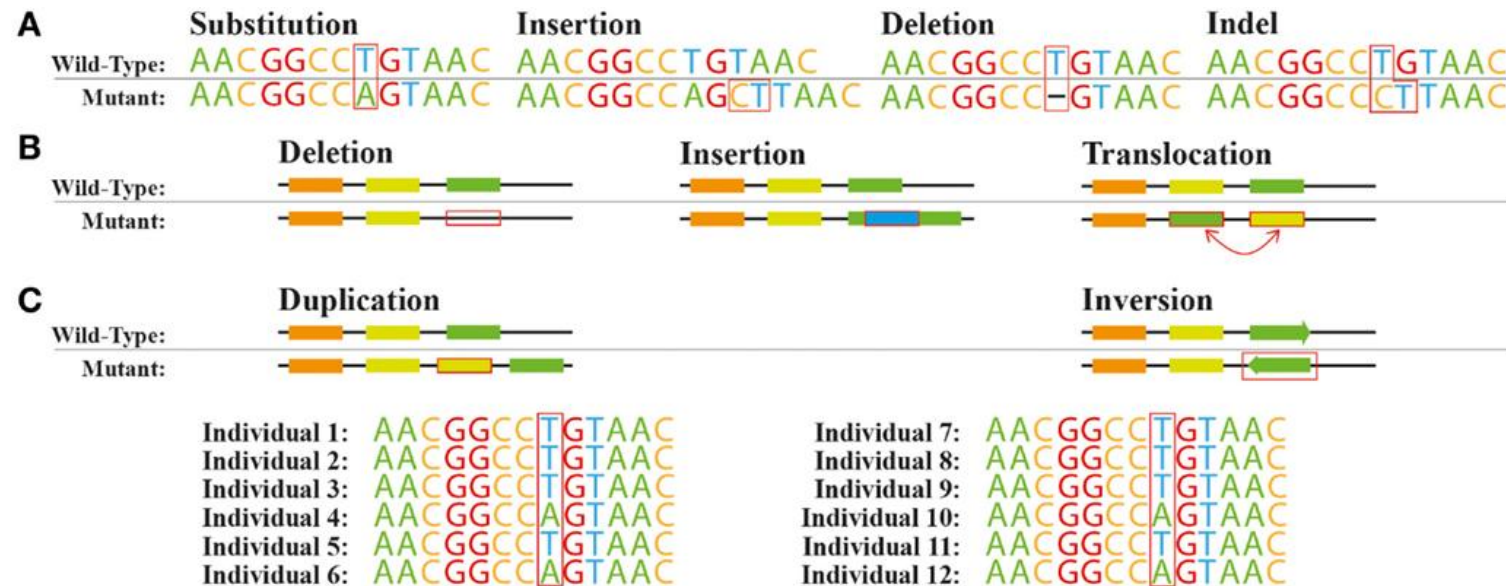# Molecular and evolutionary aspects of genetic variability
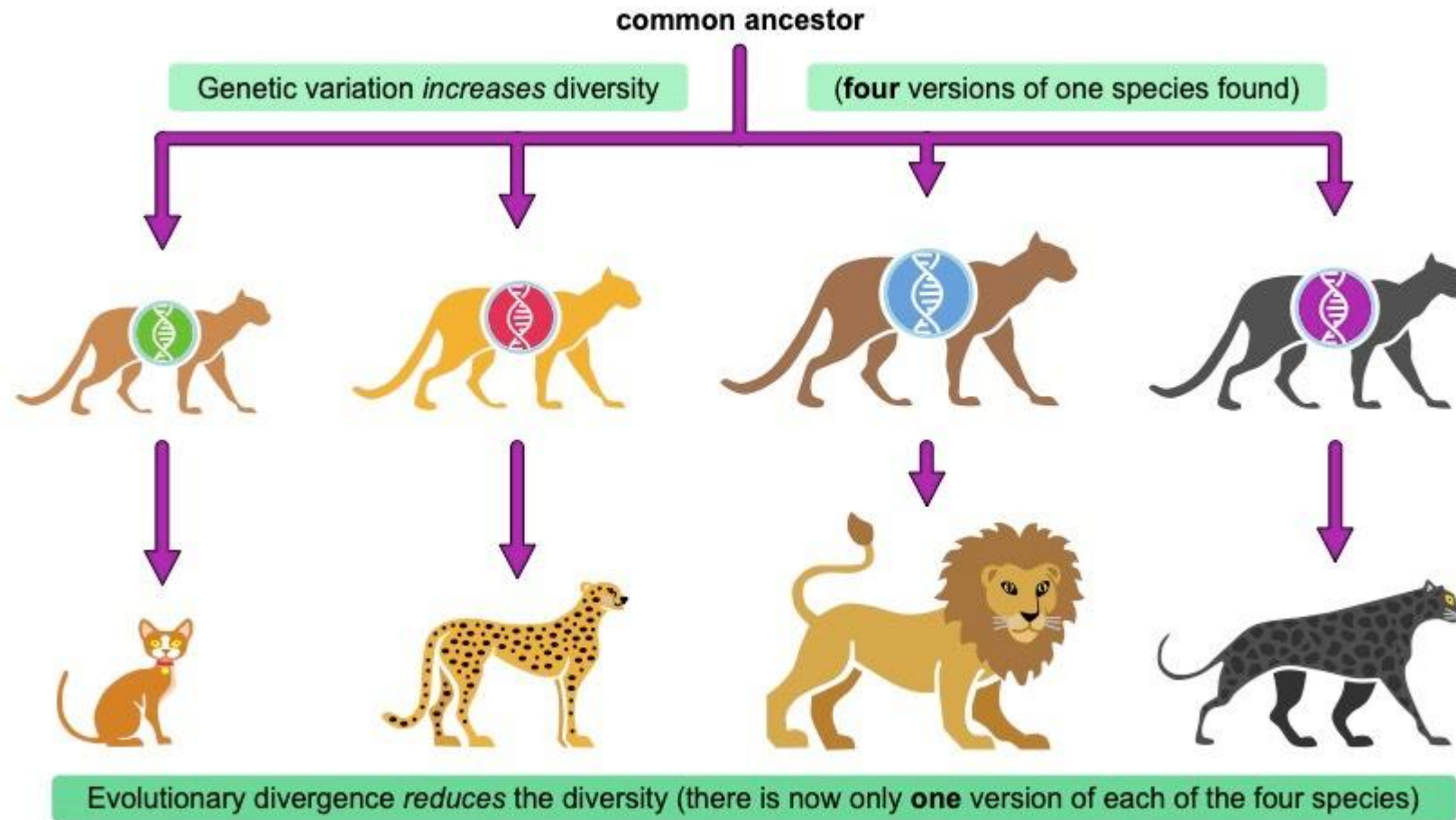

