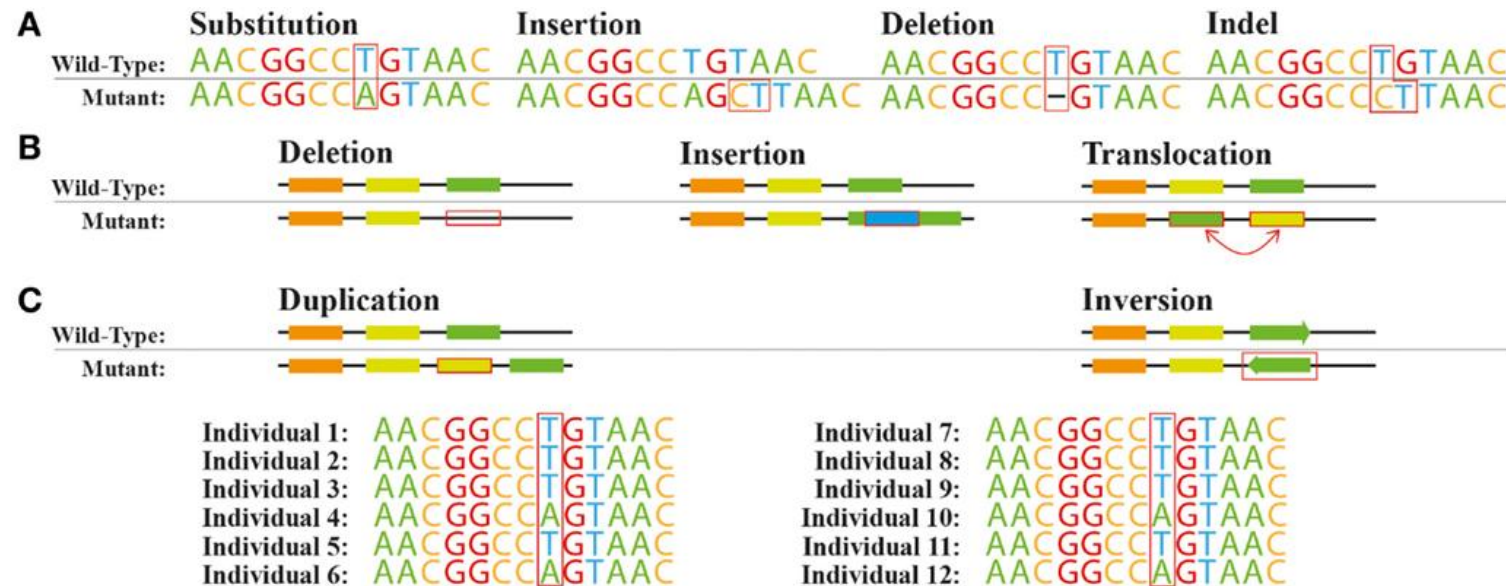# Molecular and evolutionary aspects of genetic variability
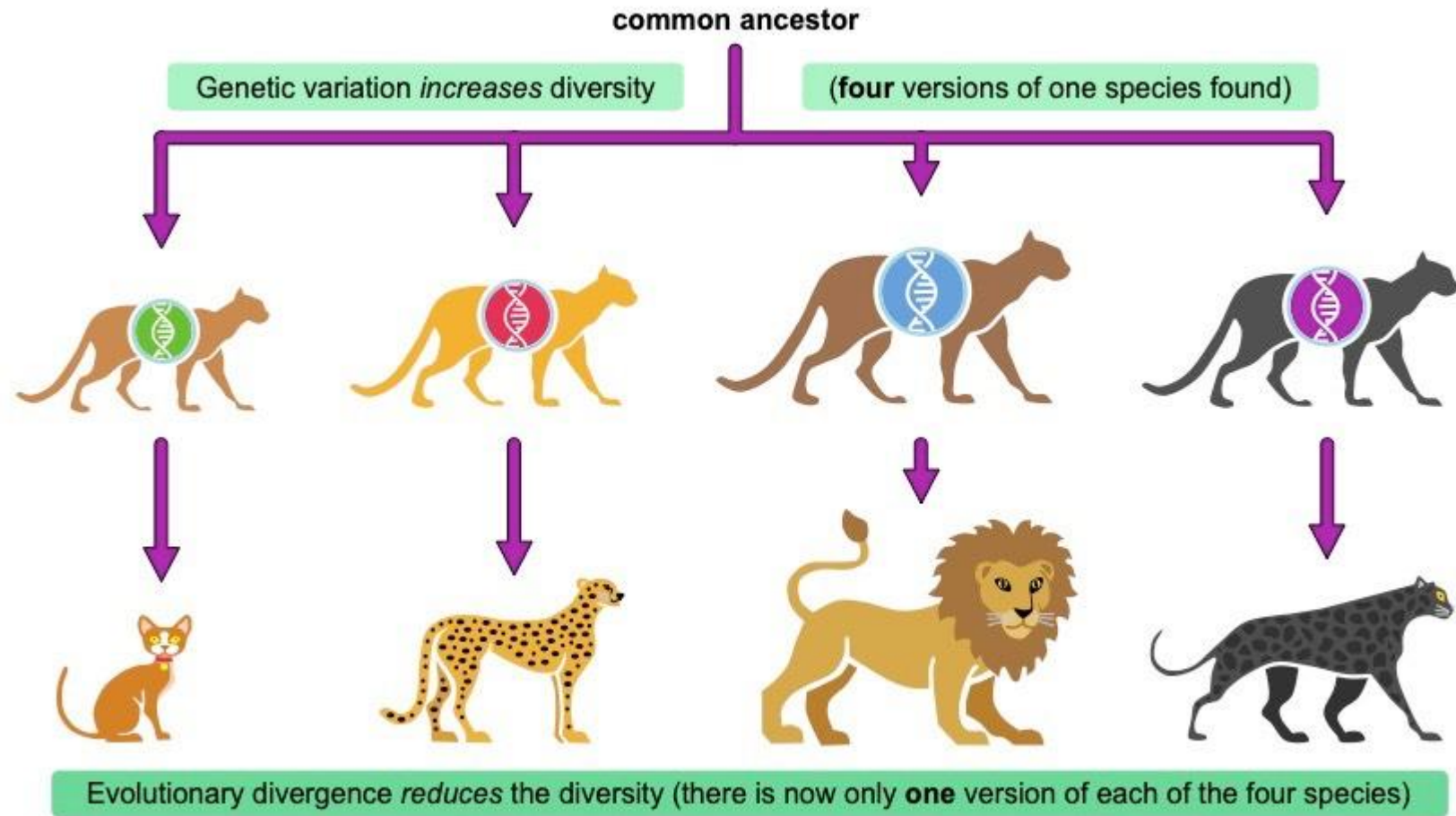

