Understanding Genetic Data

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DNA Sequencing Revolution
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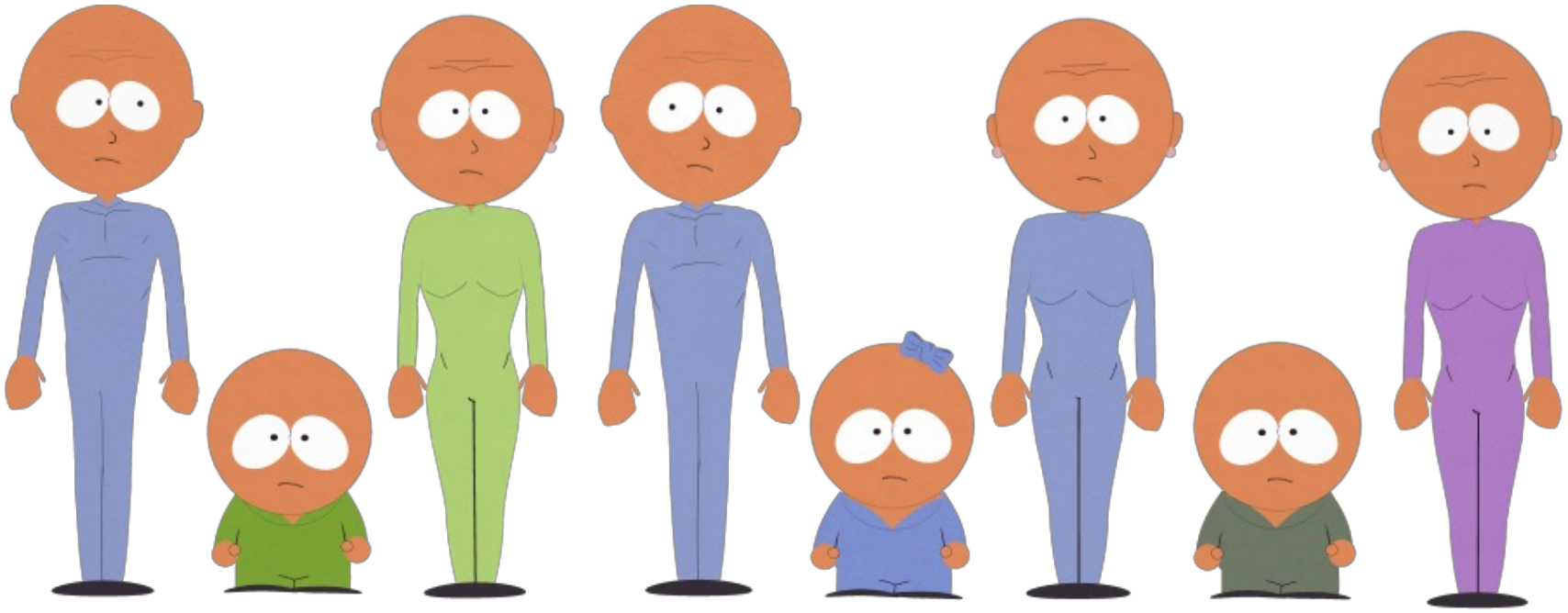
Darwin's major problem – blending inheritance

"The process (natural selection) will often be greatly retarded by ***free inter-crossing****. Differences, however slight, between any two forms, if not blended by intermediate gradations, are sufficient to raise both forms to the rank of species. All the individuals whatever their quality may be will generally be allowed to breed and this* ***will effectively prevent selection****."*

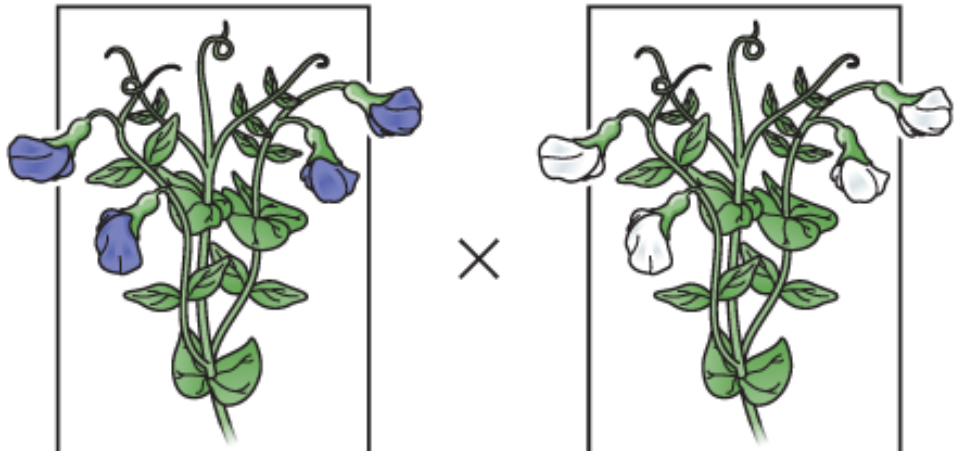
Darwin's major problem – blending inheritance

Blended inheritance prevents the evolution of novel traits
(and thus the evolution of new species by natural selection)



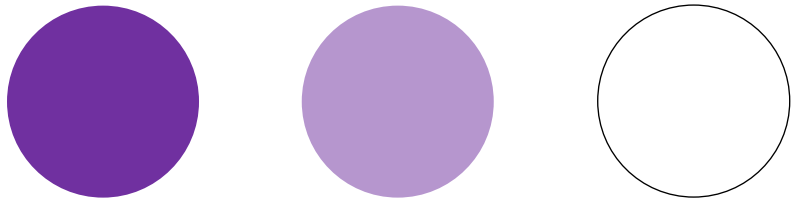
South Park Future Humans – 2004

Does inheritance follow a blending or particulate (solid) model?



P generation

Gregor Mendel



????

Does inheritance follow a blending or particulate (solid) model?