Peter DOVC

University of Ljubljana, Biotechnical Faculty
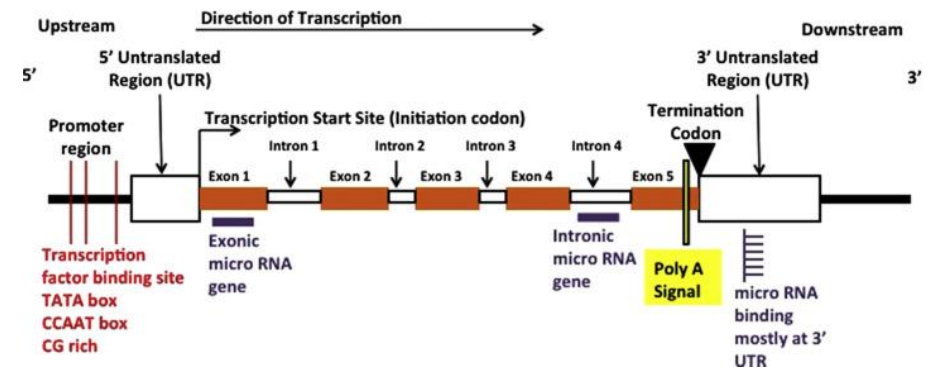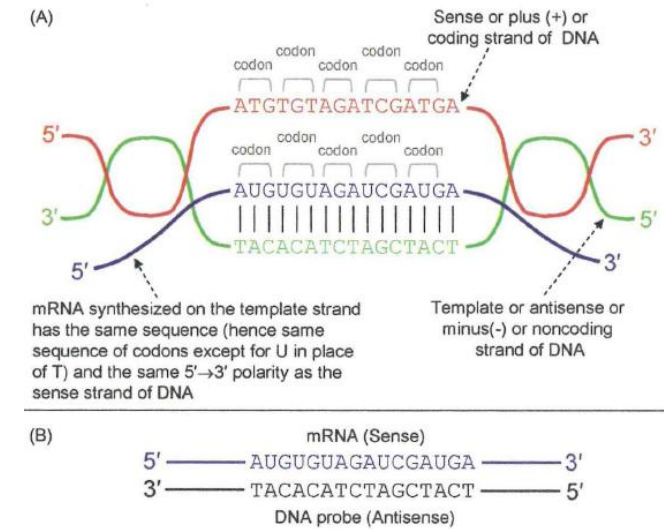
What is genetic variability?