Peter DOVC

University of Ljubljana, Biotechnical Faculty

What is genetic variability?

- Genetic variability, the diversity in genetic makeup among individuals within a population, is the **fundamental raw material** for evolution, driven by molecular processes such as **mutations, gene flow**, and **sexual reproduction**.

- **Variations in DNA**, and consequently in RNA, and protein sequences, along with **alterations in gene expression** and **epigenetic modifications**, are caused by evolutionary forces like **natural selection** and **genetic drift**, and can ultimately lead to the development of new species and adaptations.

Genetic variation and diversity

common ancestor

Genetic variation *increases* diversity

(**four** versions of one species found)

Evolutionary divergence *reduces* the diversity (there is now only **one** version of each of the four species)

Eukaryotic gene structure

- Sense and anti-sense strand

- Exon-intron structure

- Intron splicing signals, intron phase and alternative splicing

- Evolution of introns

- 5'- UTRs (Cap structure G7-met)

- 3'- UTRs (polyadenylation signal)

Genome structure and organization
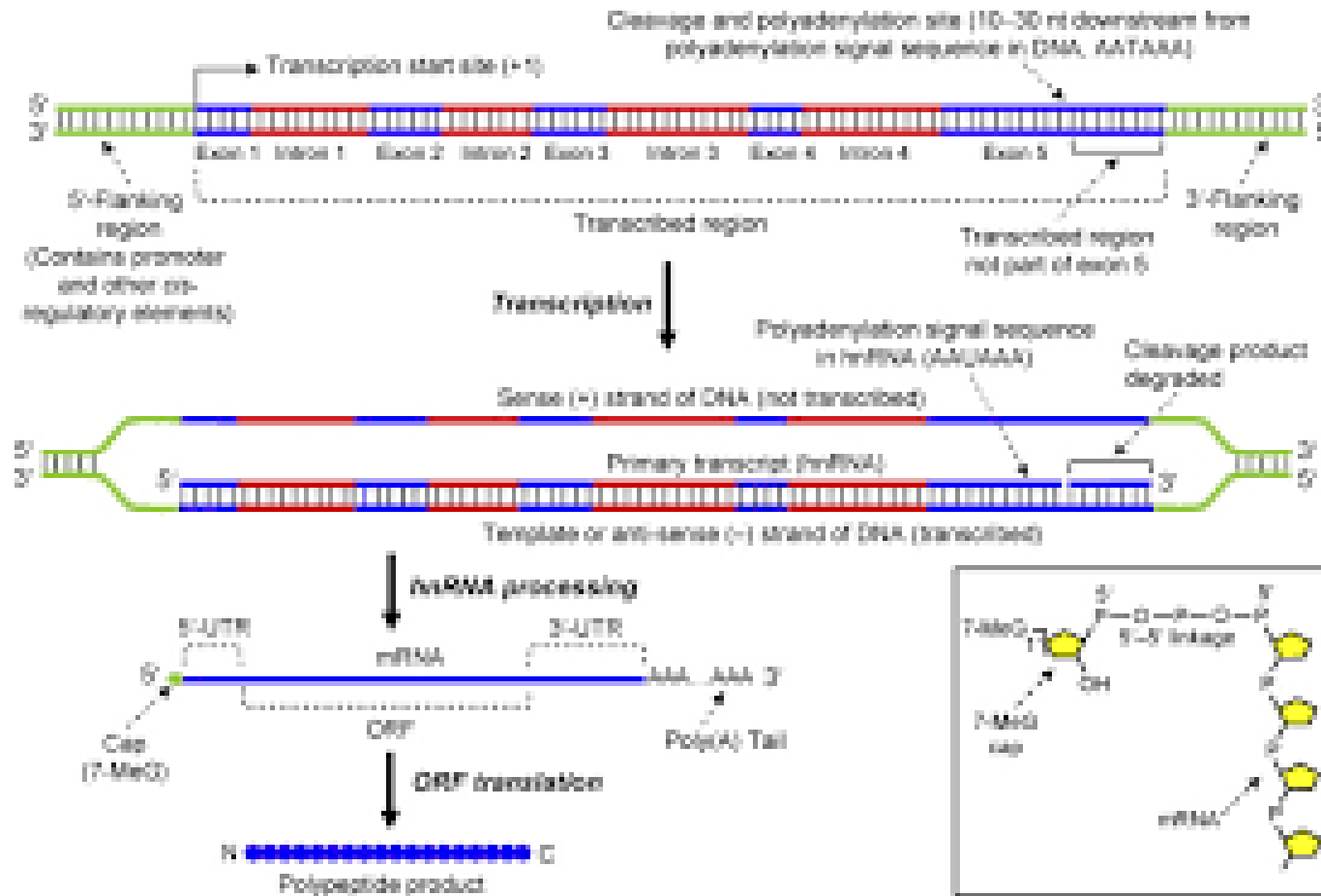
Regulation of gene expression through functional sequence elements

