

Molecular Evolution

Chapter 18

I) Scope of Molecular Evolutionary Studies

A) Molecular polymorphisms as markers and tools

- 1) Genetic variation within and among populations
 - a) Individual, parentage and lineage identification
 - i) DNA fingerprinting
 - b) gene flow and individual movements
 - c) population size stability
 - 2) Studies on, and the detection of, natural selection
 - 3) Evolutionary relationships and phylogeny of species and beyond

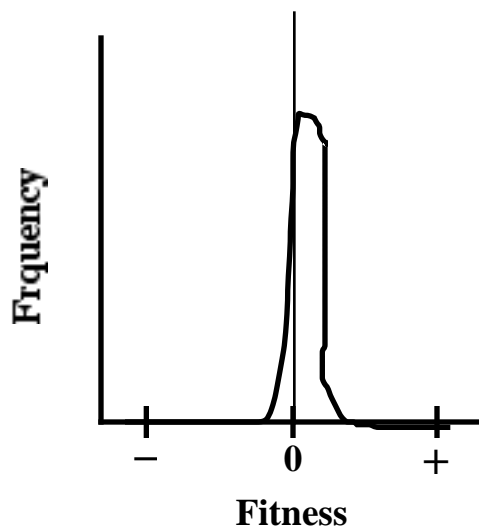
B) Genes and the evolution of Phenotype

- 1) hox genes, quantitative genetics, etc.

C) Evolution of genes and genomes – how does DNA and the entire genome evolve?

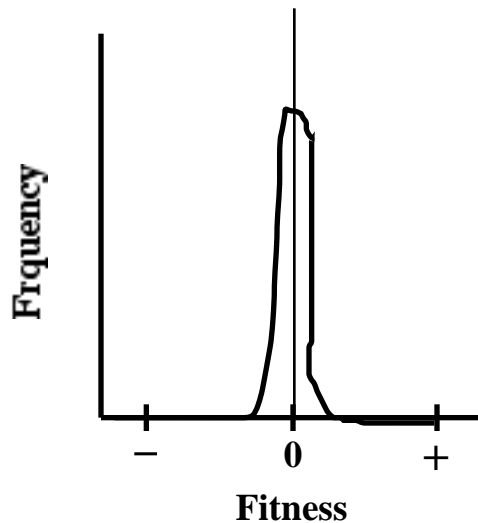
II) Selectionist and Neutralist Debate in Brief

- #### A) Classical View – The variation in natural populations is fairly limited (i.e., not a lot of it) and that all alleles and variation are under selection and mutations are most likely negative.



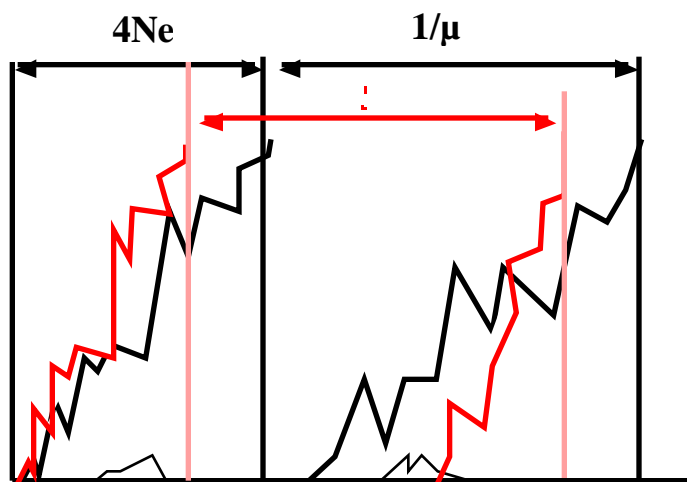
- 1) Molecular studies revealed a lot of genetic variation that appeared not to change the phenotype. Much more than can be explained if all is under selection
- 2) Variation in natural populations must be due to some sort of balancing selection (i.e., overdominance, temporally varying, etc.)
- 3) The rate of evolution is dependent on the mutation rate (μ) and the magnitude of selection.
 - a) negative (purifying or background) and positive selection

B) Neutralist View – The variation in natural populations is extensive (i.e., there is a lot) and that most alleles are NOT under selection (i.e., neutral).