- 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

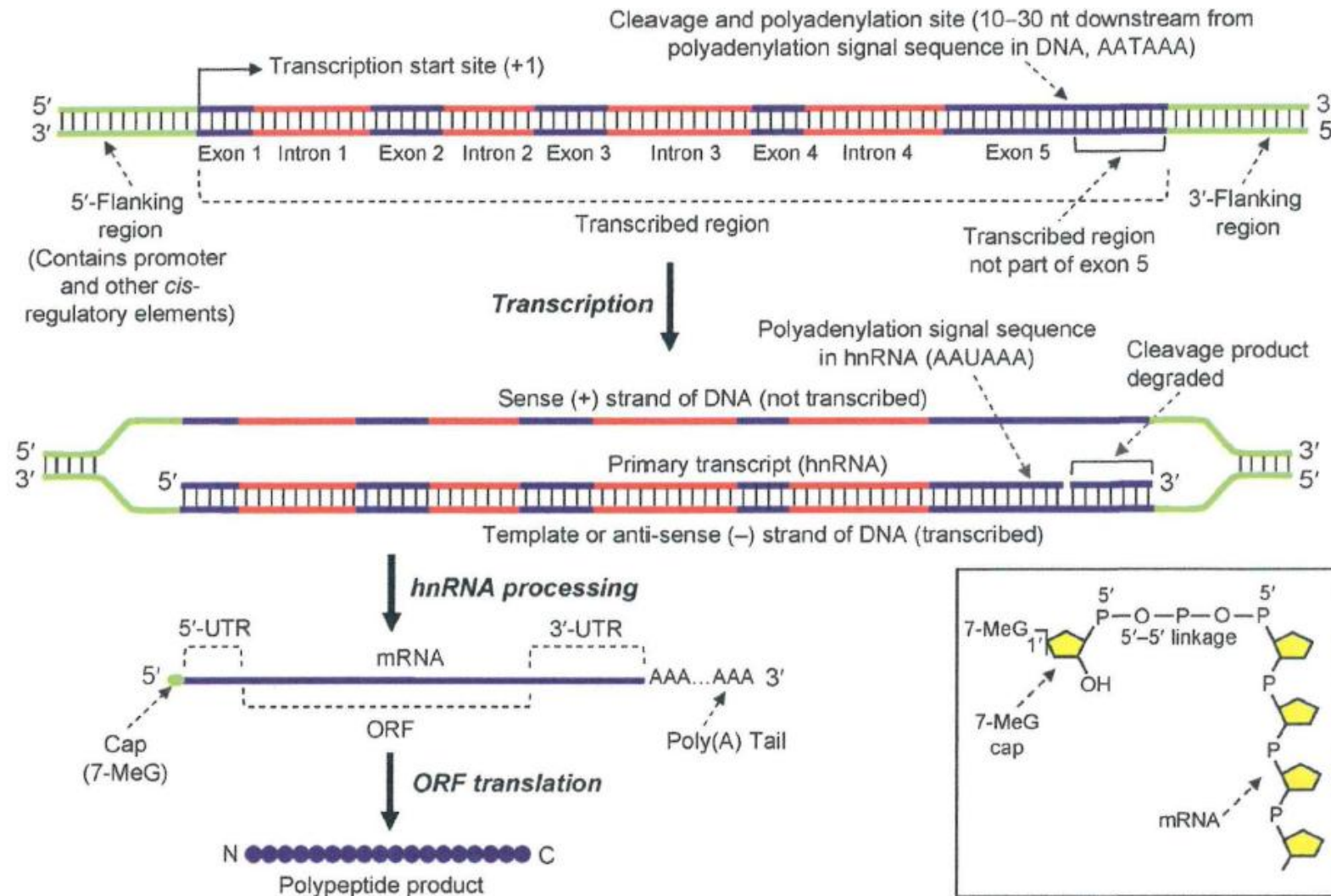- Sense and anti-sense strand

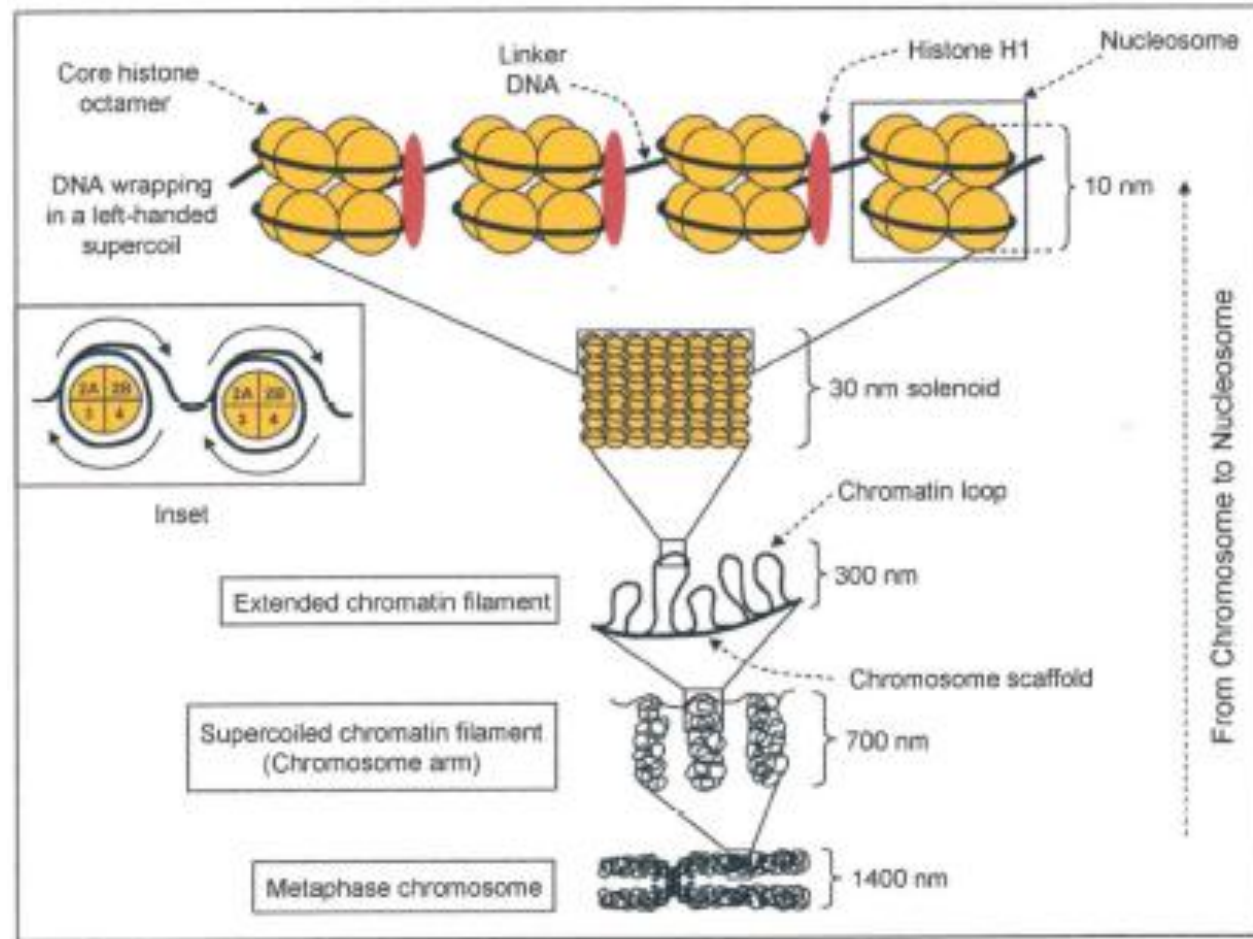- Exon-intron structure

Eukaryotic gene structure

- Intron splicing signals, intron phase and alternative splicing
- Evolution of introns
- 5'- UTRs (Cap structure G7-met)
- 3'- UTRs (polyadenylation signal)
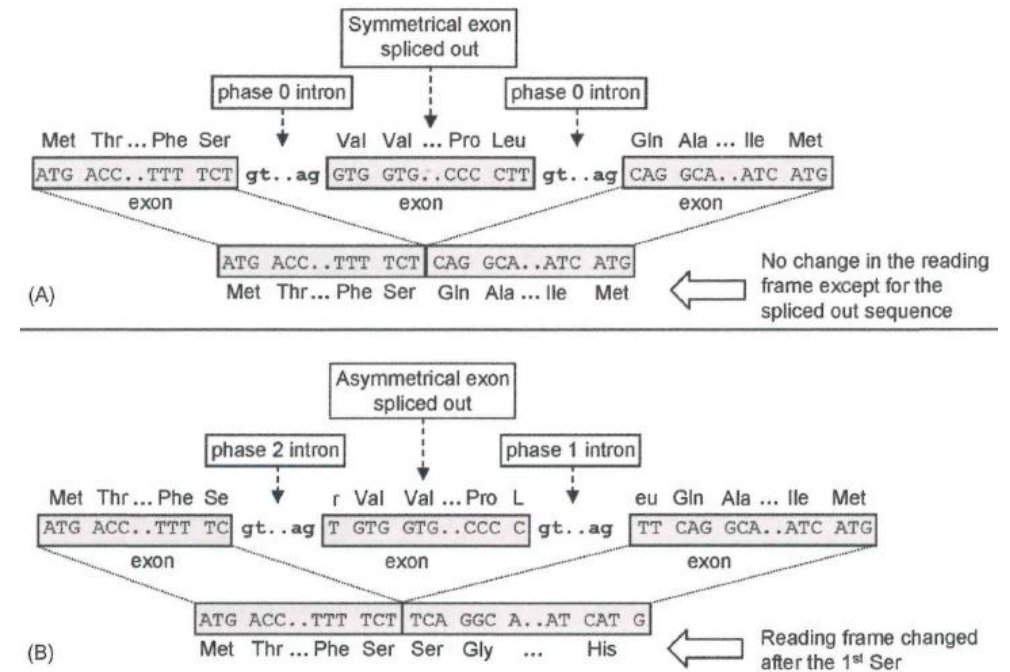
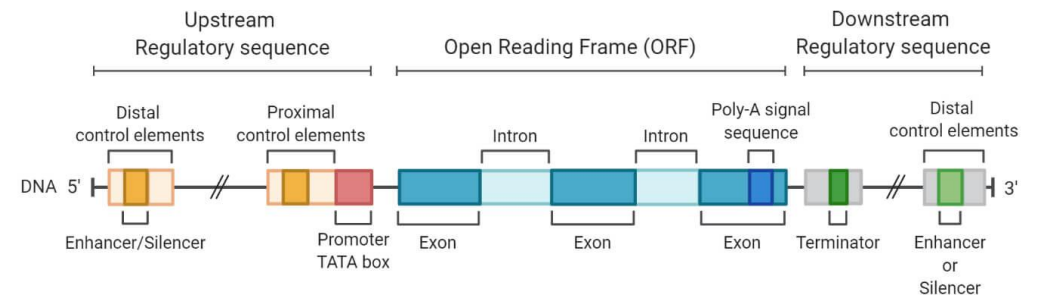# Genome structure and organization

Genome structure and organization

Regulation of gene expression through functional sequence elements
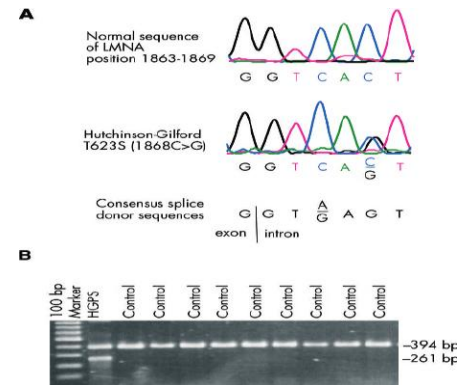
- Promoters

- Enhancers

- LCR (Locus Control Regions)

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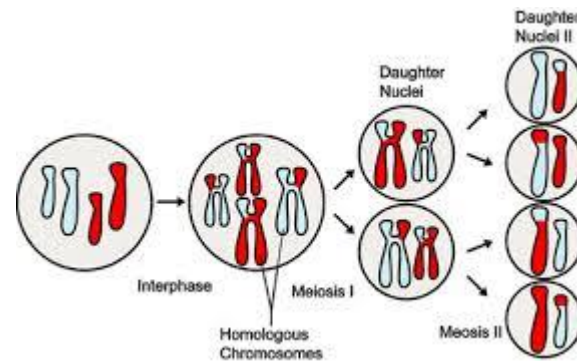