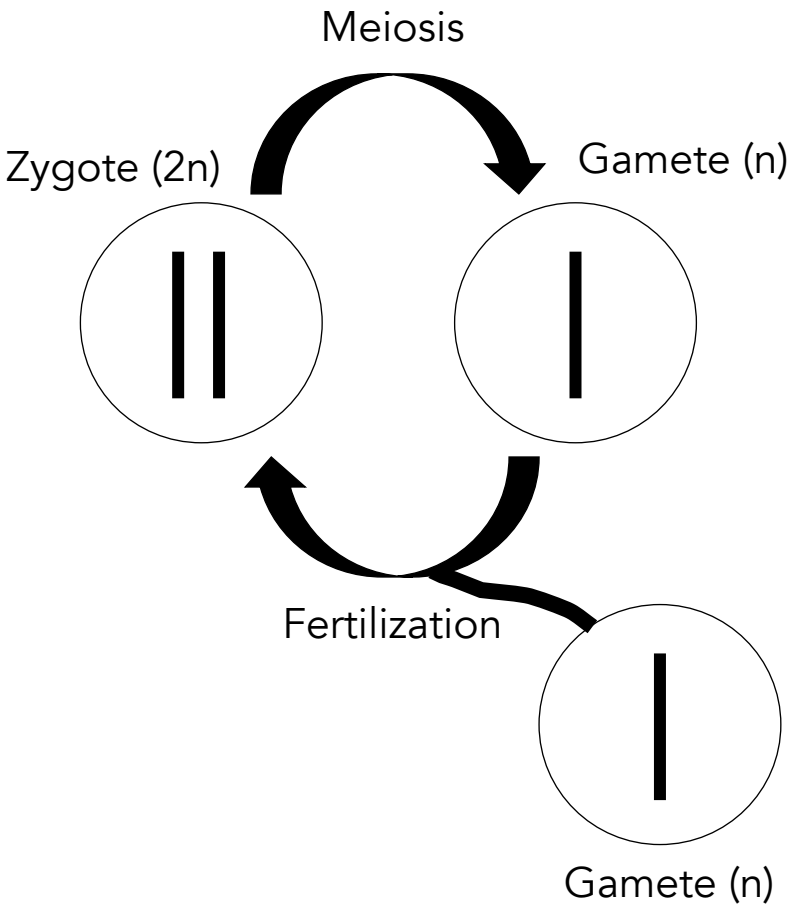
1. Parent cross, hybrid selfing results **incompatible with blending model**

2. Maintenance of both forms of the trait imply two **segregating** elements (alleles)

3. Elevated purple vs. white flowers in F2 progeny indicates **dominance**

Gregor Mendel

Particulate inheritance at the cellular level – meiosis



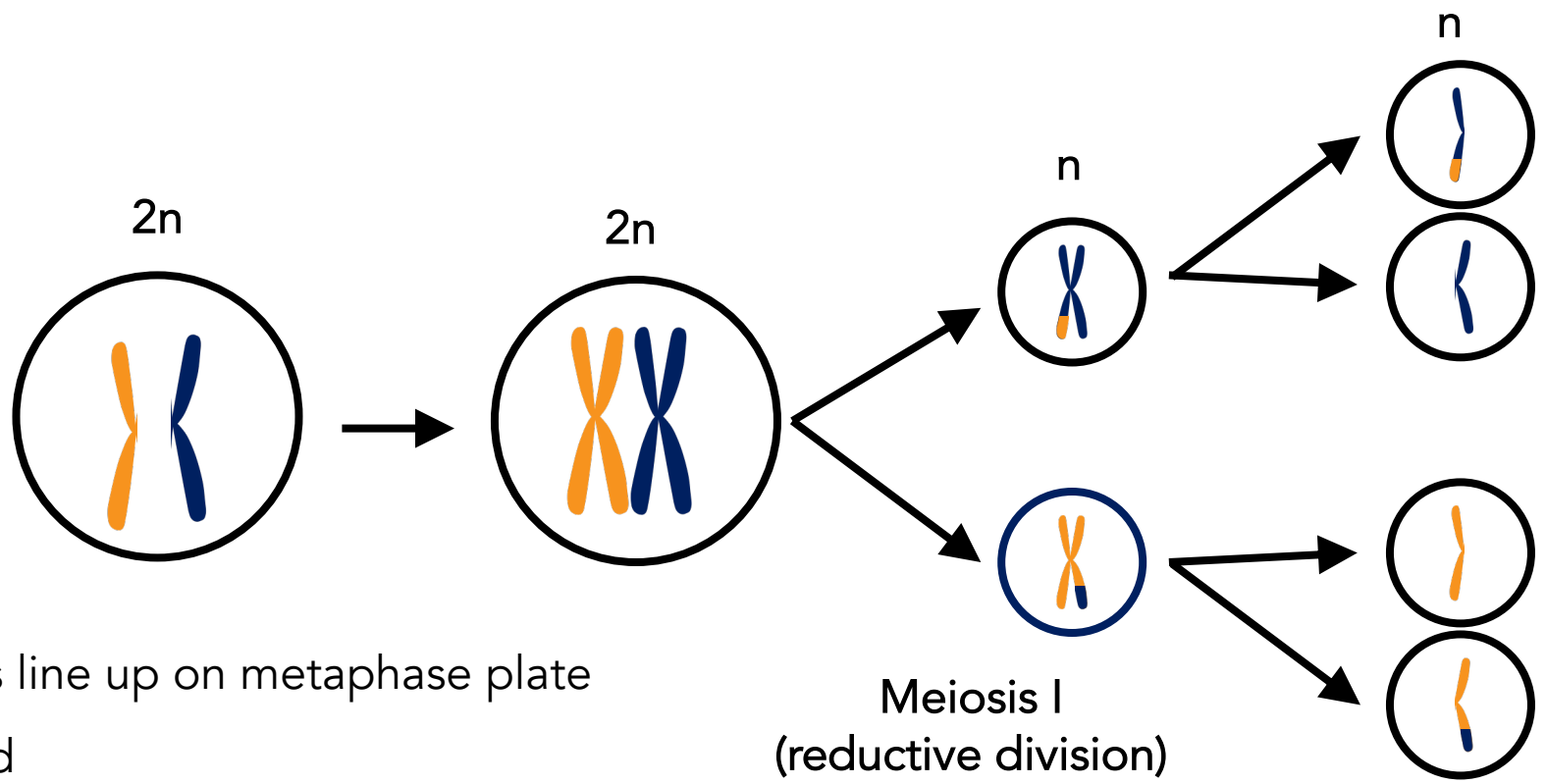
1. **Ploidy** – Number of copies of the genome present inside a cell