1) Drift is a dominant force resulting in evolution of neutral polymorphisms.

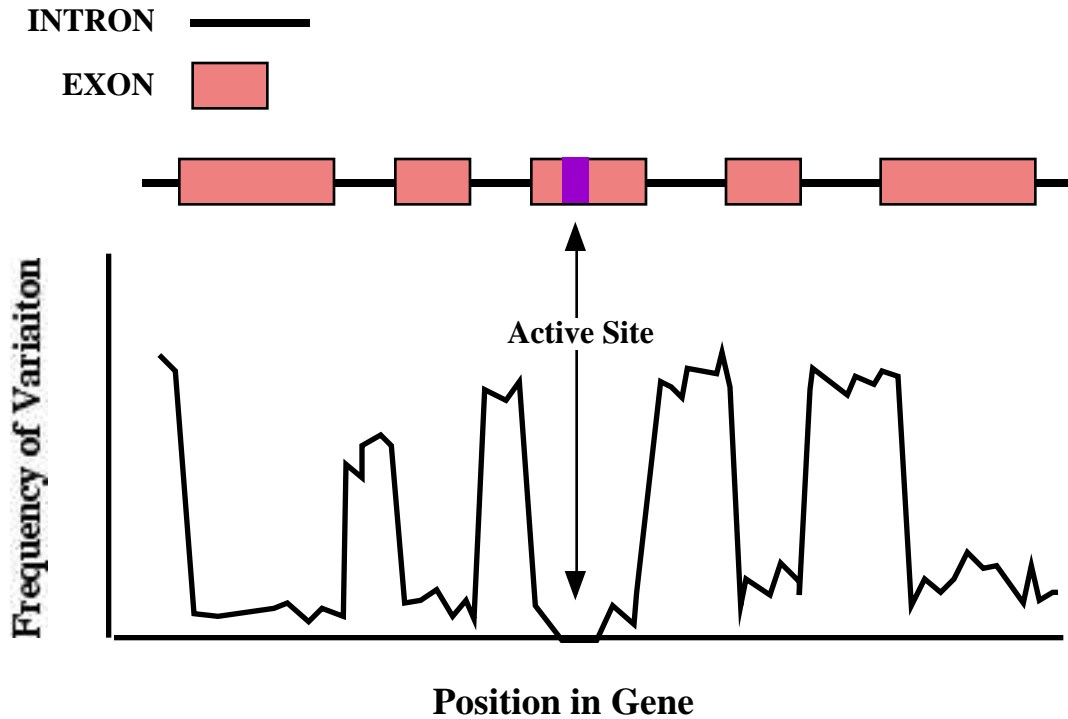
2) The alternate fixation of alleles in a population will occur at a constant rate that is equal to the mutation rate (μ) and is independent of population size



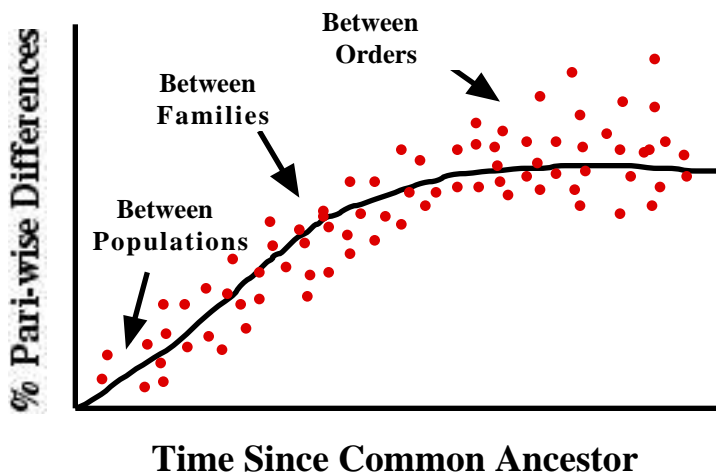
III) Evolution of DNA Sequences

A) Pattern of Variation in DNA Sequences

- 1) Non-synonymous mutation rate is less than Synonymous
i) functionality
- 2) The rate of evolution in the introns is faster than in exons



- 3) Mutational Saturation – the rate of evolution appears to slow down with time since sharing a common ancestor.