Eukaryotic Gene Structure

Molecular basis of mutation

- Point mutations

- Recombinations

Other mechanisms generating genetic diversity

- Gene flow (vertical and horizontal)
- 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
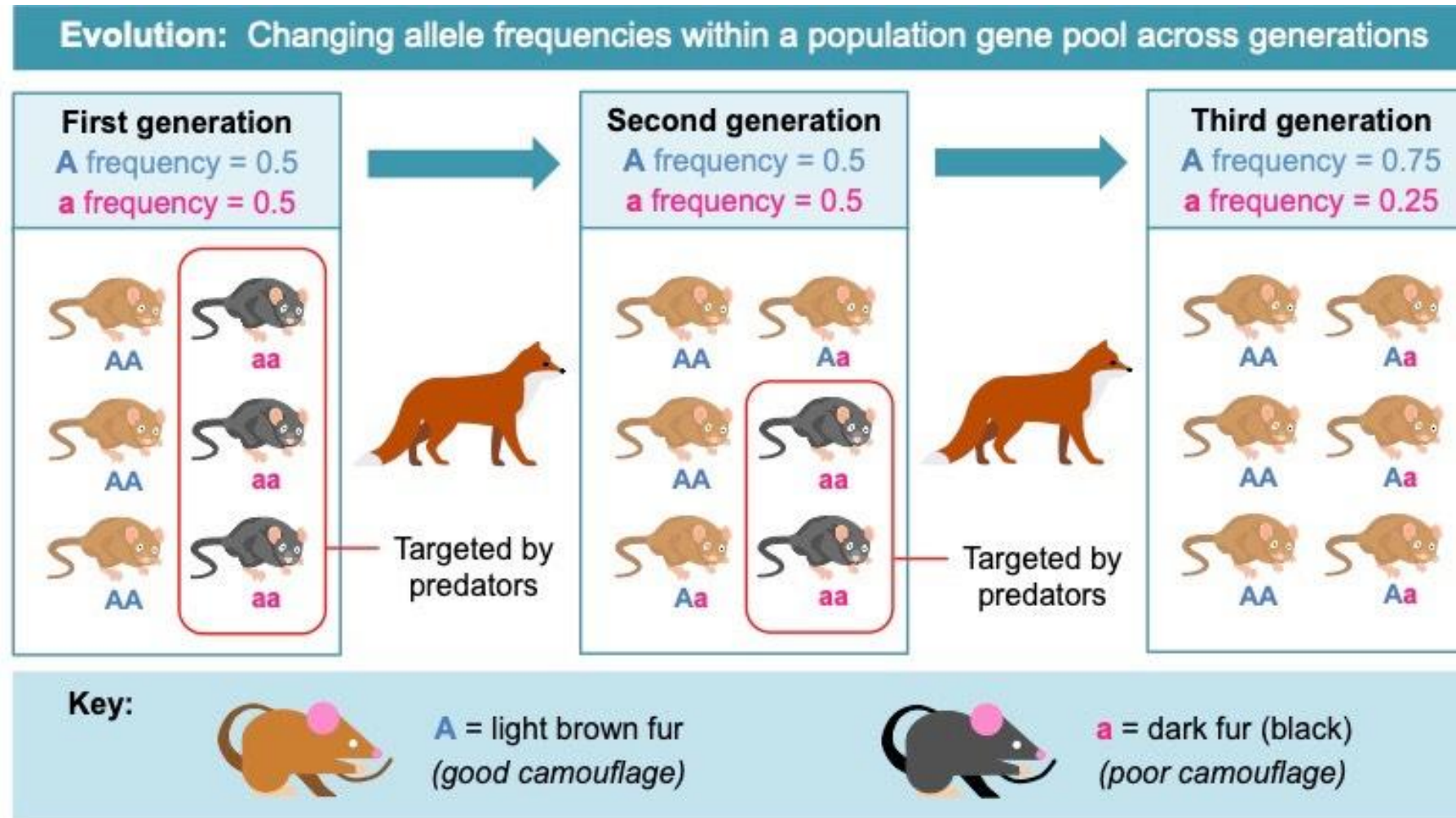
- Genetic drift

- Inbreeding
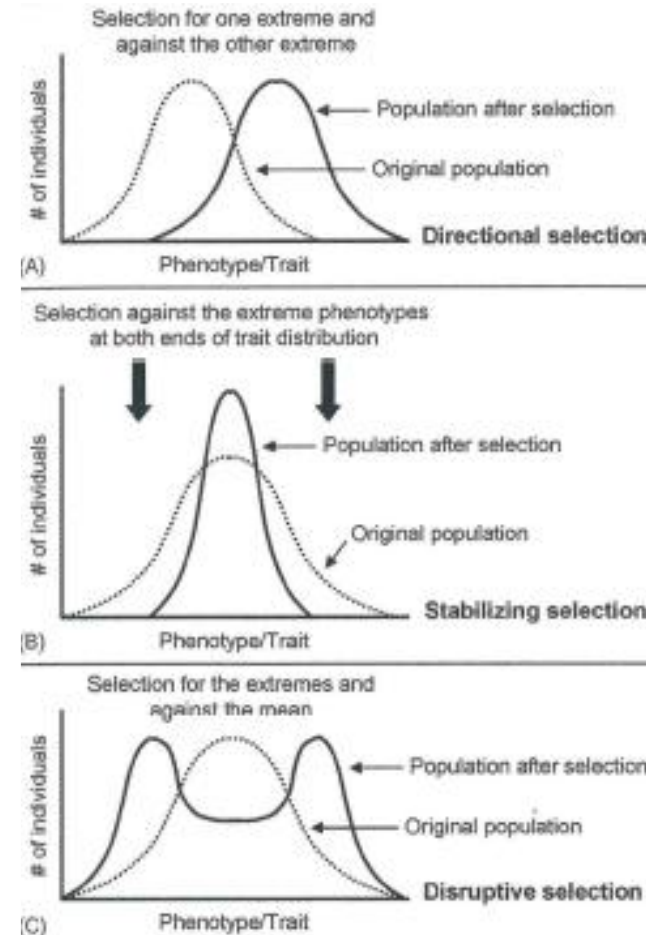
Example of natural selection

Figure 19-10
Introduction to Genetic Analysis, Ninth Edition
© 2008 W. H. Freeman and Company

Figure 19-11
Introduction to Genetic Analysis, Ninth Edition
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Example of natural selection

Evolution: Changing allele frequencies within a population gene pool across generations

First generation
A frequency = 0.5
a frequency = 0.5

Second generation
A frequency = 0.5
a frequency = 0.5

Third generation
A frequency = 0.75
a frequency = 0.25

Targeted by predators

Targeted by predators

Key:
A = light brown fur (good camouflage)
a = dark fur (black) (poor camouflage)