- Promoters

- Enhancers

- LCR (Locus Control Regions)

- Epigenetic modifications of the genome (DNA methylation, histone code)

Molecular basis of mutation

- Point mutations
- Recombinations

Other mechanisms generating genetic diversity

- Gene flow

- Origin of new genes from coding sequences
  - Gene duplication
  - 2R hypothesis
  - Unequal crossing over
  - Chromosomal duplication
  - Exon shuffling
  - Gene fusion and fission

- Origin of new genes from noncoding sequences (*de novo*)

Factors affecting allele frequency in the population
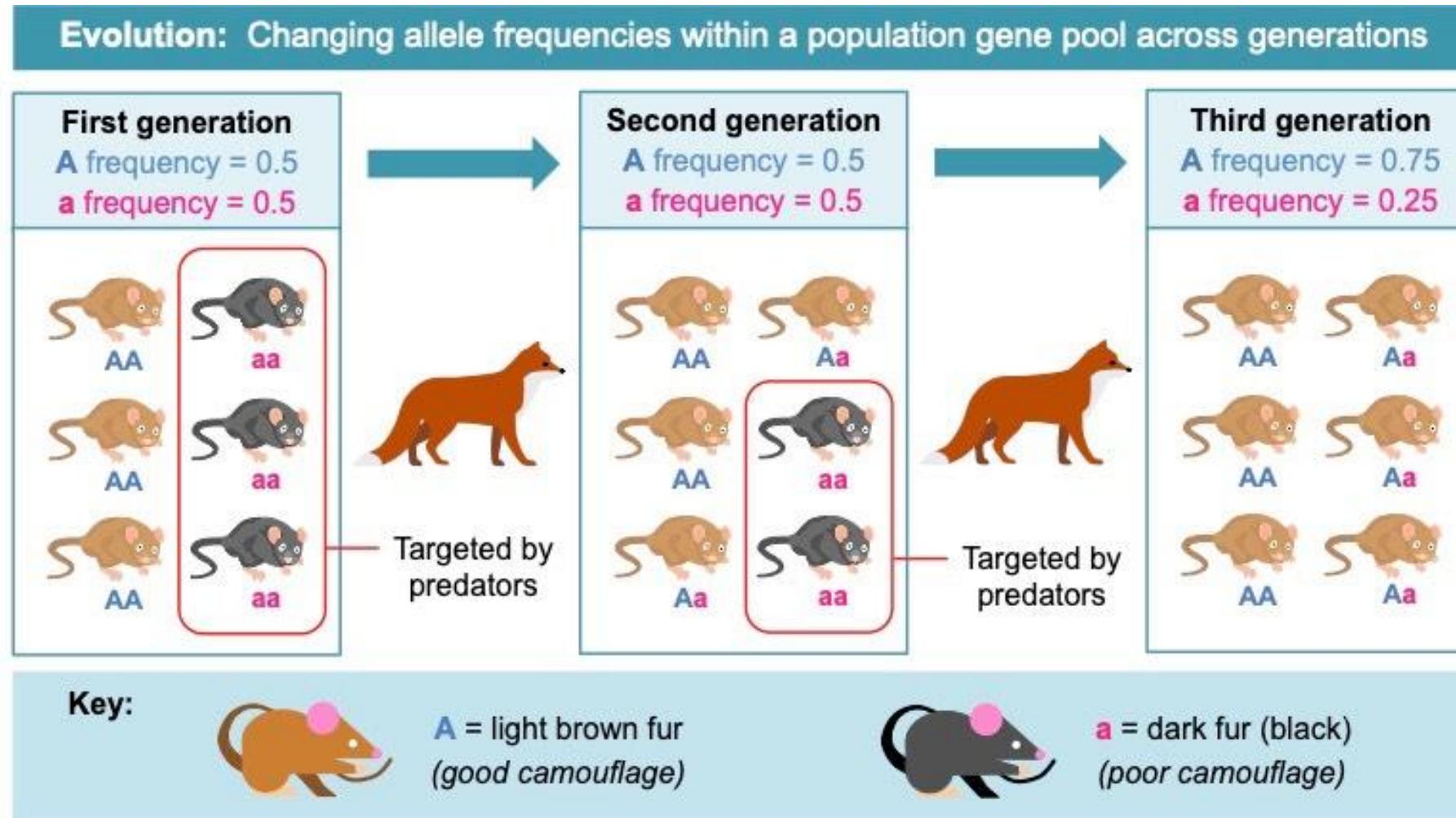
- Mutation

- Migration (gene flow)

- Natural selection

- Genetic drift

- Inbreeding

Example of natural selection

Figure 19-10
Introduction to Genetic Analysis, Ninth Edition
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Figure 19-11
Introduction to Genetic Analysis, Ninth Edition
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Example of natural selection
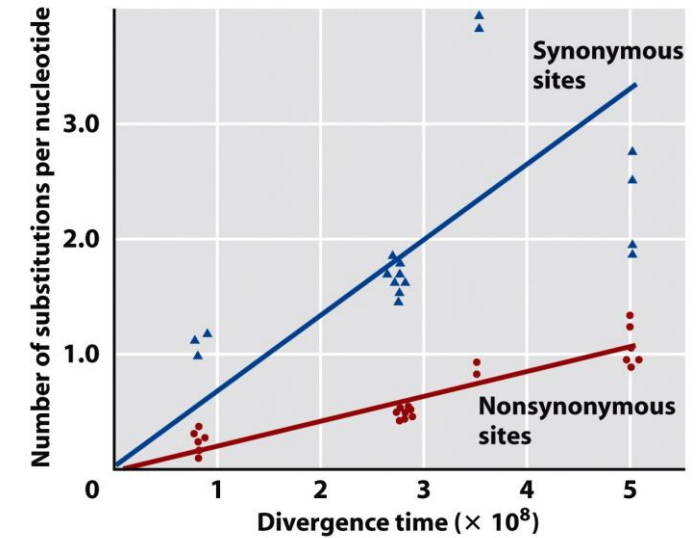
The neutral theory of evolution