2. **Diploid (2n)** – Two copies of every chromosome

3. **Haploid (n)** – One copy of every chromosome

Sexual Reproduction **...why?**

Meiosis is really good at separating alleles

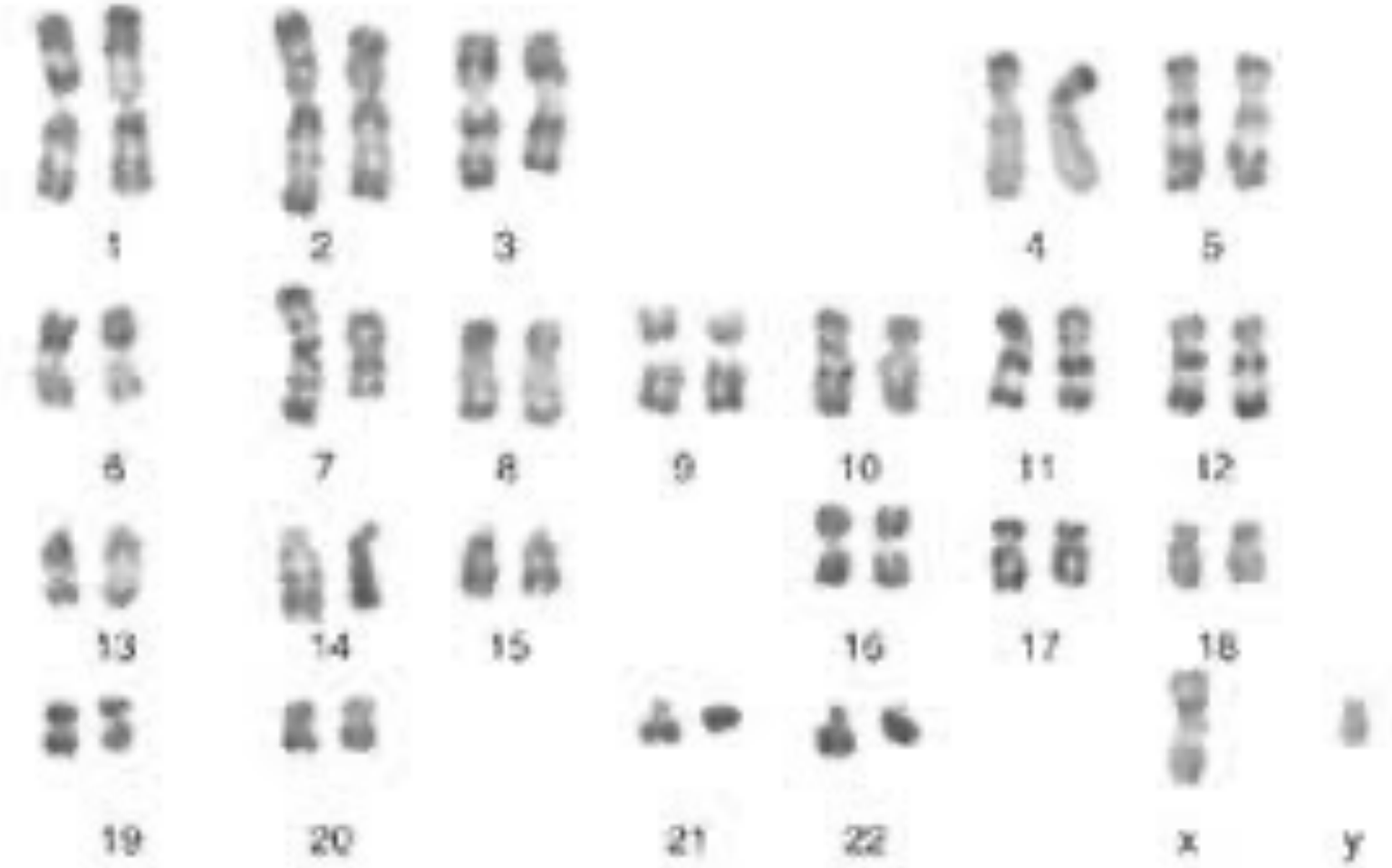


- Homologues line up on metaphase plate
- Ploidy halved
- Meiosis II ~ Mitosis
- Daughter cells not identical to mother cell
- Recombination

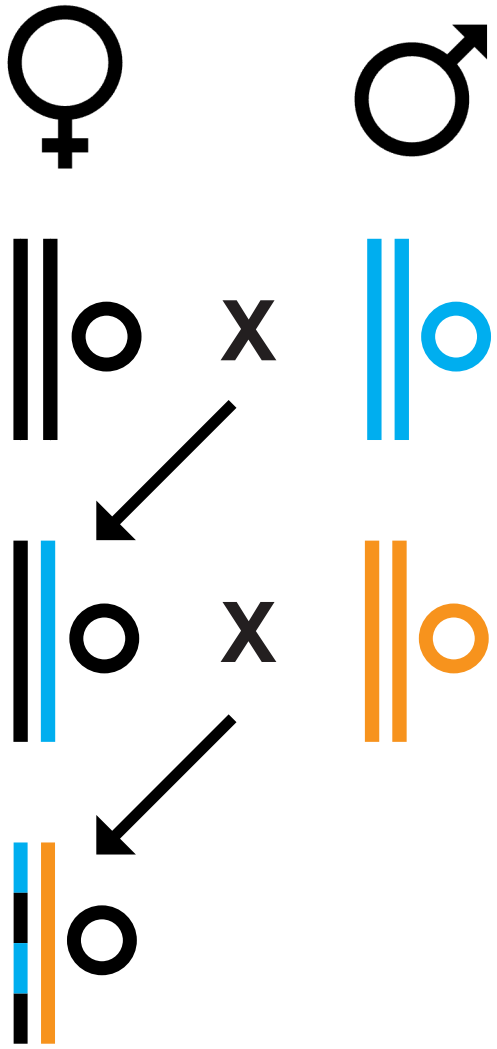
But many traits look like blended inheritance (e.g., my children). How can that be?

Almost all traits are encoded by many genes!

Many thousands of genes per chromosome!