The neutral theory of evolution

- Synonymous and nonsynonymous substitutions
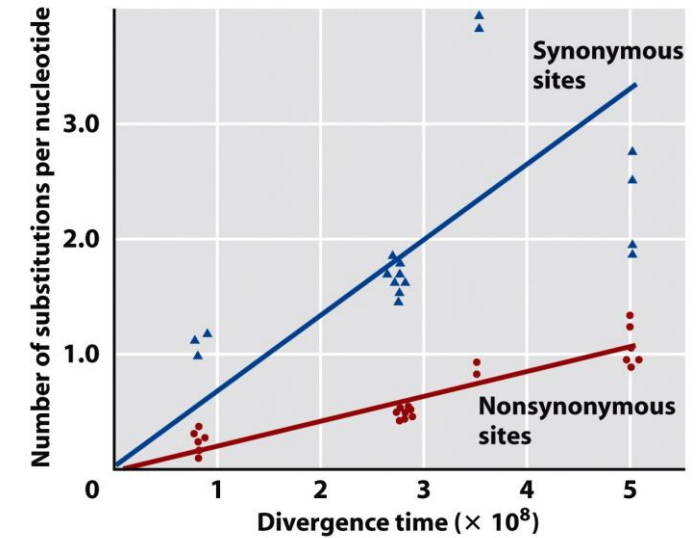
Figure 19-8
Introduction to Genetic Analysis, Ninth Edition
© 2008 W. H. Freeman and Company
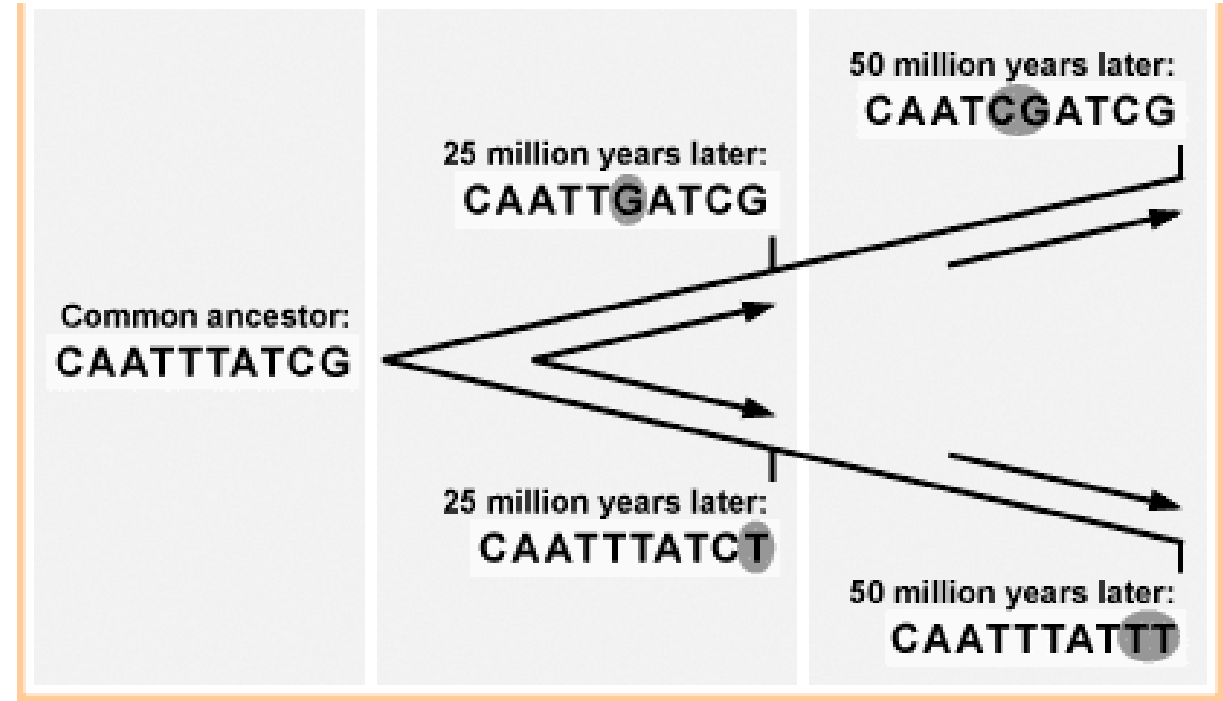
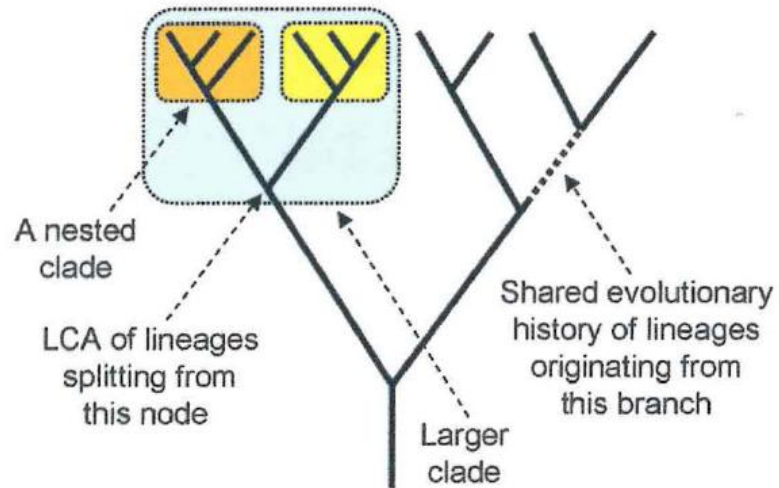- Signatures of positive selection
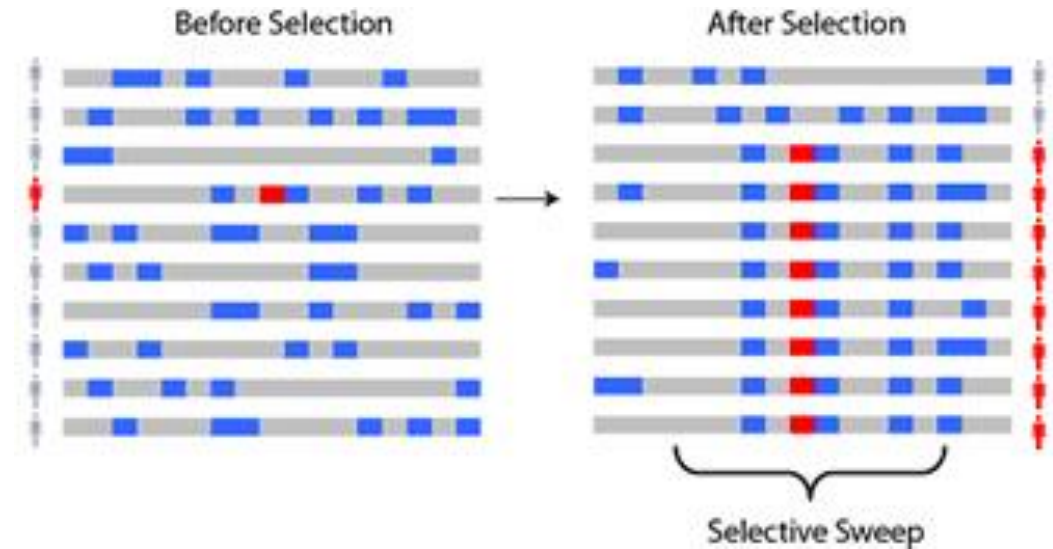
Molecular clock hypothesis

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

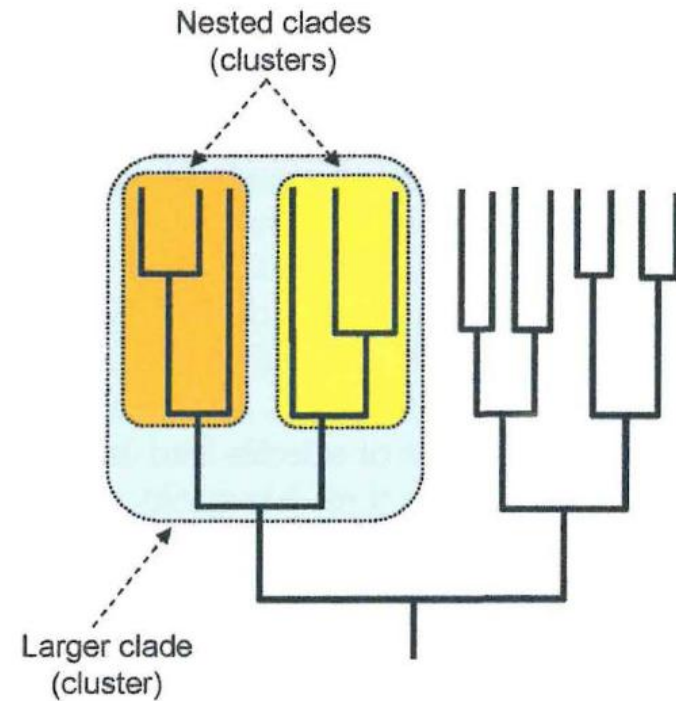The rate of mutations is the same for all positions along the sequence

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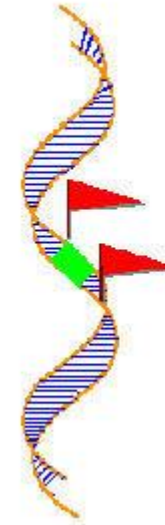
Molecular phylogenetics

Cladogram

Dendrogram

Genetic markers

- Different types of variation
- SNP, VNTR

- Dominant and co-dominant markers
- Mini- and micro-satellites

- Detection method
  - Direct detection
   - Restriction
    - DNA synthesis
  - Hybridisation

GENETIC MARKERS

"The green section indicates the presence of a desirable gene in an organisms' genetic code that is associated with two genetic markers (red flags)."