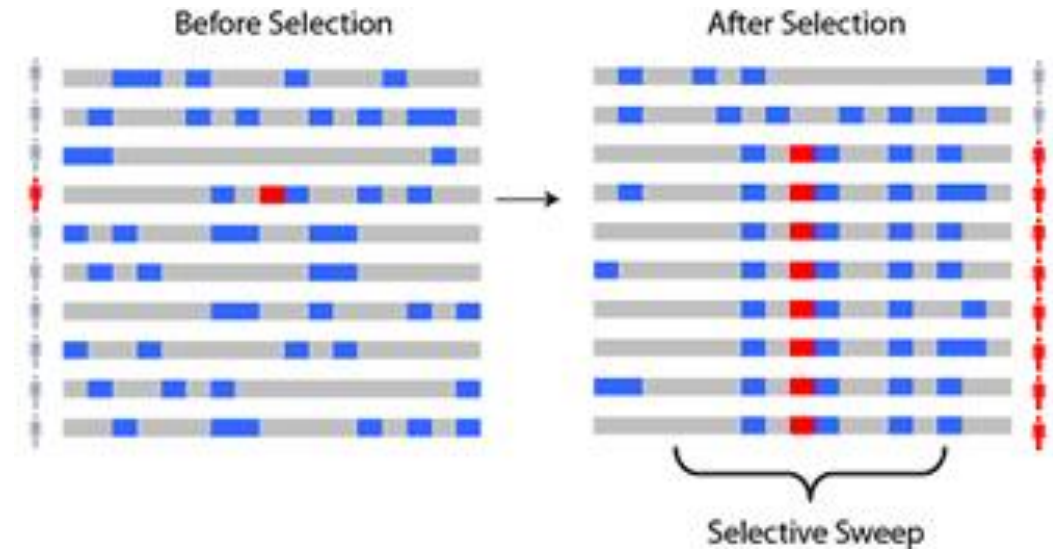- Synonymous and nonsynonymous substitutions

Figure 19-8
Introduction to Genetic Analysis, Ninth Edition
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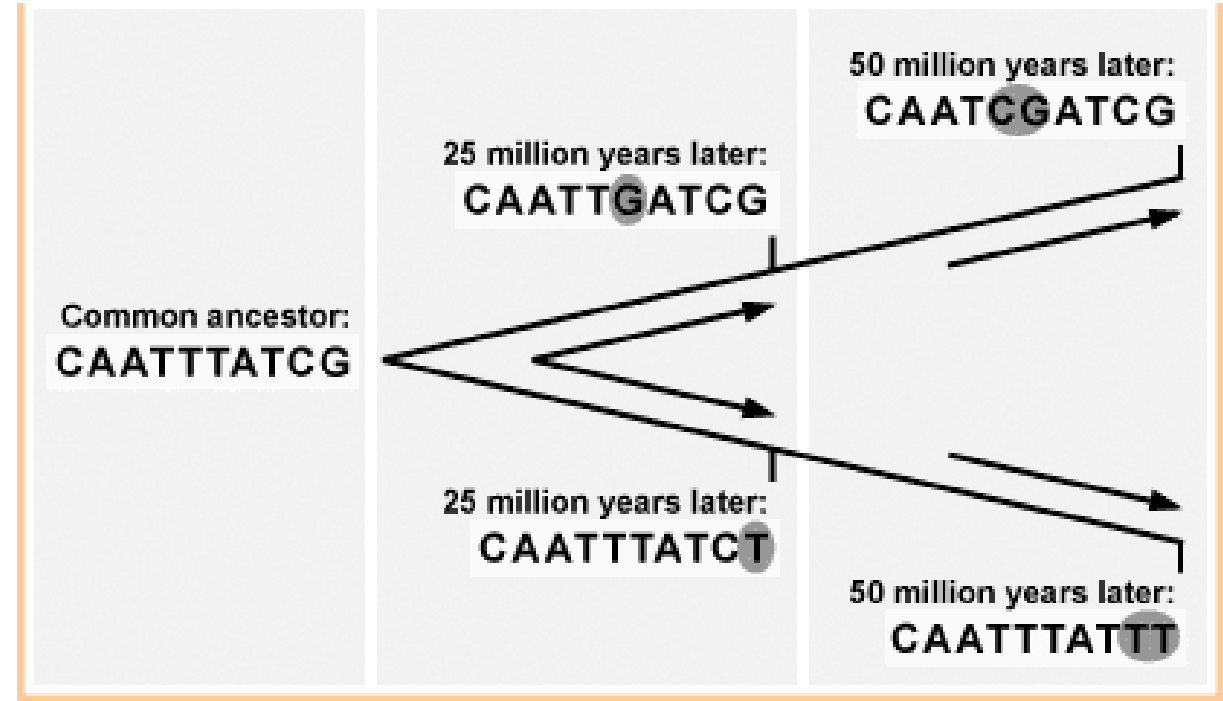- Signatures of positive selection
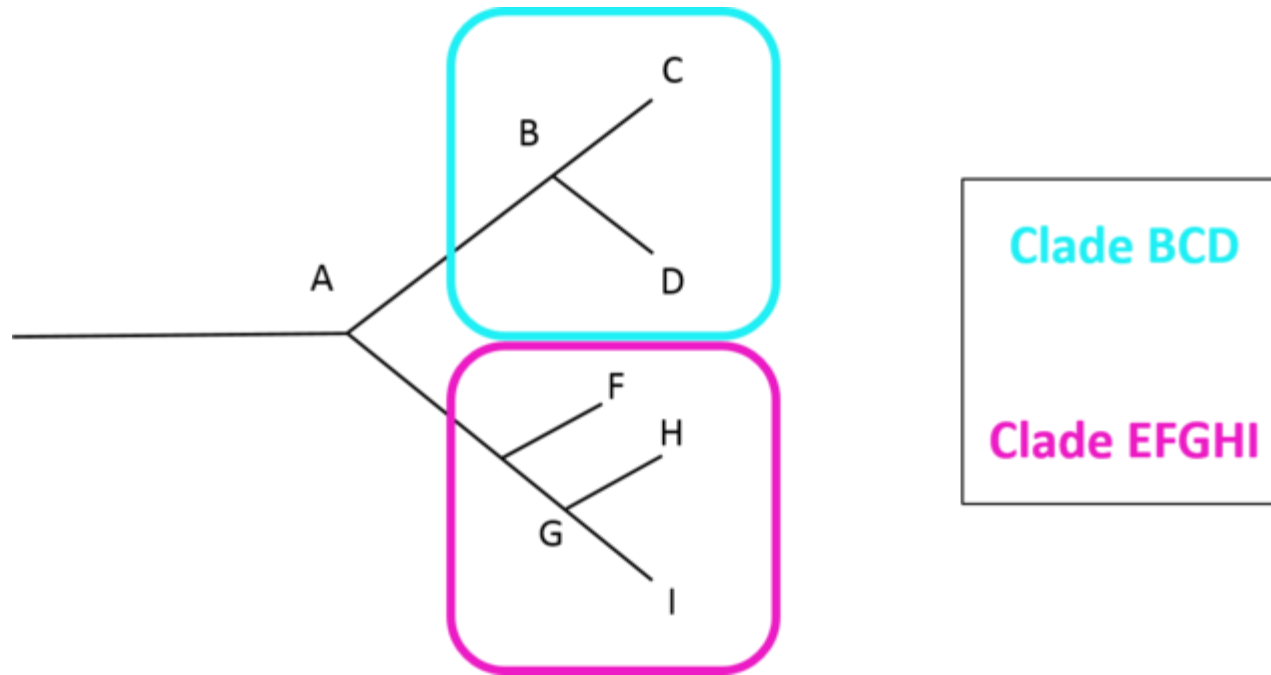
Molecular clock hypothesis