Non-mendelian inheritance is also common



Camus et al 2022. *Heredity*

Mutations are the source of genetic variation

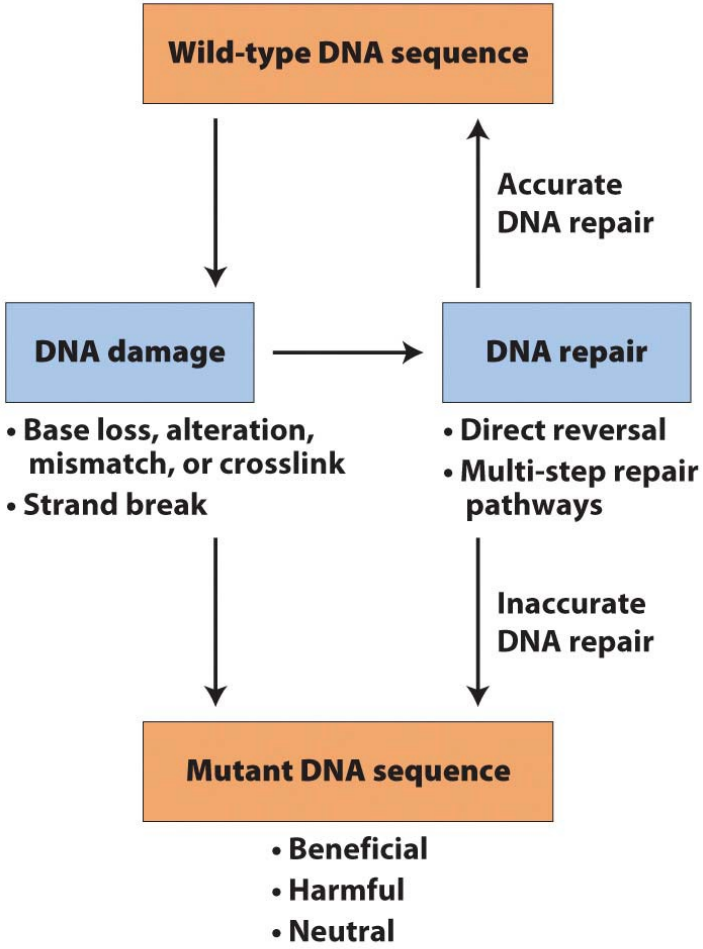
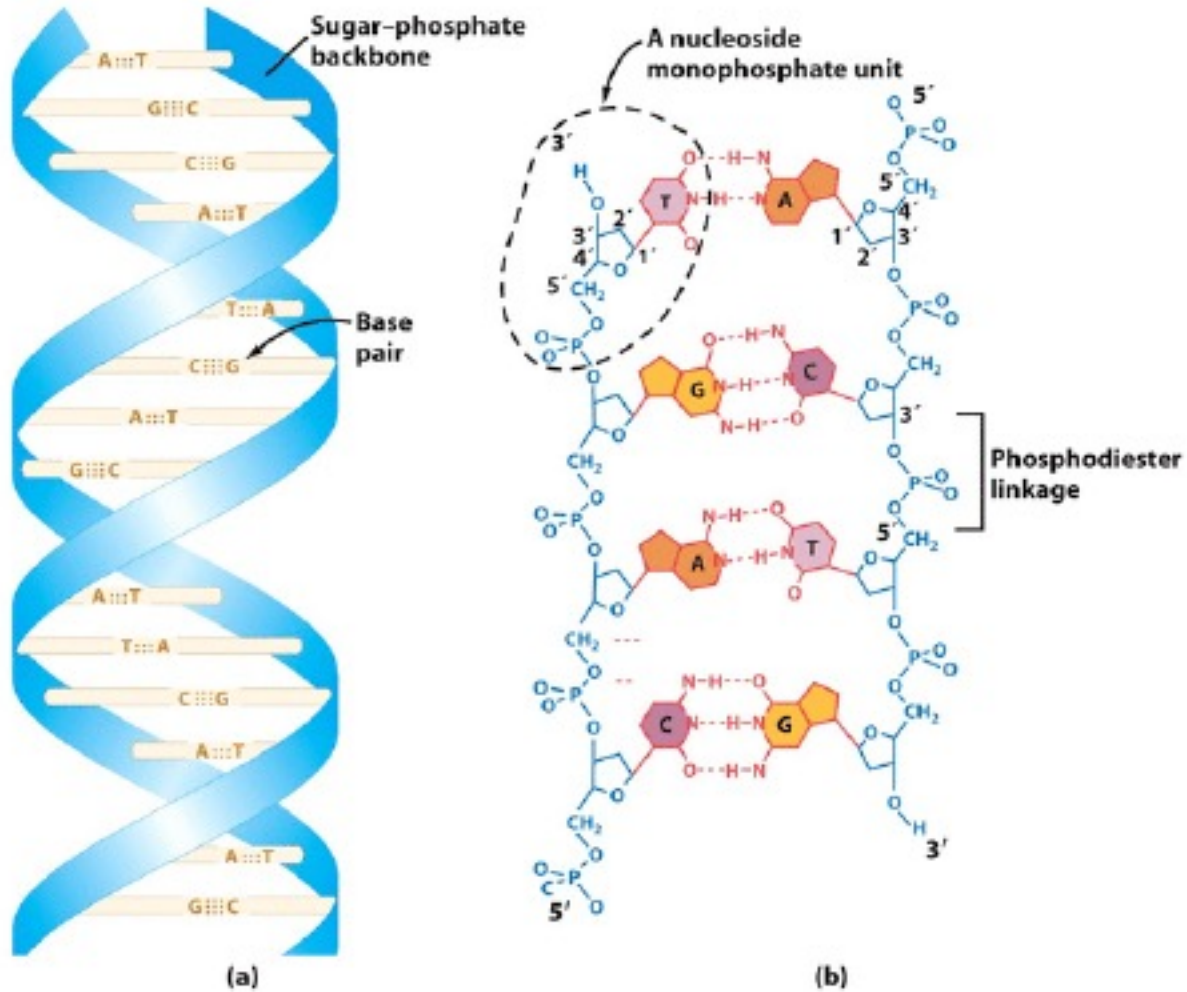
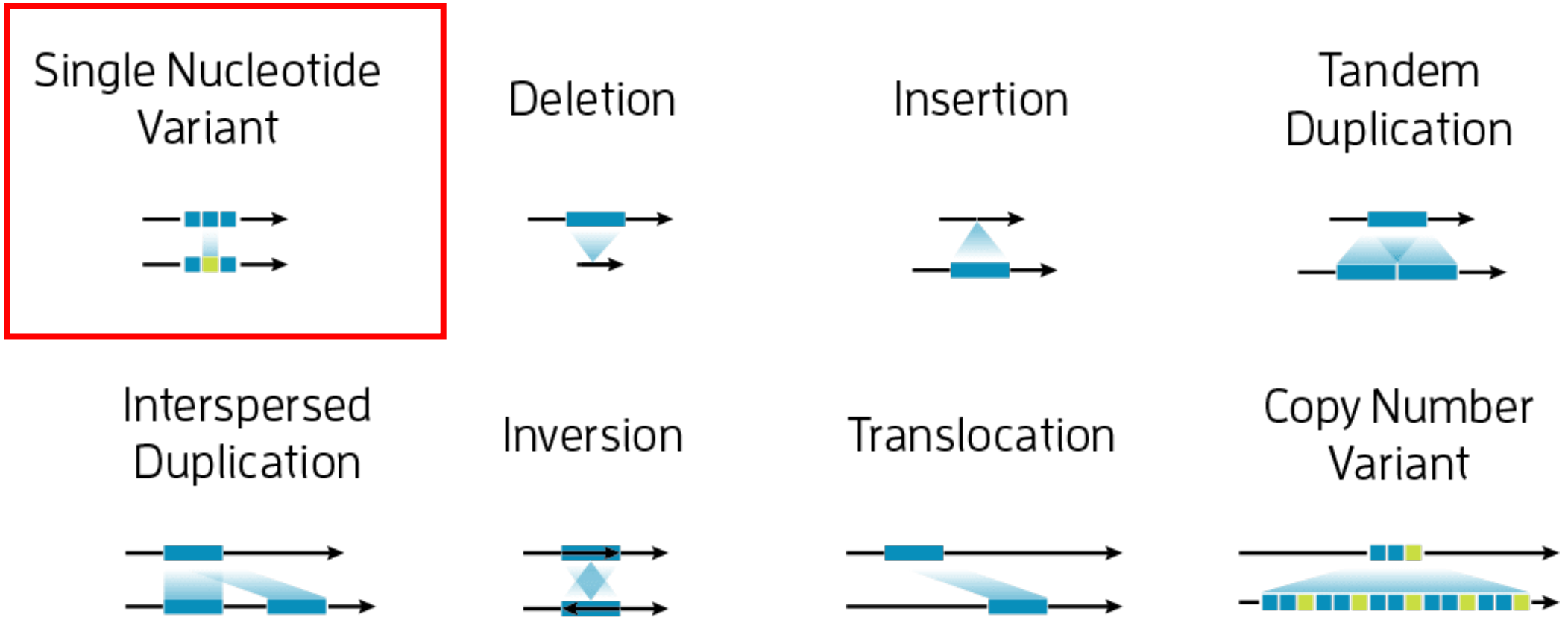


