THE ORIGINS OF CELLULAR ARCHITECTURE

INTRODUCTION

1. Evolutionary Cell Biology.
   The dominance of unicellular life.
   What is evolutionary cell biology?
   The completeness of evolutionary theory.
   Nonadaptive hypotheses and our understanding of evolution.
   The grand challenges.
      The origin of life.
      The roots of organismal complexity.
      Molecular stochasticity.
      Molecular complexes.
      Cellular networks.
      Cellular surveillance systems.
      Growth regulation.
      Biological scaling laws.

2. The Origin of Cells.
   The earliest stages.
      The alkaline hydrothermal-vent hypothesis.
      The terrestrial geothermal-field hypothesis.
   An early RNA world?
   Membranes and the origin of individuality.
   Genomic constraints on the establishment of life.

3. The Major Lines of Descent.
   The major domains of life.
   Times of origin.
   The emergence of eukaryotes.
      The stem eukaryote.
      The eukaryotic radiation.
      A eukaryotic big bang?

THE GENETIC MECHANISMS OF EVOLUTION

   Demystifying random genetic drift.
   The genetic effective sizes of populations.
   Probability of fixation of a mutant allele.
   Evolution of the mutation rate.
      High mutability of mutation rates.
Error-prone polymerases.
Optimizing the mutation rate.
The nonrandom nature of mutations.
Recombination.
Evolution of the recombination rate.

The perils of the adaptive paradigm.
The fitness effects of new mutations.
The classical model of sequential fixation.
Vaulting barriers to more complex adaptations.
Sequential fixation vs. stochastic tunneling.
Two-locus transitions.
More complex scenarios.
The effects of recombination.
The phylogenetic dispersion of mean phenotypes.
Two-state traits.
Multistate-traits and the drift-barrier hypothesis.

Illusions of grandeur.
Constructive neutral evolution.
Ribosomes.
Evolution by gene duplication.
The masking effect.
Neofunctionalization.
Subfunctionalization.
Adaptive-conflict resolution.
The case for subfunctionalization.
The emergence of modular gene subfunctions.
The passive origin of species via gene duplication.

BASIC CELLULAR FEATURES

Molecular composition of cells.
Water.
Elemental composition.
Biomolecules.
Numbers of molecules per cell.
Passive transport of particles through the cytoplasm.
Intermolecular encounter rates.
Temperature-dependence of biological properties.
Energy, carbon skeletons, and cell yield.
   Describing allometric relationships.
   Scaling laws in cellular bioenergetics.
   Metabolic rate.
   Lifetime energy requirements of a cell.
   The speed limit on cell-division rates.
   The limits to natural selection imposed by the drift barrier.
   Membrane bioenergetics and the prokaryote-eukaryote transition.
   Energy production and the mitochondrion.
   Cellular investment in ribosomes.
   The mitochondrion as a driver of eukaryotic evolution.

   Ribosomes and cell growth.
   Models for cellular growth.
   Control of cell size at maturity.
   Division-size determination.
   Environmental determinants of cell size.
   Scaling of intracellular features.
   Phenotypic variation in cell size and division time.
   Stochastic partitioning of cell contents at division.
   Phenotypic variation and adaptation.
   Environmental variation and the efficiency of selection.
   Inheritance of environmental effects.
   The adaptive value of phenotypic variation.

    The eukaryotic cell cycle.
    Phylogenetic diversity.
    Network complexity.
    Mitosis.
    Meiosis.
    Origin and evolutionary modifications.
    Rapid evolution of meiosis-associated proteins.
    Recombination mechanisms.
    Evolutionary consequences of sexual reproduction.
    Mating types.
    Mating-type determination.
    Mating-type number.
    Cell fusion.
    Coevolution of pheromones and their receptors.
    Sexual systems in unicellular and multicellular organisms.
    Isogamy vs. anisogamy.
    Sex ratio.
    Sex chromosomes.
11. Senescence.
   Physiological load.
   Error catastrophe.
   Cellular vs. population immortality.
Molecular and cellular determinants.
Evolution of senescence.
Mutational meltdown.

STRUCTURAL EVOLUTION

12. The Protein World.
   The essential features of proteins.
   Amino-acid composition.
   Origin of amino acids.
Protein folding and stability.
   The rate of protein folding.
   Stability of folding.
Determinants of protein-sequence evolution.
   Lessons from phylogenetic comparisons and experimental mutagenesis.
   Expression level and the propensity for sequence change.
   Mutation pressure and biased amino-acid usage.
   Convergent and parallel evolution.
   Epistasis and compensatory mutation.
A general model for protein evolution.

