MAST10016 - Mathematics for Biomedicine - Notes

Exercise Sheet 1: (approximately correlates to week number)

Population Genetics

Allele Frequencies:
$f^A = f^{AA} + \frac{1}{2} f^{Aa}, f^a = f^{aa} + \frac{1}{2} f^{Aa}$
$f^A + f^a = 1$

Genotype Frequencies:
$f^{AA} = \frac{N^{AA}}{N}, f^{Aa} = \frac{N^{Aa}}{N}, f^{aa} = \frac{N^{aa}}{N}$

Random mating:
$P(offspring\ is\ AA) = (f^A)^2$
$P(offspring\ is\ Aa) = 2f^A f^a = 2f^A(1 - f^A)$
$P(offspring\ is\ aa) = (f^a)^2$

Segregation Principle:
By the segregation principle, a gamete will inherit one of the two alleles with equal probability. Hence half of the man's gametes will possess the dominant A allele. Since a child is formed from a randomly selected gamete, 50% of the man's offspring will inherit the A allele from him.
If the man is homozygous, then all gametes will possess the A allele, and all children will inherit the trait.

Random mating for a population of N size:
$N^{AA} \sim Bi(N, (f^A)^2)$
$N^{AA} \sim Bi(N, 2f^A(1 - f^A))$
$N^{AA} \sim Bi(N, (f^a)^2)$

Expected number of genotypes in new generation:
$E(N^{AA}) = np = N \times (f^A)^2$

Expected genotype frequency in new generation:
$E(f^{AA}) = np = \frac{1}{N} E(N^{AA}) = (f^A)^2$
$E(f^{Aa}) = 2f^A f^a$
$E(f^{aa}) = (f^a)^2$

Note:
Use genotype frequencies of generation 0 to work out allele frequencies of generation 0
Use random mating and allele frequencies of 0 to work out generation 1 genotype frequencies
Repeat.

Exercise Sheet 2:

Hardy-Weinberg equilibrium:
Under the assumptions of random mating, large population size, no mutation, no selection and no migration, the **allele frequencies never change,** and **after the 1st generation, genotype frequencies are constant.**

$$\boldsymbol{AA:Aa:aa = p^2:2pq:q^2}$$

The biological significance of these results is that random matings drive genotype frequencies to equilibrium rapidly in 1-2 generations. In the absence of mechanisms that change alleles, Mendelian inheritance preserves genetic diversity.

Testing for HW equilibrium
1. Are allele frequencies constant in time?
2. Are genotype frequencies in the ration required for some p, q = 1-p?

Including sexual reproduction
- Consider an autosomal gene with A, a alleles. Since sex is determined by X/Y chromosomes, by the Segregation Principle, the A/a/ alleles and the sex are passed to offspring **independently**
- **Allele frequencies are constant from GEN 1+, Genotype frequencies are constant from GEN 2+**
- Use same principle of random mating but with male/female subscripts

Mutation
- Use state diagram to illustrate probabilities and state of play:
- $A \overset{u}{\rightarrow} a$
- P(gamete is A) = $f^A(n) \cdot (1-u)$ = P(allele from A pool)*(A doesn't mutate) = p
- **Allele frequencies change over time (A↓, a↑) (non-reversible only)**
- **Genotypes are ALWAYS in H-W proportions each generation (but with changing p, q)**
- **Reversible:** $f^A(n+1) = (1-u-v)f^A(n) + v$
  $f^a(n+1) = (1-u-v)f^a(n) + u$

Difference equations:
- Homogeneous difference equation
  - $\boldsymbol{x_{n+1} = a \cdot x_n}$
    - **General Solution:** $\boldsymbol{x_n = C \cdot a^n}$
      - **a > 1:** Xn grows exponentially to infinity, as n→∞, Xn diverges monotonically to infinity.
      - **a = 1:** Xn is constant (trivial) solution, eqm depends on Xo
      - **0 < a < 1:** Xn decays exponentially, converges monotonically to 0
      - **a = 0:** Xn = 0, constant solution independent of Xo
      - **-1 < a < 0:** Xn decays/converges with oscillations to 0
      - **a = -1:** Xn oscillates, doesn't decay, Xn diverges with bounded osciallation
      - **a < -1:** Xn diverges with unbounded oscillations, magnitude of Xn grows monotonically
- Inhomogeneous difference equations
  - Uses **Principle of Superposition**
  - **1. GUESS, 2. SUBSTITUTE, 3. SOLVE**