All the mutations occur in the same rate in all the taxa of a tree

The rate of mutations is the same for all positions along the sequence

The molecular clock hypothesis is most suitable for closely related taxa
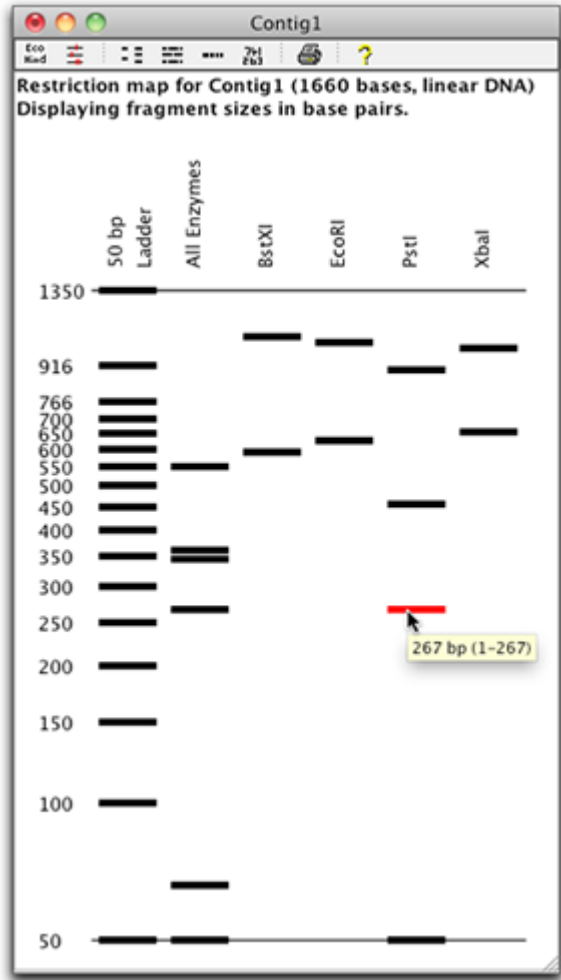
Molecular phylogenetics

Genetic markers (their background, character - affecting evaluation, detection technology)

- Different types of variation
- Dominant and co-dominant markers
- Direct detection, hybridisation

Genomic technologies

- Restriction analysis

- Short tandem repeats (microsatellites)