Genomic technologies

- Restriction analysis
- Short tandem repeats (microsatellites)
- Sanger sequencing
- Pyrosequencing
- SNP genotyping
- NGS (Roche 454, Illumina Solexa, ABI SOLiD)
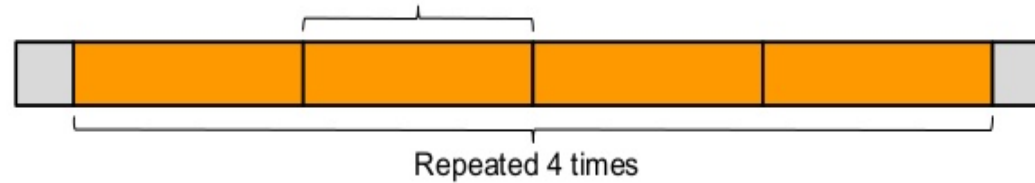- Tiling Arrays
- Optical mapping

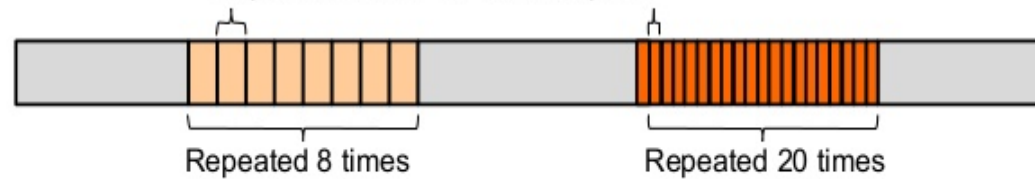# Restriction analysis, VNTRs and STRs
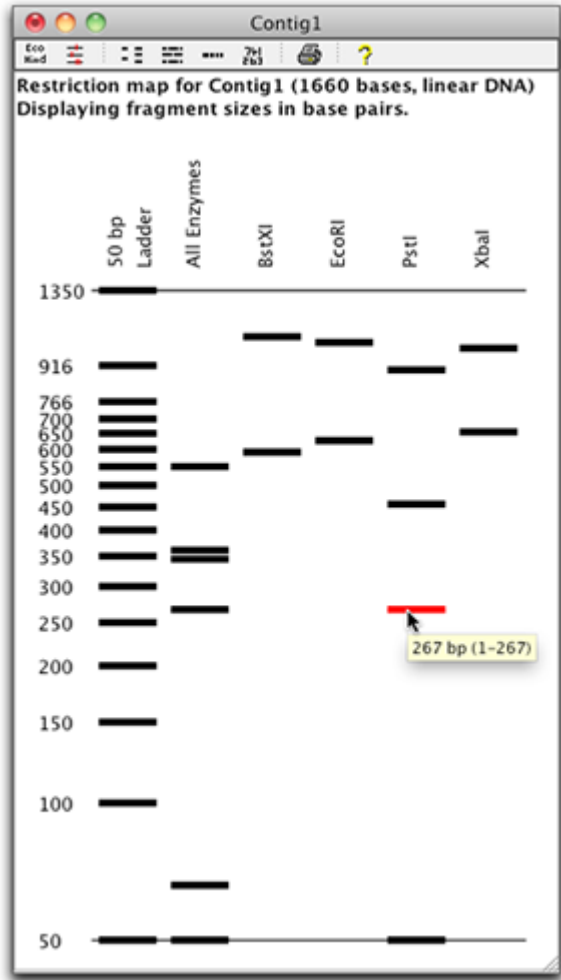
Tandem Repeat elements

Minisatellite: Variable Number Tandem Repeats (VNTR)