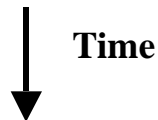
a) Mutation Saturation

... 1 2 3 4 5 6 7 8 9 10 11 12 13 14 ...
 ... A C A G T T A G C T C T A G ...

$$P(\text{position 3 mutates}) = \frac{1}{14}$$

$$P(\text{position 3 does not mutate}) = \frac{13}{14}$$

$$P(\text{position has been previously mutated}) = 0$$



... 1 2 3 4 5 6 7 8 9 10 11 12 13 14 ...
 ... A **T** **G** G T **C** A G C **C** C **C** **G** G ...

$$P(\text{position has not been previously mutated}) = \frac{8}{14}$$

$$P(\text{position has been previously mutated}) = \frac{6}{14}$$

$$P(\text{position 3 mutates AND has been previously mutated})$$

$$= \frac{1}{14} \times \frac{6}{14} = 3.06\%$$

b) Multiple mutations to a sequence

... 1 2 3 4 5 6 7 8 9 10 11 12 13 14 ...
 ... A T A G T C A G C C C C G G ...

A => G mutation

... A T **G** G T C A G C C C C G G ...

= 1 difference between

i) Reversions – a second mutation at the same site that changes the nucleotide back to the original

G => A (reversion)

... A T **A** G T C A G C C C C G G ...

= 0 differences between

ii) any other mutation:

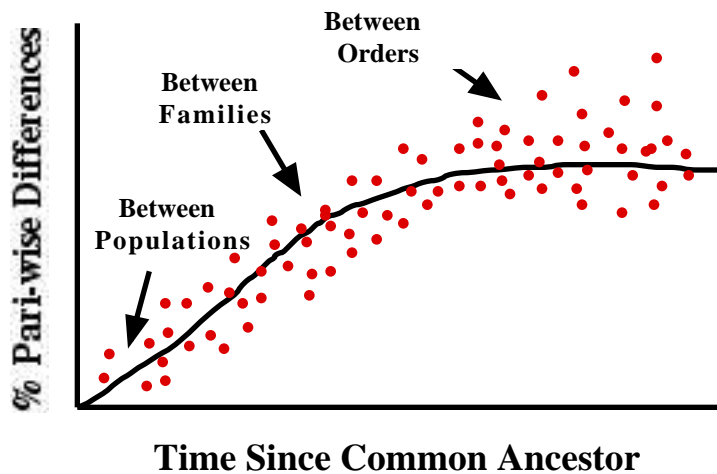
G => C

G => T

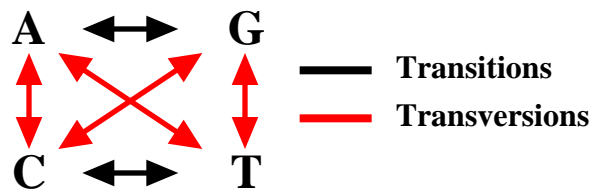
... A T **C** G T C A G C C C C G G ...

