BGEN 55 - Advanced Genetics II

The Properties of Mutation

Week 5, Part 2: Mutation as Source of Variation

🎯 Learning Objectives

After studying this lecture, you will be able to:

- Define mutation rate (μ) and explain its significance in evolutionary genetics
- Describe why mutation is considered a weak but constant evolutionary force
- Classify mutations based on their fitness effects and molecular mechanisms
- Explain the relationship between mutation rates and evolutionary change
- Calculate expected allele frequency changes due to mutation pressure

🧬 Fundamental Concepts of Mutation

Mutation: A heritable change in the DNA sequence that can be passed from one generation to the next.

The Ultimate Source of Variation

Mutation is the **ultimate source of all genetic variation** in populations. Every allele, every nucleotide difference that exists in any gene pool originated as a mutation at some point in evolutionary history.

Key Insight: Without mutation, there would be no genetic variation for natural selection to act upon, and evolution would eventually cease.

Mutation Rate (μ)

The mutation rate (denoted by μ, the Greek letter mu) is defined as:

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μ = Probability of mutation per generation
per base pair or per locus
```

Typical mutation rates in eukaryotes:

- **Per base pair:** 10^{-8} to 10^{-11} per generation
- **Per gene locus:** 10^{-5} to 10^{-6} per generation
- **Genome-wide:** ~70 new mutations per generation in humans

Example Calculation: If $\mu = 1 \times 10^{-6}$ per locus per generation, and a population has 1,000,000 individuals, we expect approximately 1 new mutation at that locus in each generation.

⚡ Properties of Mutation as an Evolutionary Force

1. Weak Force

Mutation rates are extremely low. To change allele frequency significantly by mutation alone requires thousands of generations.

$$\Delta p = -\mu p_0$$

Very small per generation

2. Constant Process

Mutation occurs in every generation, continuously introducing new variation into populations regardless of environmental conditions.

3. Random Process

Mutations occur randomly with respect to:

- Organism's needs
- Environmental conditions
- Genomic location

4. Mostly Irreversible

While reverse mutations can occur, they are rare. For modeling purposes, we typically treat mutation as a one-way process: A → a.

Evolutionary Significance: Despite being weak individually, mutation's constant action over geological time scales makes it a powerful creative force in evolution.

📊 Classification of Mutations

By Fitness Effect

Type	Fitness Effect	Frequency	Evolutionary Significance
Neutral	No effect on fitness	Most common	Subject to genetic drift; molecular clock
Deleterious	Reduces fitness	Common	Removed by selection; genetic load
Advantageous	Increases fitness	Rare	Basis of adaptation; positive selection

By Molecular Mechanism

- **Point mutations:** Single nucleotide changes (transitions, transversions)

- **Insertions/Deletions:** Addition or removal of nucleotides
- **Chromosomal rearrangements:** Inversions, translocations, duplications
- **Copy Number Variations:** Changes in number of gene copies

🧮 Mathematical Modeling

One-Way Mutation Model

For recurrent one-way mutation (A → a) at rate μ:

$$p_1 = p_0(1 - \mu)$$
$$\Delta p = p_1 - p_0 = -\mu p_0$$

Where:

- p_0 = initial frequency of allele A
- p_1 = frequency after one generation
- Δp = change in frequency per generation

Time Scale of Mutation

The frequency after t generations:

$$p_t = p_0(1 - \mu)^t$$

> **Numerical Example:** If $p_0 = 1.0$ and $\mu = 1 \times 10^{-5}$:
> After 1,000 generations: $p \approx 0.990$
> After 10,000 generations: $p \approx 0.905$
> After 100,000 generations: $p \approx 0.368$

This demonstrates why mutation is considered a **slow evolutionary force**.

🌍 Real-World Implications

Genetic Disorders

Many inherited diseases are caused by deleterious mutations. Despite selection against them, they persist due to:

- Recurrent mutation
- Heterozygote advantage (e.g., sickle cell anemia)
- Late onset (e.g., Huntington's disease)

Molecular Clock

The relatively constant rate of neutral mutations allows us to estimate evolutionary divergence times between species.

```
Divergence time = (Number of differences) / (2 × Mutation rate)
```

Antibiotic Resistance

Bacteria evolve resistance through spontaneous mutations that are then selected for in antibiotic-rich environments.

💡 Key Takeaways

- Mutation rate (μ) is typically very small (10^{-5} to 10^{-8})
- Mutation is a **weak but constant** evolutionary force
- Most mutations are **neutral or deleterious**
- Mutation provides the **raw material** for evolution
- The one-way mutation model: $p_1 = p_0(1 - \mu)$
- Mutation-selection balance explains persistence of deleterious alleles

> **Looking Ahead:** In the next section, we will explore how mutation interacts with selection in the important concept of mutation-selection balance.
