## THE ORIGINS OF CELLULAR ARCHITECTURE

## **INTRODUCTION**

- 1. Evolutionary Cell Biology.
- 2. The Origin of Cells.
- 3. The Major Lines of Descent.

## THE GENETIC MECHANISMS OF EVOLUTION

- 4. The Population-genetic Environment.
- 5. Evolution as a Population-genetic Process.
- 6. Evolution of Cellular Complexity.

#### **BASIC CELLULAR FEATURES**

- 7. The Cellular Environment.
- 8. Evolutionary Scaling Laws in Cell Biology.
- 9. Cell Growth and Division.
- 10. The Cell Life Cycle.
- 11. Cellular Senescence.

#### STRUCTURAL EVOLUTION

- 12. The Protein World.
- 13. Multimerization.
- 14. Protein Management.
- 15. Lipid and Membranes.
- 16. Cytoskeleton, Cell Shape, and Motility.

## **ENERGETICS AND METABOLISM**

- 17. The Costs of Cellular Features.
- 18. Resource Acquisition and Homeostasis.
- 19. Enzymes and Metabolic Pathways.

#### INFORMATION PROCESSING

- 20. Intracellular Errors.
- 21. Intracellular Communication: Transcription.
- 22. Environmental Sensing and Extracellular Communication.

### ORGANISMAL COMPLEXITY

- 23. Endosymbiosis.24. Origins of Organismal Complexity.

#### **FOUNDATIONS**

- 2.1. The proton-motive force and the evolution of ATP synthase.
- 2.2. Evolution prior to self-replication.
- 2.3. The limits to replication fidelity and genomic maintenance.
- 4.1. The amount of neutral nucleotide variation maintained at selection-drift equilibrium.
- 4.2. Relationship of the recombination rate to physical distance between sites.
- 5.1. Divergence under uniform selection.
- 5.2. Mean probabilities of alternative alleles at steady state.
- 5.3. The detailed-balance solution for the evolutionary distribution of alternative molecular states.
- 7.1. Intracellular diffusion.
- 7.2. Rates of encounter by molecular diffusion.
- 7.3. The Boltzmann probability distribution for alternative molecular states.
- 7.4. The yield of cellular biomass per ATP usage.
- 8.1 The cost of building a cell.
- 9.1. The scaling of ribosome number and cell growth rate.
- 9.2. Nutrient limitation and cell growth.
- 9.3. Scaling models for the development of cellular features.
- 9.4. Parent-offspring resemblance and the response to selection.
- 9.5. Transient response to selection without genetic change.
- 11.1. The physiological damage load in a cell lineage.
- 13.1. Association / dissociation equilibria.
- 14.1. The CCT chaperonin complex.
- 14.2. Evolution of a digital trait.
- 15.1. Probability of preservation and subdivision of labor by duplicated interactions.
- 16.1. The eukaryotic cellular investment in the cytoskeleton.
- 16.2. The physical challenges to cellular locomotion.
- 16.3. The construction costs of flagella.
- 18.1. The response of uptake rate to nutrient concentration.
- 18.2. Encounter and capture rates.
- 18.3. The cost of osmoregulation.

- 19.1. Michaelis-Menten enzyme kinetics.
- 19.2. Evolutionary sensitivity of pathway steps.
- 19.3. Optimization of the glycolytic flux rate.
- 19.4. Extension / contraction of a metabolic pathway.
- 20.1. Kinetic proofreading.
- 20.2. The evolutionary bounds on the transcription-error rate.
- 21.1. Number of transcripts per cell.
- 21.2. Occupancy probability for a transcription-factor binding site.
- 21.3. The biophysics of TFBS localization.
- 21.4. The evolutionary dispersion of TFBS matching profiles.
- 22.1. Behavior of a monocycling system.
- 22.2. Accuracy of environmental sensing.
- 23.1. Messenger RNA editing.

#### **FIGURES**

- 1.1. A broad overview of the Tree of Life.
- 1.2. The major dimensions of the triad of environmental features influencing cellular evolution.
- 2.1. Amino-acid synthesis via the Strecker reaction.
- 2.2. The reductive citric-acid cycle.
- 2.3. Two proposed settings for the origin of life.
- 2.4. The structure of ATP synthase.
- 2.5. The building blocks of DNA and RNA.
- 2.6. A family of polymeric sequences with binary alternatives for the monomeric subunits.
- 3.1. An idealized view of the two-domain view of the Tree of Life.
- 3.2. Alternative forms of phospholipids deployed by the three major lineages of life.
- 3.3. An approximate phylogenetic tree for some of the major eukaryotic supergroups.
- 3.4. Emergence of reproductive incompatibility following the relocation of a mitochondrial gene.
- 4.1. An overview of the influence of random genetic drift on allele frequencies.
- 4.2. Effects of chromosomal linkage on the efficiency of natural selection.
- 4.3. The negative scaling of effective population size with organism size across the Tree of Life.
- 4.4. Quasi-equilibrium distributions of mutation rates under the drift-barrier hypothesis.
- 4.5. Negative scaling of mutation rates with effective population sizes across the Tree of Life.
- 4.6. The physical mechanics of recombination.
- 4.7. Scaling of the recombination rate per nucleotide site with genome size.
- 4.8. Temporal changes of allele frequencies under asexual vs. sexual reproduction.
- 5.1. The distribution of fitness effects of new mutations.
- 5.2. Allele-frequency changes in experimental populations of *E. coli*.
- 5.3. Some possible routes to the establishment of adaptations involving two or more mutations.
- 5.4. Origin of a complex adaptation involving three mutations in small and large populations.
- 5.5. Expected frequency of an allele under the joint forces of drift, mutation, and selection.
- 5.6. Schematic for transition rates between adjacent classes under the sequential-fixation model.
- 5.7. Long-term mean genotypic states under a two-locus, two-allele model.
- 5.8. Equilibrium mean frequencies of favorable alleles for a trait under directional selection.
- 6.1. Evolution of increased complexity by constructive neutral evolution.
- 6.2. Variation in the structural complexity and size of ribosomal RNA.
- 6.3. The DDC model for the alternative fates of duplicate genes.
- 6.4. Evolution of the yeast galactose-utilization pathway following duplication and subfunctionalization.
- 6.5. Duplication and subfunctionalization of components of yeast vacuolar ATP synthase.
- 6.6. The emergence of modular gene-regulatory structure by small duplications and deletions.
- 6.7. Speciation by reciprocal silencing of an ancestral duplicate gene.
- 7.1. Relationship between dry weights and volumes of individual cells.
- 7.2. Physical features of water molecules.
- 7.3. Fractional contributions of major biomass components to the cell dry weights.