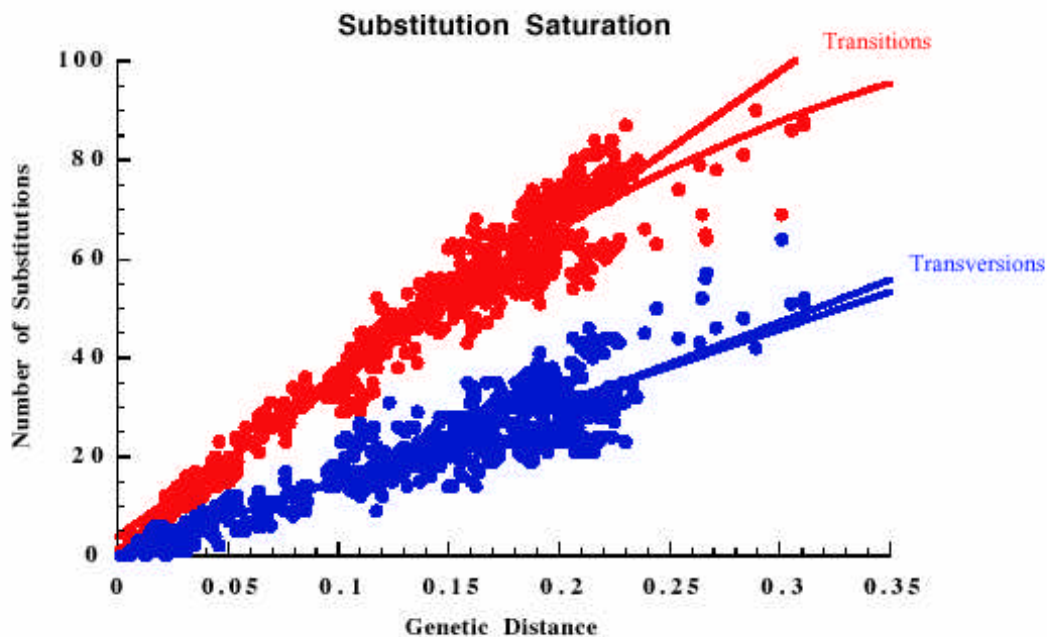
= 1 differences between

(although there has actually been two mutations to the same site)



4) Transition Bias – usually there are many more transitional differences (i.e., purine ↔ purine, or pyrimidine ↔ pyrimidine) than transversional (i.e., purine ↔ pyrimidine).