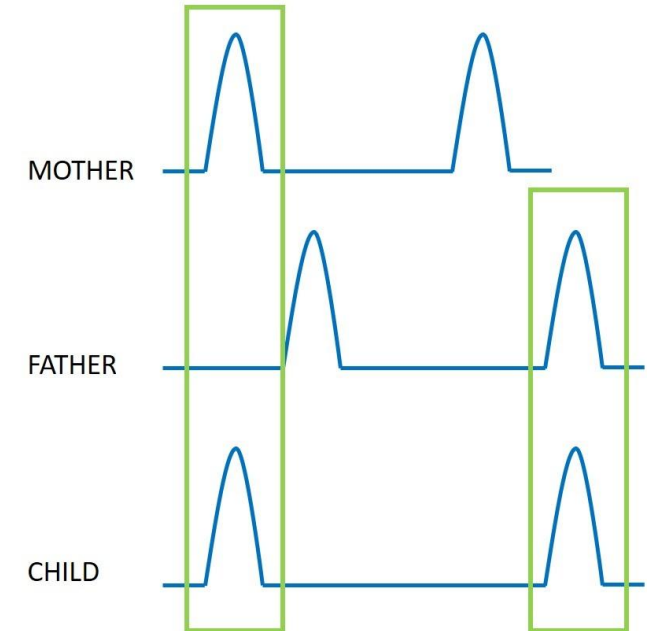Repeat unit size = hundreds base pairs

Repeated 4 times

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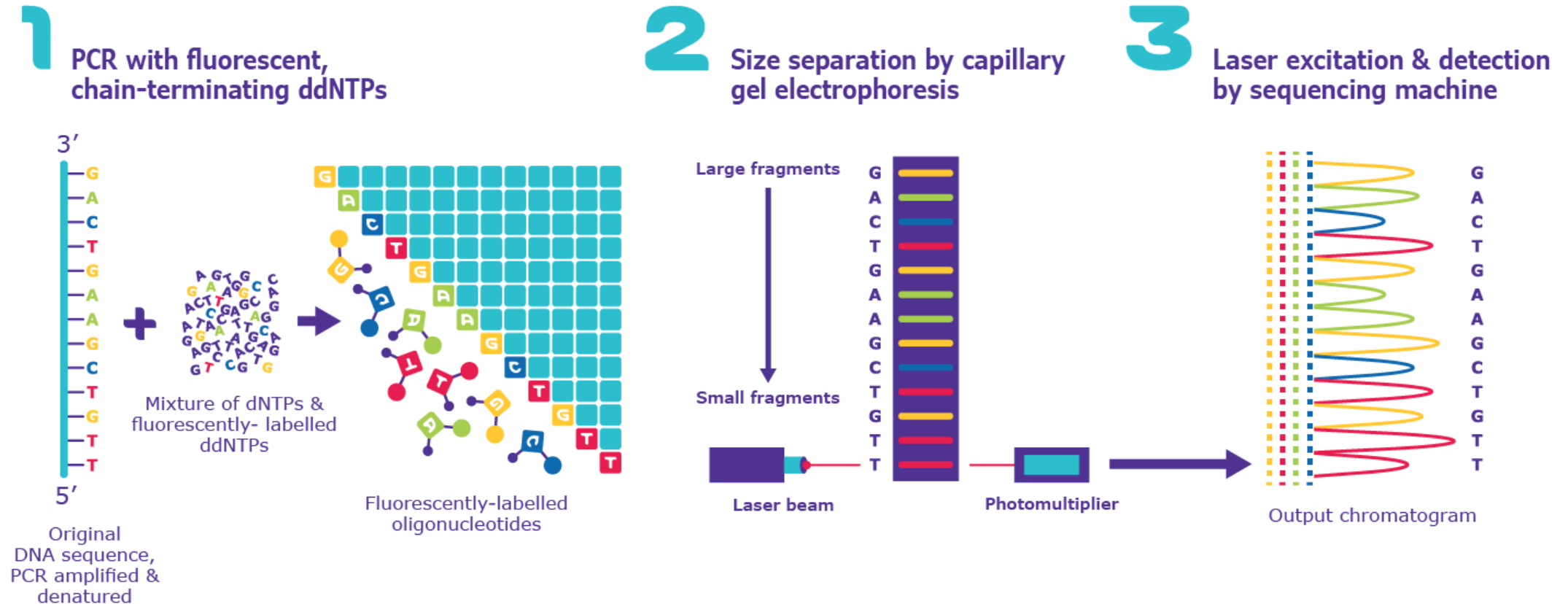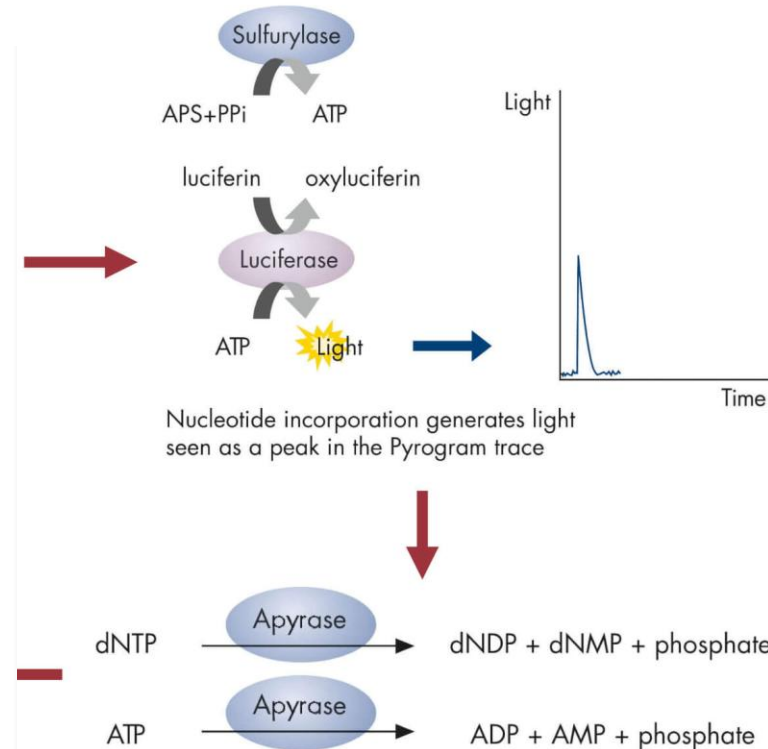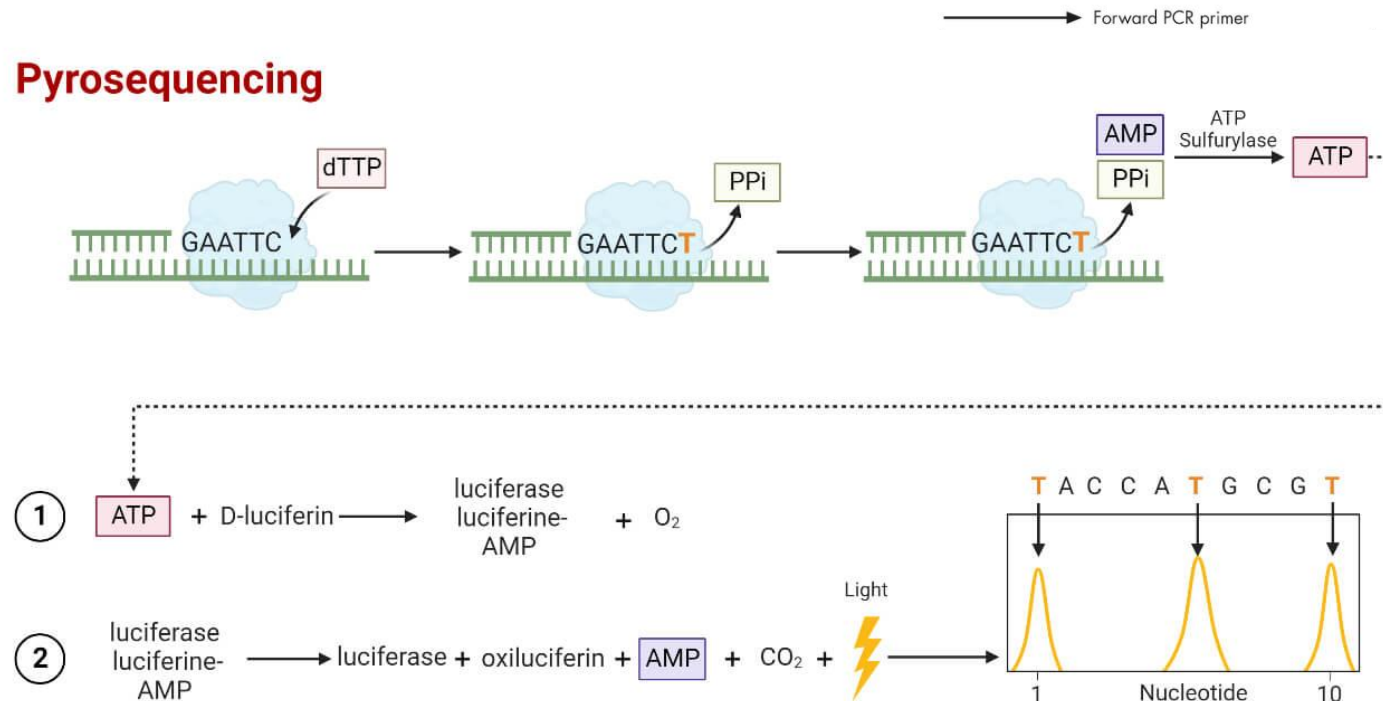
Repeat unit size = 2 - 6 base pairs