- Sanger sequencing

- Pyrosequencing

- SNP genotyping
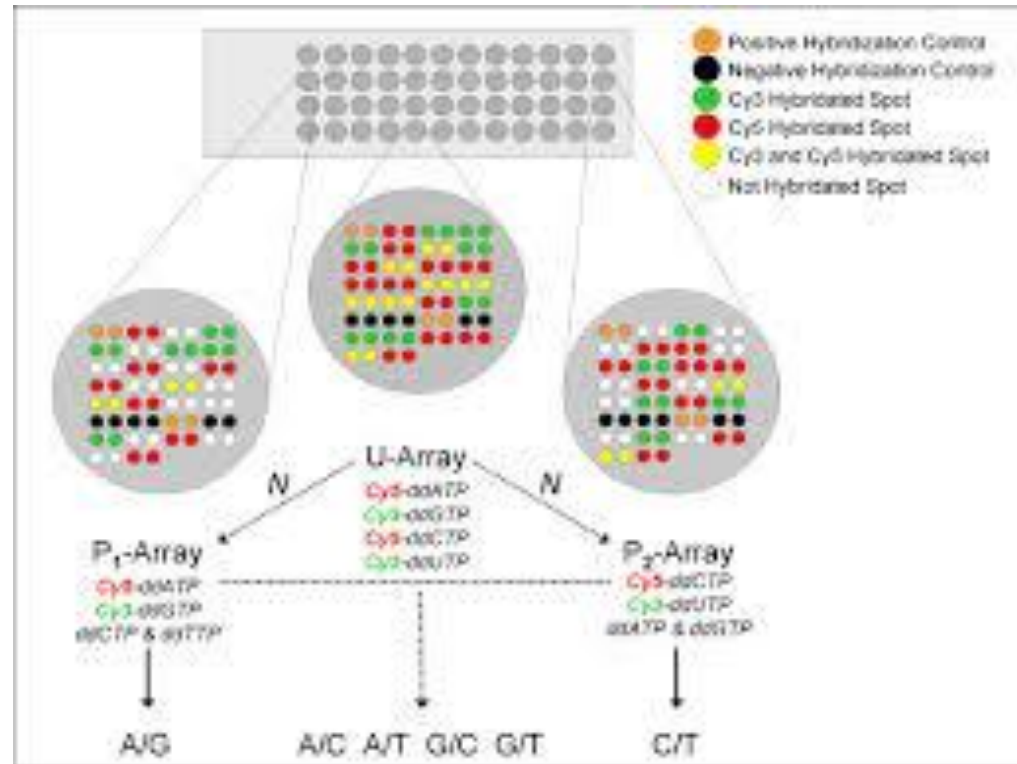
- NGS (Roche 454, Illumina Solexa, ABI SOLiD)
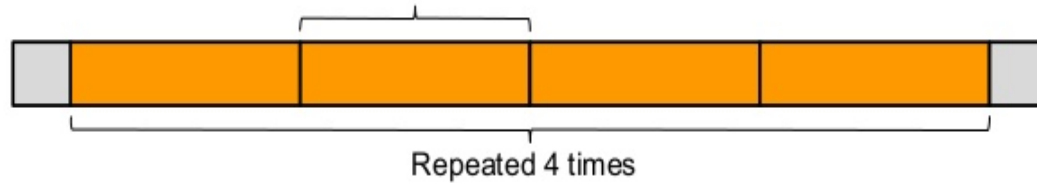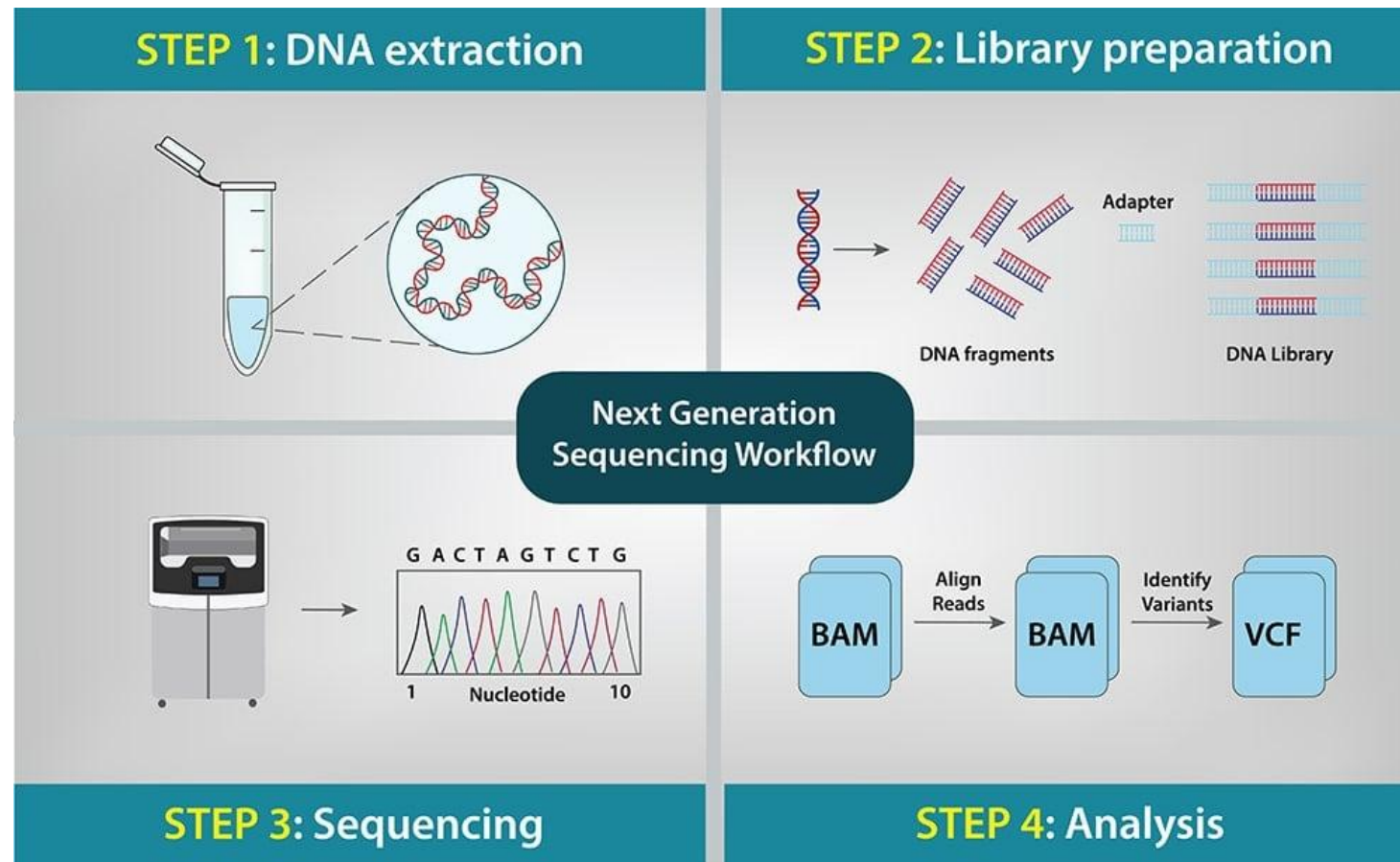
- Tiling Arrays