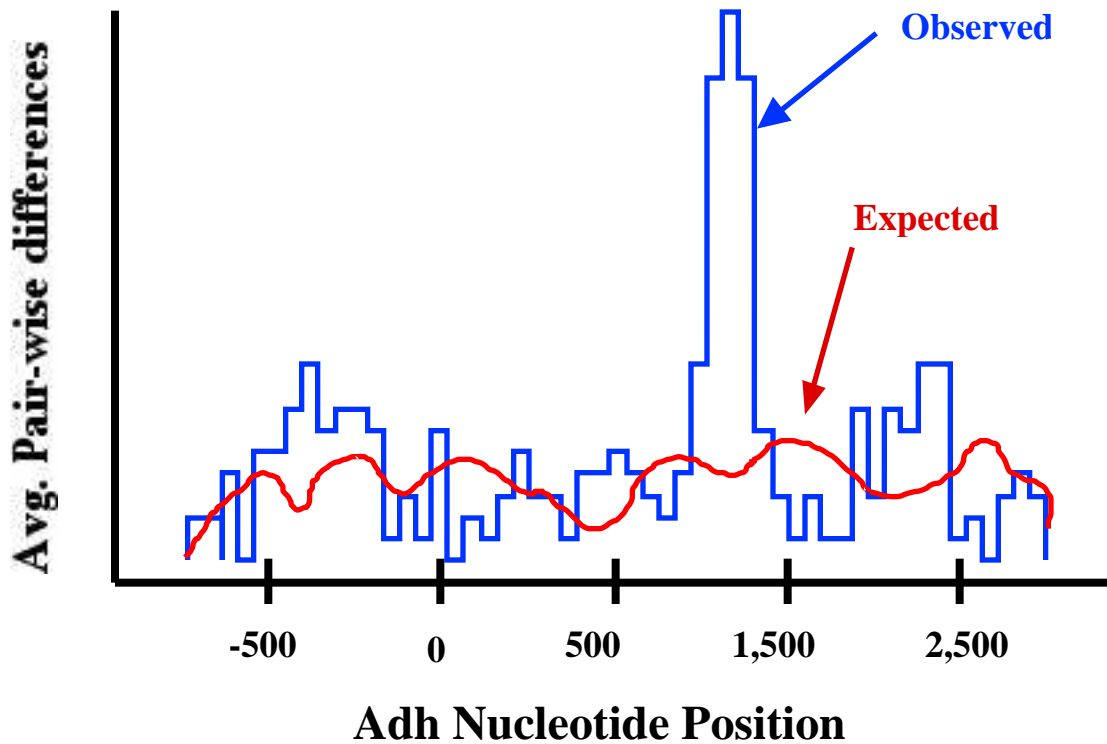




B) Detecting Natural Selection on DNA Sequences

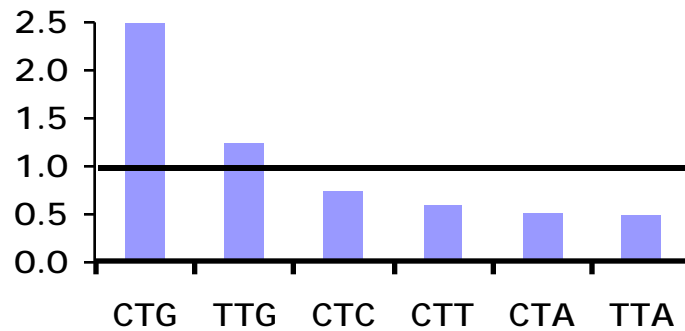
- 1) **Positive selection** – given the redundancy in the genetic code (i.e., on the whole, more than one sequence specifies a single amino acid) and the functional importance of the amino acid sequence, the number of silent (synonymous) substitutions should outnumber the number of replacement (i.e., non-synonymous).
 - a) MHC, bindin, Table 18.2, etc. #replacement > #silent
- 2) **Hitchhiking, Selection and linked sites** – since each nucleotide is not strictly independent from all others, those sites that are genetically linked tend to evolve similarly to nearby selected sites.
 - a) **Purifying or Background selection** – mutations are negative and lineages containing them are selectively removed faster than if not under selection. The amount of variation seen at linked sites is lower than expected under neutrality

- b) **Positive Selection** – some mutations are advantageous so mutations go to fixation faster than neutral expectations and therefore the amount of variation at linked sites is lower than expected.
- c) **Balancing Selection** – since overdominance keeps alleles in the population longer than they otherwise would be, the neutral sites linked to them have accumulated more polymorphisms than expected.
- i) **Fast and Slow allele in Adh of Drosophila.**



3) Codon Bias – General assumption given the redundancy in the genetic code (i.e., more than one sequence can specify the same amino acid) is that all silent mutations are equally likely.

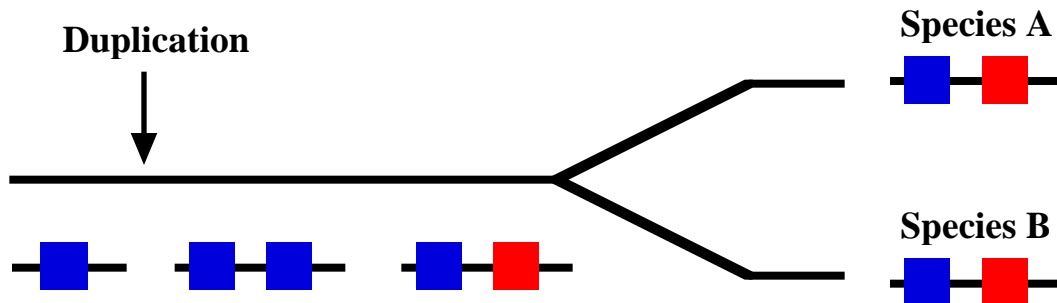
e.g., Leucine codon bias in *Drosophila melanogaster*



a) regulatory role and translational efficiency.

IV) Multi-gene families

A) Gene duplication is very common



Blue versus Blue }
 Red versus Red } : Orthologous

Blue versus Red: Paralogous

1) very important to the evolution of new genes and new gene functions (i.e., regulatory Adh).

B) Concerted Evolution – although most duplicated genes tend to evolve independently, some have the paralogous sequences homogenized by a process known as biased gene conversion



Duplication



Divergence



Speciation



Divergence



Conserted Evolution



1) mechanism is not well understood

C) Evolution of New Genes

- 1) Duplication and differentiation – as before**
- 2) Exon shuffling – gene structure in exons and introns may be an important evolutionary mechanisms to create new genes. Exons and domains of genes can be put together in new combinations to form new functions.**