   The incidence and architectural features of multimers.
   Propensity to aggregate.
   Theory of association.
   The physical features of interfaces.
Evolutionary considerations.
   Transitions from monomeric to higher-order states.
   The domain-swapping model.
   Dimerization by compensatory mutation.
   Heteromers from homomers.

14. Protein Management.
   Chaperone assistance.
   Phylogenetic diversity of chaperones.
   Client-chaperone coevolution.
   Chaperone-mediated phenotypic evolution.
   Disposal by proteosomes.
   Post-translational modification.

15. Lipid and Membranes.
Molecule structure.
Membrane structure.
Eukaryotes and the organellar explosion.
  Vesicle trafficking.
  Vesicle production.
  Vesicle delivery.
Evolutionary issues.
The nuclear envelope.
  Nuclear-pore architecture.
  Nuclear transport.
  Evolutionary considerations.

The basic cytoskeletal infrastructure.
  Actins.
  Tubulins.
  Intermediate filaments.
Molecular motors.
Motility.
  **Gliding motility.**
  Prokaryotic flagella.
  Eukaryotic flagella.
  The costs of motility.
Cell shape.
Cell walls.

**ENERGETICS AND METABOLISM**

17. The Costs of Cellular Features.
The energetic cost of a cellular feature.
The evolutionary cost of a cellular feature.
The costs of maintaining and expressing a gene.
The cost of lipid production.

18. Resource Acquisition and Homeostasis.
Elemental composition of cells.
  Adaptive fine-tuning of elemental composition?
Nutrient uptake kinetics.
  Channels and transporters.
  Physiological acclimation.
  Advantages of motility.
Photosynthesis.
  The transformation of solar to chemical energy.
  The world’s most abundant enzyme.
Osmoregulation.
Circadian rhythms.

19. Enzymes and Metabolic Pathways.
   Enzymes.
   - Basic enzymology
   - Degree of molecular perfection.
   - Enzyme promiscuity.
   Pathway flux control.
   - Pathway position and the strength of selection.
   - Speed vs. efficiency.
   Pathway expansion and contraction.
   - Stochastic meandering of pathway architecture.
   - The origin of novel enzymes.
   Pathway remodeling.
   - Nonorthologous gene replacement.
   - Internal pathway expansion via multifunctional enzymes.
   - Pathway duplication and divergence.

INFORMATION PROCESSING

20. Intracellular Errors.
   Transcript fidelity
   Translational fidelity.
   - Biophysical limits to substrate discrimination and the cost of proofreading.
   - The limits to selection on error rates.
   - The evolutionary consequences of proofreading.
   - Adaptive significance of errors.

   Transcription factors and their regulatory motifs.
   - Biophysics of recognition.
   - Facilitated diffusion and the search for regulatory motifs.
   - Evolution of the regulatory vocabulary.
   - Evolutionary rewiring of transcription networks.
   RNA-mediated expression.

22. Environmental Sensing and Extracellular Communication.
   Bacterial signal-transduction systems.
   - Origin and diversification.
   - Coevolutionary integration of components.
   - Emergence of new pathways.
   - Interconvertible proteins and ultrasensitivity.
   - The cost of signal transduction.
   - Similarities and differences in eukaryotic systems.
   Chemoreception.
Accuracy of environmental assessment.
Phenotypic bimodality and bet-hedging.
Adaptive fine-tuning vs. inadvertent by-products of pathway structure.

ORGANISMAL COMPLEXITY

23. Endosymbiosis.
Mitochondria.
   Origins.
   Energetic boost or burden.
   Functional remodeling.
The extreme population-genetic environments of mitochondria.
   Mutation rates.
   Modes of inheritance.
   Muller’s ratchet.
Organelle genome degradation.
   Animal mitochondrial tRNAs.
   Coevolutionary drive and compensatory mutations.
Plastid evolution.
Addiction to endosymbionts.

24. The Road to Multicellularity.
The population-genetic consequences of large organism size.
Development at the intracellular level.
The passive emergence of organismal complexity.
Shake-up via a basal genome-duplication event?
Antecedents in bacteria.
   Quorum sensing.
Evolutionary rewiring: recap.
The cost of living.
The energetic cost of multicellularity.
Decision making, altruism, and the evolution of multicellularity.
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.
9.4. 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.

12.1. Magnitude of selection on amino-acid sequences under the cost hypothesis.


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.

19.2. 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.
7.9. 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.

9.2. 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.

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.
TABLES

7.1. Elemental compositions of cells.
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.