- Optical mapping

Restriction analysis and STRs

Tandem Repeat elements

Minisatellite: Variable Number Tandem Repeats (VNTR)
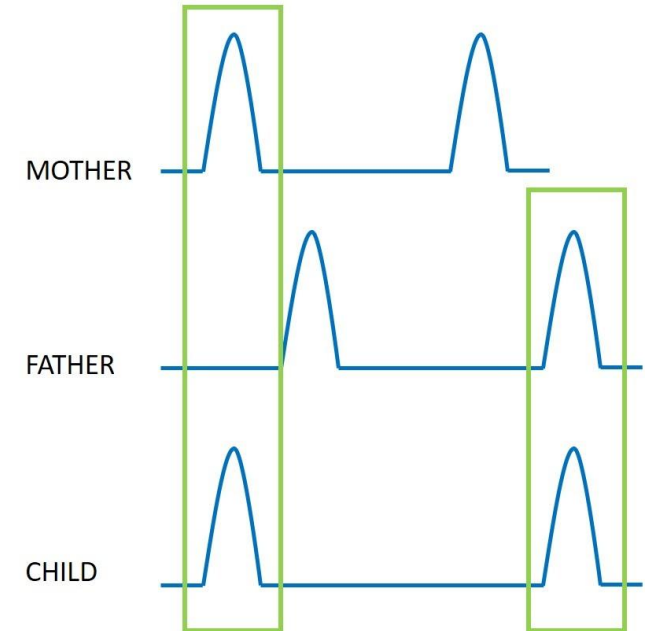
Repeat unit size = hundreds base pairs

Repeated 4 times

Microsatellite: Short Tandem Repeats (STR) – Simple Sequence Repeats (SSR)
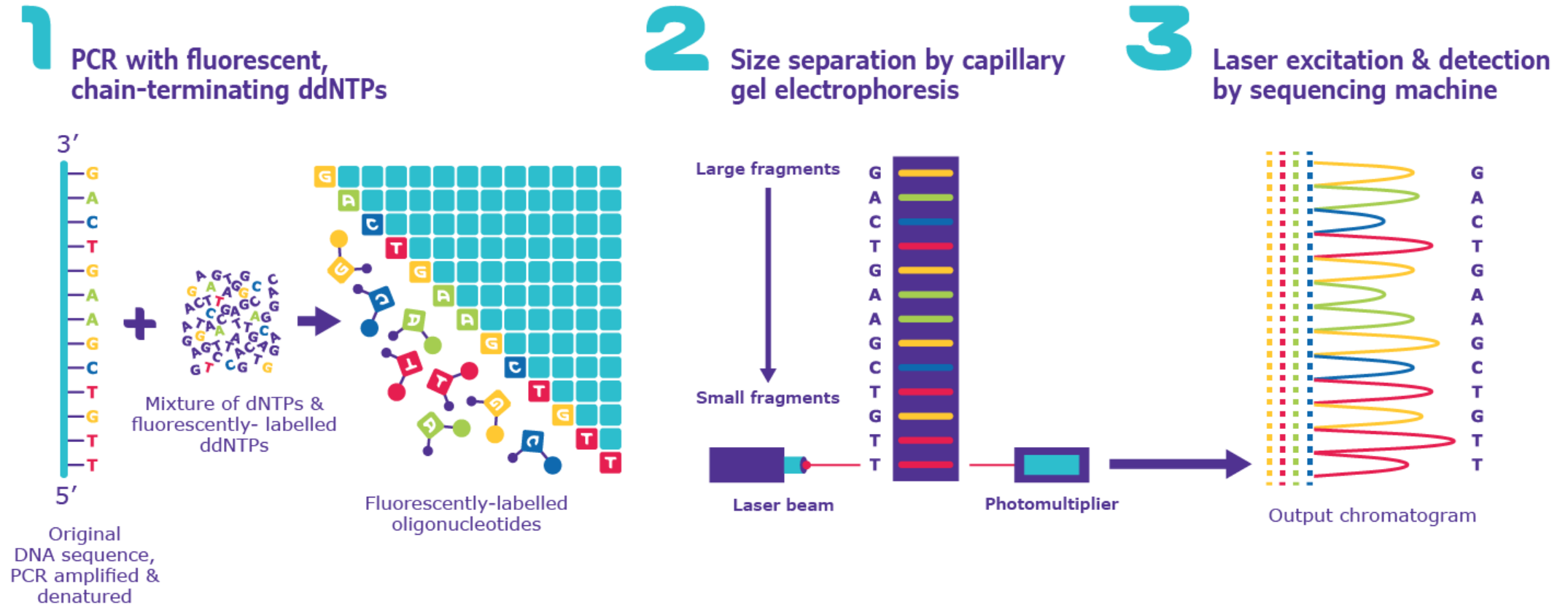
Repeat unit size = 2 - 6 base pairs