Figure 15-1
Introduction to Genetic Analysis, Twelfth Edition

The Structure of DNA double helix

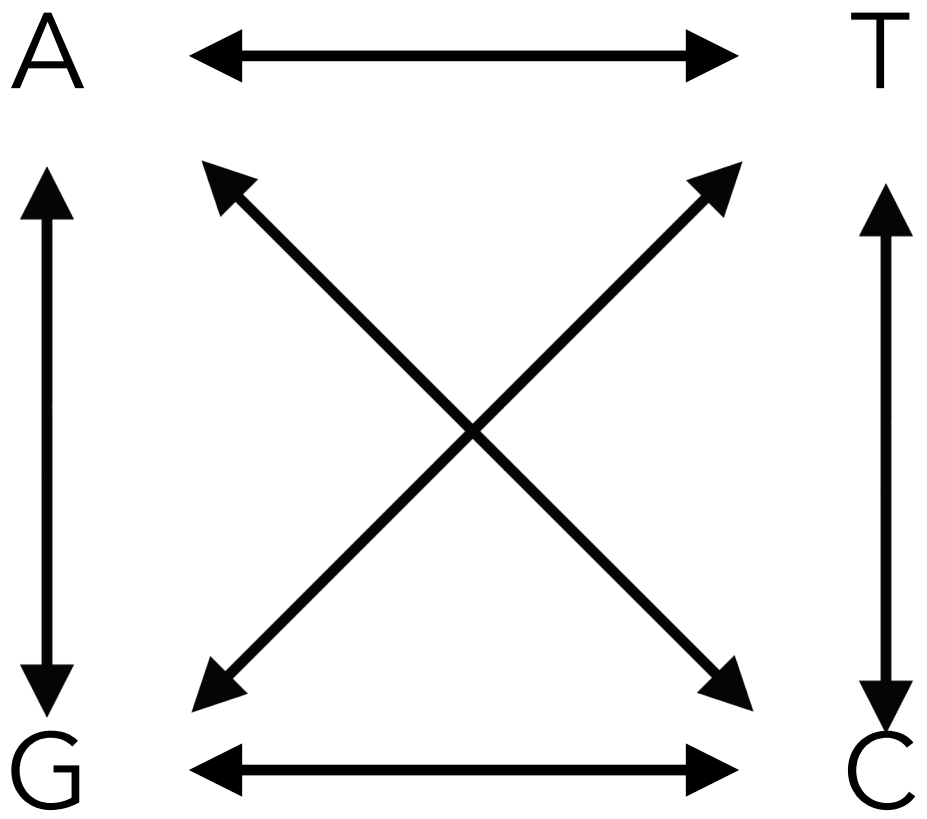


Many different kinds of mutations



Types of Variants

Mutations – Inherited changes in nucleotide sequence



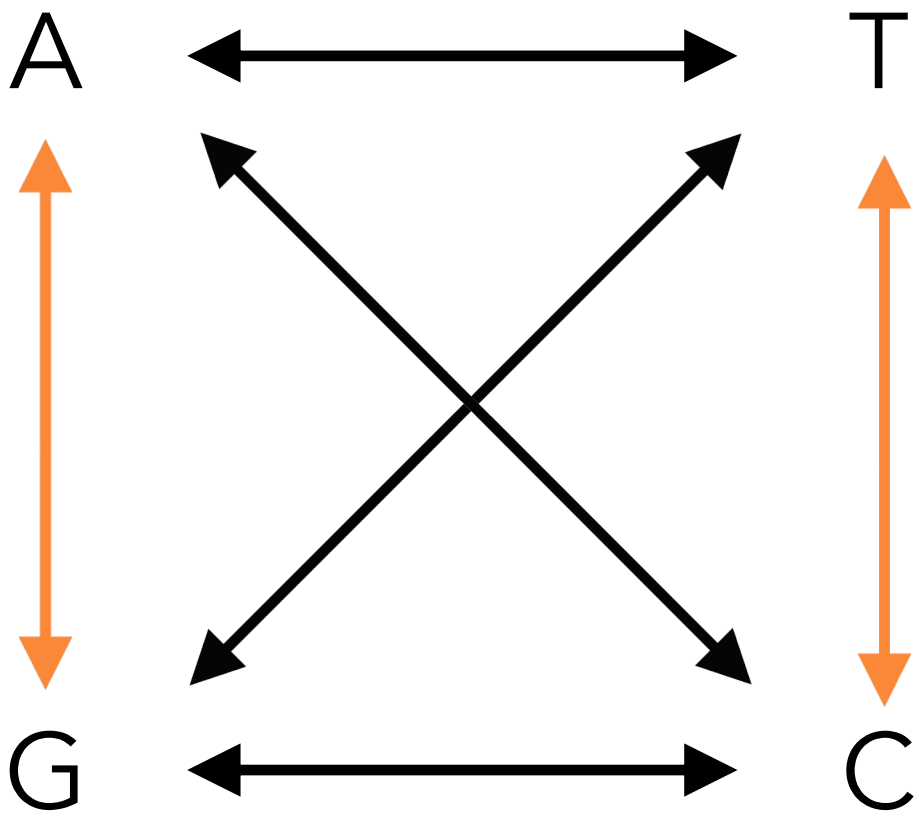
