proteins	187
Mutations influencing splicing	189
Non-sense mediated RNA decay	190
Alarm generation	192
Turning polypeptides into proteins	193
Factors influencing polypeptide folding and structure	194

Chaperones	196	
Regulating protein activity, concentrations and stability (half-life)		198
Allosteric and post-translational regulation	199	
Diseases of folding and misfolding	200	
Molecular machines	202	
Chapter 9: Organizing and expressing genes in regulatory networks		203
Locating information within DNA	205	
Interaction networks and model systems	209	
E. coli as a model system	210	
Adaptive behavior and gene networks (the lac response)		211
Final thoughts on (molecular) noise, for now	215	
Chapter 10: Cellular topology and intercellular signaling		216
Targeting proteins to where they need to be: membrane proteins		217
Nuclear targeting and nuclear exclusion in eukaryotes	218	
Intercellular signaling: signals, receptors & responses	219	
Signaling molecules and receptors	220	
Cellular reprogramming: embryonic and induced pluripotent stem cells	221	
Part II: From molecular biology to genetics and genetic technologies		223
A brief review of concepts with which we hope you should already be familiar with		224
Words, terms, and processes we (really) need to understand:	224	
Where do genes, alleles, and mutations come from?	226	
Alleles	226	
Phenotypes	227	
Muller's Morphs	228	
Chapter 11: Reproduction in prokaryotes and horizontal gene transfer		232
Asexual reproduction in bacteria and archaea	232	
Conjugation: what counts as sex in prokaryotes	233	
Other naturally occurring horizontal gene transfer mechanisms	235	
Transformation	235	
Viruses moving genes: transduction	236	
Chapter 12: Asexual and sexual reproduction in eukaryotes		238
Asexual reproduction in a eukaryote: making a (somatic) clone	238	
Ploidy during the cell cycle	239	
Molecular choices and checkpoints	240	
Meiosis, fertilization, and embryogenesis	244	
Steps in meiosis: from diploid to haploid	245	
Recombination & independent segregation	246	
Linkage & haplotypes	249	
X-inactivation and sex-linked traits	250	
X-linked diseases and mono-allelic gene expression	251	
Chapter 13: Generating mutations and becoming alleles		253
Mutations into alleles	253	
Luria & Delbrück: Discovering the origin of mutations	254	
Forward and reverse genetics	256	
Generating mutations rationally - CRISPR CAS9 and related technologies		259
Longer term mutation / evolution studies	260	
Chapter 14: Genome dynamics and pathogenic somatic mutations		262
Rates and effects of somatic mutation	263	
Non-disjunction: a disease of aberrant chromosome segregation meiosis		264
Genome dynamics	265	
Gene duplications and deletions	266	
Orthologs and paralogs	267	
Transposons: moving DNA within a genome (and weird genetics)	268	
Chapter 15: Becoming Mendelian: analyzing alleles in terms of phenotypes & pathways		271
Chi square analysis, hypothesis testing, and numbers that are less than infinity	274	

Dihybrid crosses and linkage	276
Using web-based bioinformatic tools: Genomicus	278
Genetic complementation	280
Interacting traits: synthetic lethality and co-dominance	282
Interacting traits: epistasis	283
Temperature sensitive alleles	285
Measuring evolution's impact on allele frequencies: Hardy-Weinberg	285
The persistence of deleterious alleles	286
Chapter 16: Germ line alleles and human pathologies	288
Developing multicellular organisms: from egg to embryo and more	288
Maternal and paternal effects	290
Conflicts between mother and fetus: imprinting	290
Genetic analysis of developmental processes: maternal and zygotic effect mutations	291
Mitochondrial inheritance	292
Traits and the number of genes involved	293
Where is a gene expressed?	294
Back to Mendelian determinants	297
Disease-associated alleles	298
Concordance between monozygotic twins and genetic influence on a trait	298
Using web-based bioinformatic tools: Exac Browser	299
Using web-based bioinformatic tools: BLAST	301
Genetic anticipation	301
Conclusions, good bye and good luck	304
Considering embryonic development	305
Coming in Spring of 2020	305