Repeated 8 times   Repeated 20 times
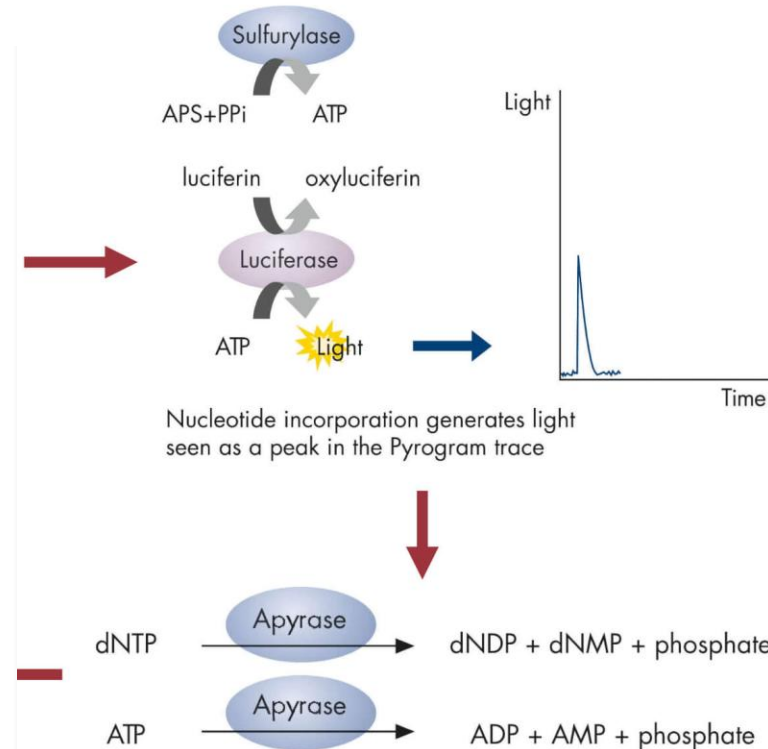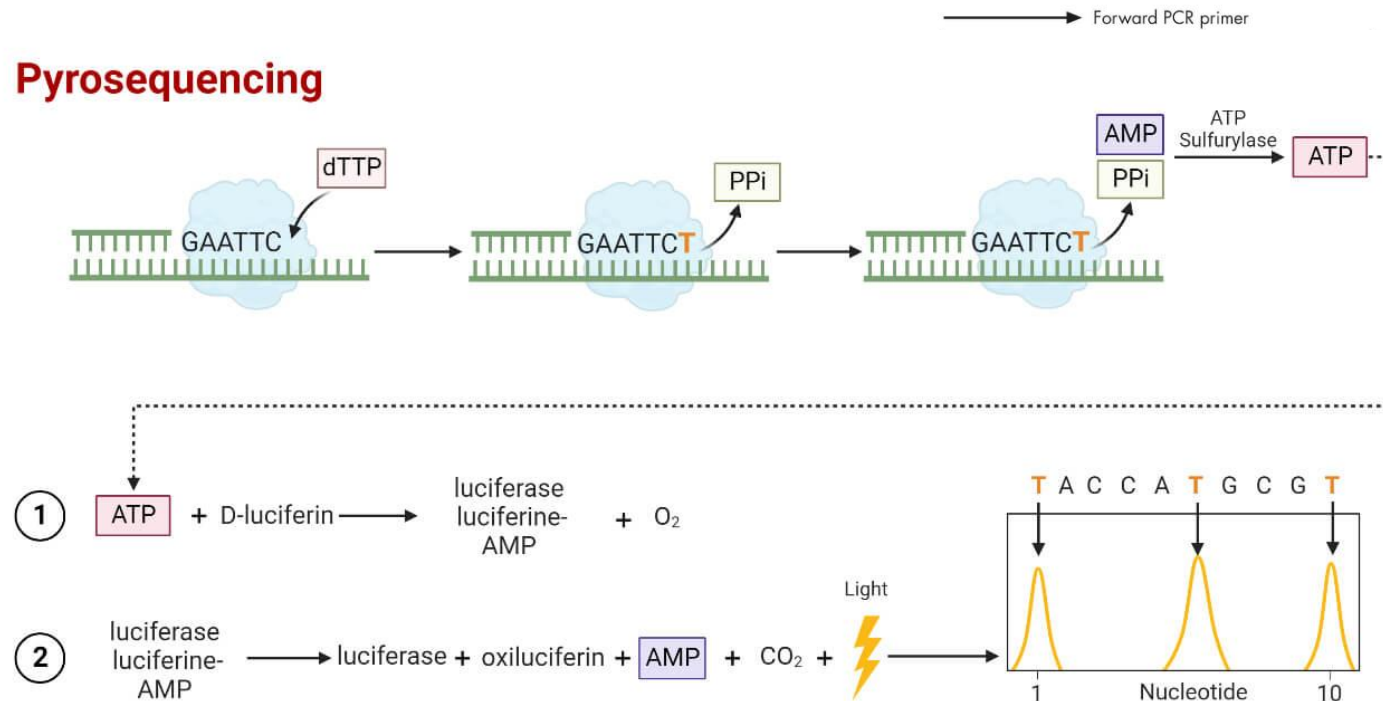
HAGenetics.org

MICROSATELLITES

MOTHER

FATHER

CHILD

Sanger sequencing

Pyrosequencing

SNP genotyping

NGS (Roche 454, Illumina Solexa, ABI SOLiD)

Tiling arrays

genomic DNA

partially overlapping probes

genomic DNA

non-overlapping probes

Optical mapping

Isolate long DNA molecules (solid tissue, blood, cell lines)

Fluorescently tag DNA at specific sequence motifs (avg every 6kb)

Pass DNA through nanochannels to linearize and separate single molecules

Continuous cycling of DNA through chip and imaging of single molecules

- Thank you for your attention!

Questions?