Mutations – Inherited changes in nucleotide sequence

Transitions

purine-to-purine

pyrimidine-to-pyrimidine

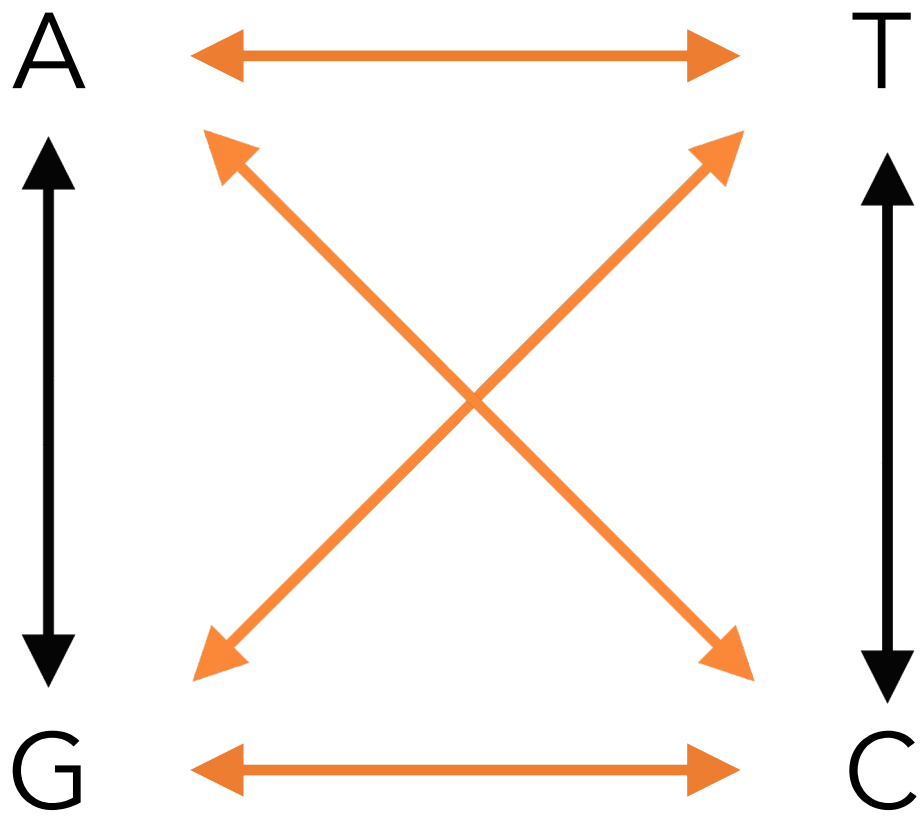
COMMON



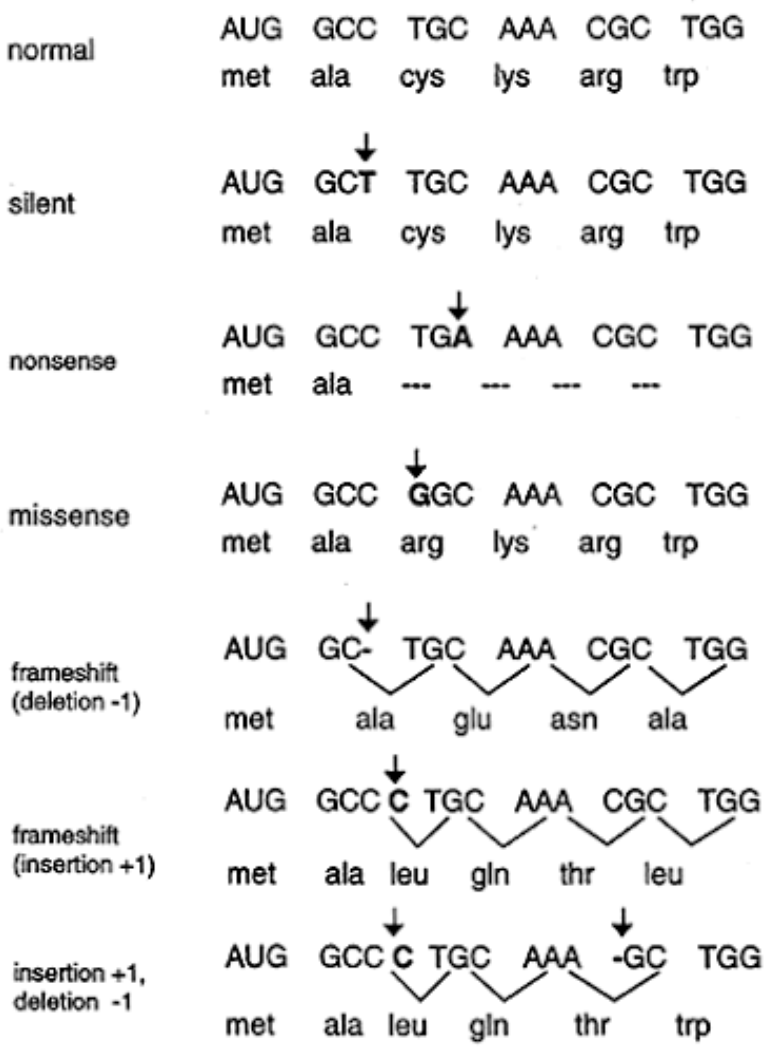
Mutations – Inherited changes in nucleotide sequence