- 7.4. Numbers of proteins and messenger RNAs per cell.
- 7.5. Two-dimensional random walks.
- 7.6. Diffusion coefficients for simple substances in water.
- 7.7. Response of cellular growth rates to temperature in bacterial species.
- 7.8. Heats of combustion of organic substrates and relationship to microbial growth rates.
- 7.9. Geometry of diffusive encounters between two particles.
- 8.1. Distribution of cell sizes for major phylogenetic groups.
- 8.2. Allometric scaling of metabolic rate with cell volume.
- 8.3. Estimating the costs of building and maintaining cells with chemostat cultures.
- 8.4. The bioenergetic costs of cellular construction and maintenance.
- 8.5. The scaling of maximum growth rate and cell volume in heterotrophs and autotrophs.
- 8.6. The drift-barrier to the performance of complex quantitative traits.
- 8.7. The scaling of mitochondrial features with cell size.
- 8.8. The scaling of ribosome number with cell size.
- 9.1. Response of ribosome-associated features with cell growth rate.
- 9.2. Growth and uptake responses to the concentration of a limiting nutrient.
- 9.3. Relationship between cell volume and growth increment under three alternative models.
- 9.4. Evidence in support of the adder growth model for *E. coli*.
- 9.5. Response of growth rate and cell volume to laboratory selection in *E. coli*.
- 9.6. Responses of cell size and growth rates at the phylogenetic and environmental plasticity levels.
- 9.7. Distributions of cell division times for different members of a population of *Bacillus*.
- 9.8. Coefficients of variation for numbers of molecules within individual cells.
- 9.9. Response to directional selection on a quantitative trait.
- 9.10. Influence of the form of the fitness function on mean fitness in a population.
- 9.11. A conceptualize partitioning of cellular proteins into functional sectors.
- 10.1. The eukaryotic cell cycle.
- 10.2. Nonorthologous gene replacement under a constant network topology.
- 10.3. Alternative surveillance architectures with the same final outcome.
- 10.4. Independent duplication / subfunctionalization events for a key cell checkpoint gene.
- 10.5. Mitosis vs. meiosis.
- 10.6. Some multimeric proteins involved in DNA replication.
- 10.7. The centromere-drive hypothesis.
- 10.8. Evolution of mating-type determination in a pheromone-receptor system.
- 10.9. The binuclear genomes in ciliates.
- 10.10. Neutral drift of a one-to-one communication system.
- 10.11. Frequency-dependent selection for alternative mating types.
- 11.1. Serial buildup and dilution of cellular damage.
- 11.2. The distribution of damage inheritance in cell pedigrees.
- 11.3. Passive relocation of a protein aggregate to the poles of cells.
- 11.4. Survivorship cures for two yeast species.
- 11.5. Continuous decline of cell-division potential in single-cell lineages.
- 11.6. History of division times in *E. coli* cells.

- 12.1. Guide to the amino acids.
- 12.2. Structure of polypeptide chains.
- 12.3. Biosynthetic pathways of amino acids.
- 12.4. Alpha helices and beta sheets.
- 12.5. Dependence of folding rate on amino-acid chain length.
- 12.6. Evolution of population mean phenotypes on a hyperbolic fitness function.
- 12.7. Frequency distributions of the destabilizing effects of mutations on proteins.
- 12.8. Bacterial phylogenetic distribution of folding stabilities of dihydrofolate reductase.
- 12.9. Exchangeability of amino acids in  $\beta$ -lactamase.
- 12.10. Distributions of fitness effects from single amino-acid substitutions.
- 12.11. Genome-wide G+C compositions relative to the neutral expectation.
- 12.12. A restricted path of evolution of a three-residue protein resulting from epistasis.

#### **TABLES**

- 7.1. Elemental compositions of cells.
- 8.1. Geometric features of common cell shapes.
- 9.1. Coefficients of variation for growth-related features of cells.
- 12.1. Properties of amino acids.

# SUPPLEMENTAL TABLES

- 4.1. Mutation-rate and effective population size estimates.
- 7.1. Dry weights and volumes of individual cells.
- 7.2. Fractional contributions of major biomass components to the cell dry weights.
- 7.3. DNA content vs. cell size.