Transversions:
purine-to-pyrimidine
pyrimidine-to-purine

RARE



Mutations – Inherited changes in nucleotide sequence

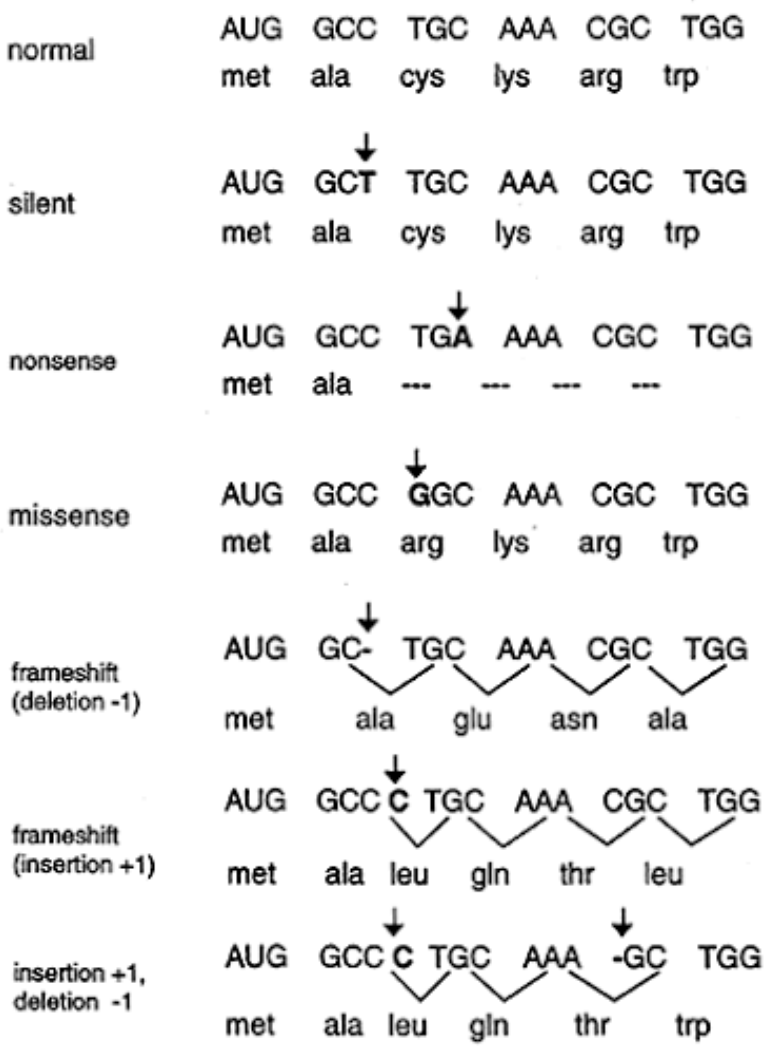


synonymous

nonsynonymous

nonsynonymous

Mutations – Inherited changes in nucleotide sequence

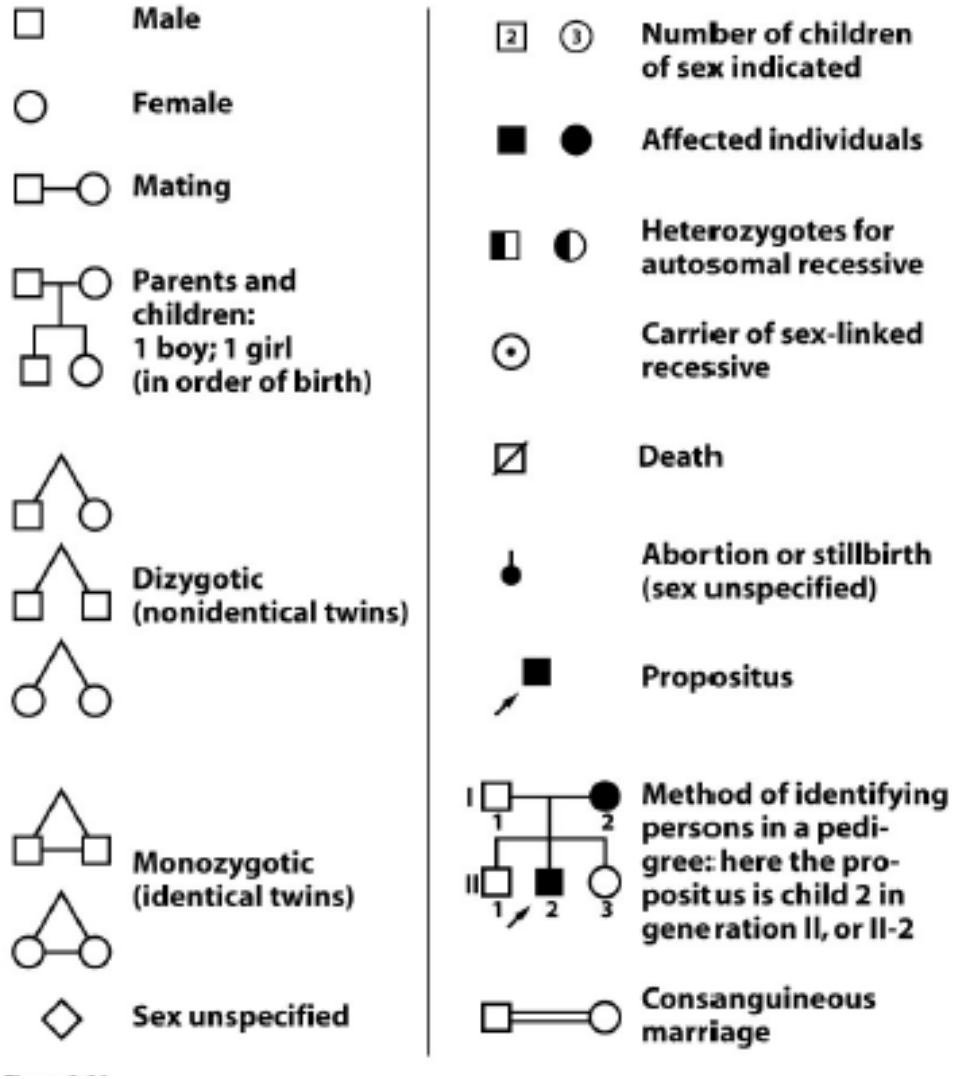


synonymous

nonsynonymous

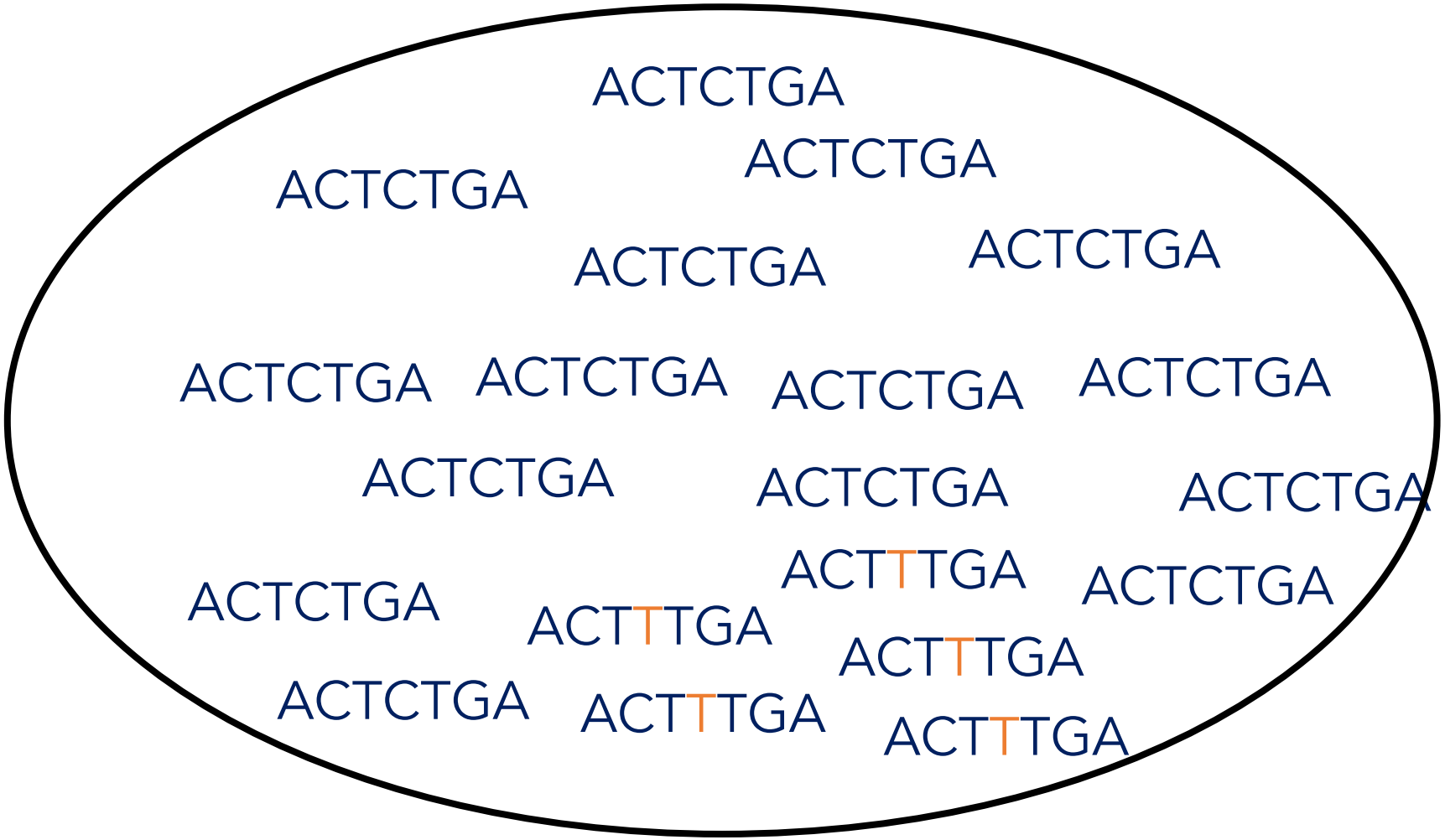
nonsynonymous

Pedigrees – genetic variation within families



Polymorphisms – genetic variation within species

Single Nucleotide Polymorphisms (SNPs)



C/T polymorphism

Single Nucleotide Polymorphisms (SNPs)

- Synonymous (sSNP) – SNP in coding region that does not have any effect on amino acid sequence

- Nonsynonymous SNP (nsSNP) – SNP in coding region that results in a different amino acid compared to the other allele

Hardy Weinberg Equilibrium

$1 = p + q$ TRUISM

$1 = p^2 + 2pq + q^2$ HWE Null Hypothesis

Hardy-Weinberg Equilibrium as null model

HWE Assumptions:

- Infinite population size
- No mutation
- No selection
- No migration/gene flow
- Random mating

$1 = p + q$ TRUISM

$1 = p^2 + 2pq + q^2$ HWE Null Hypothesis

Frequency of heterozygotes, given the frequency of alleles

Phylogenetic trees – genetic variation between species