Repeated 8 times   Repeated 20 times

HAGenetics.org

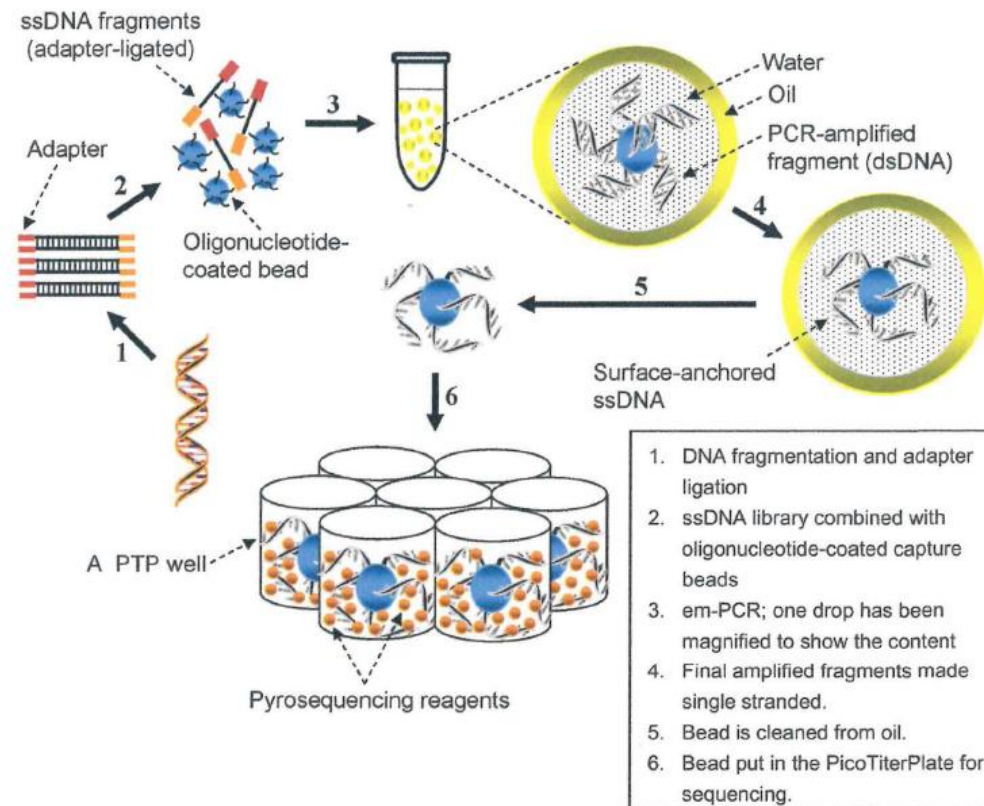## MICROSATELLITES

MOTHER

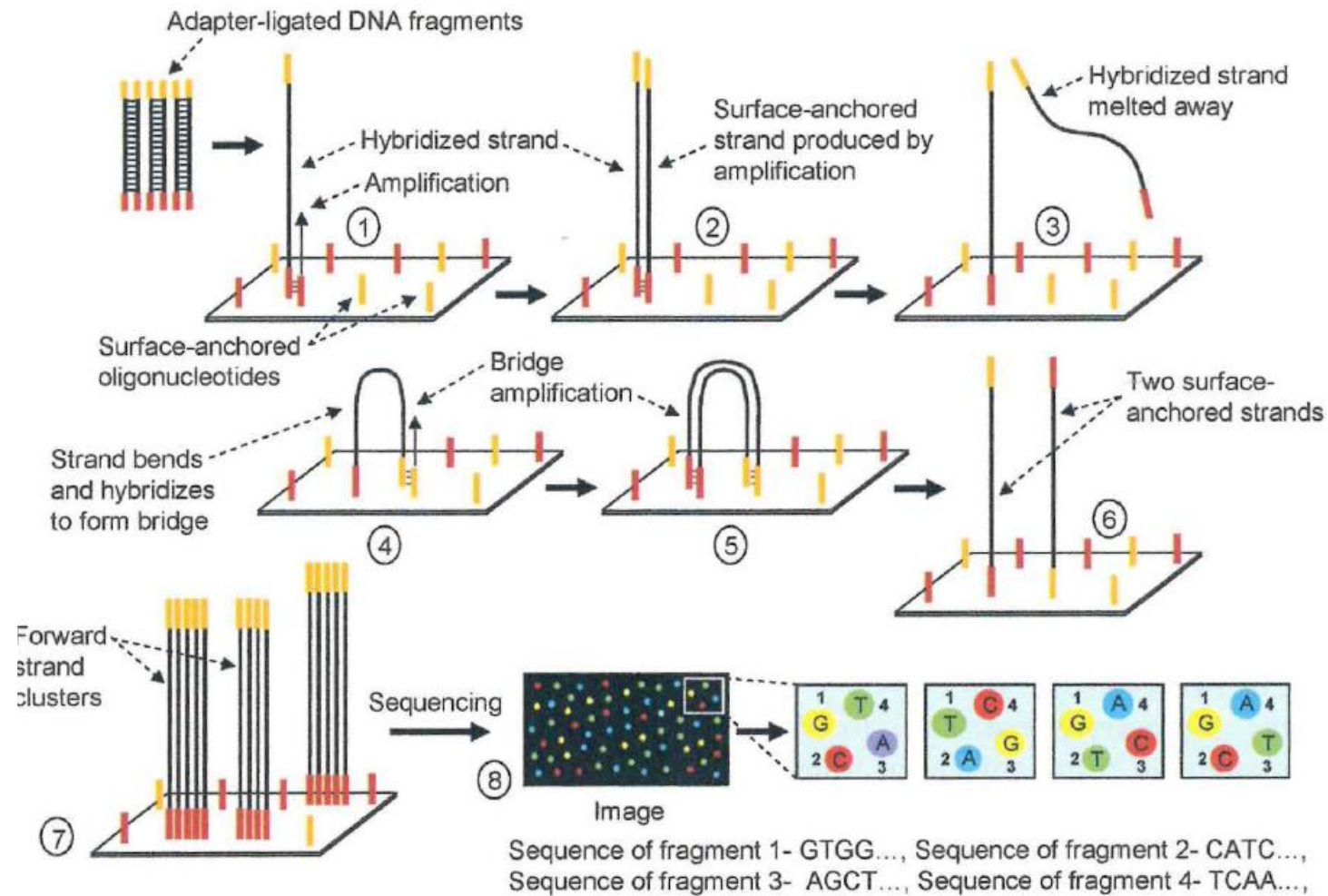FATHER

CHILD

Sanger sequencing

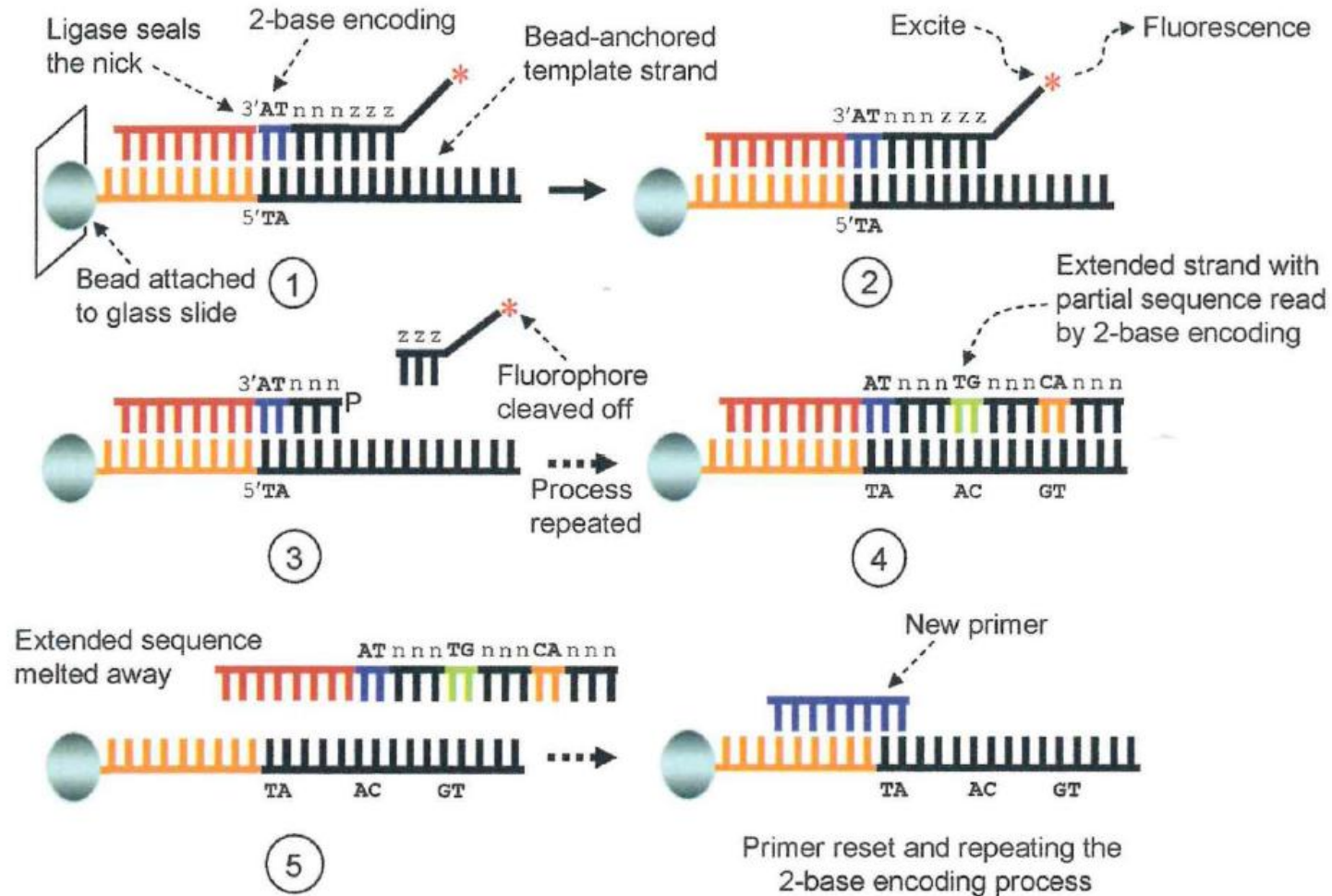# Pyrosequencing

NGS (Roche 454, Illumina Solexa, ABI SOLiD)
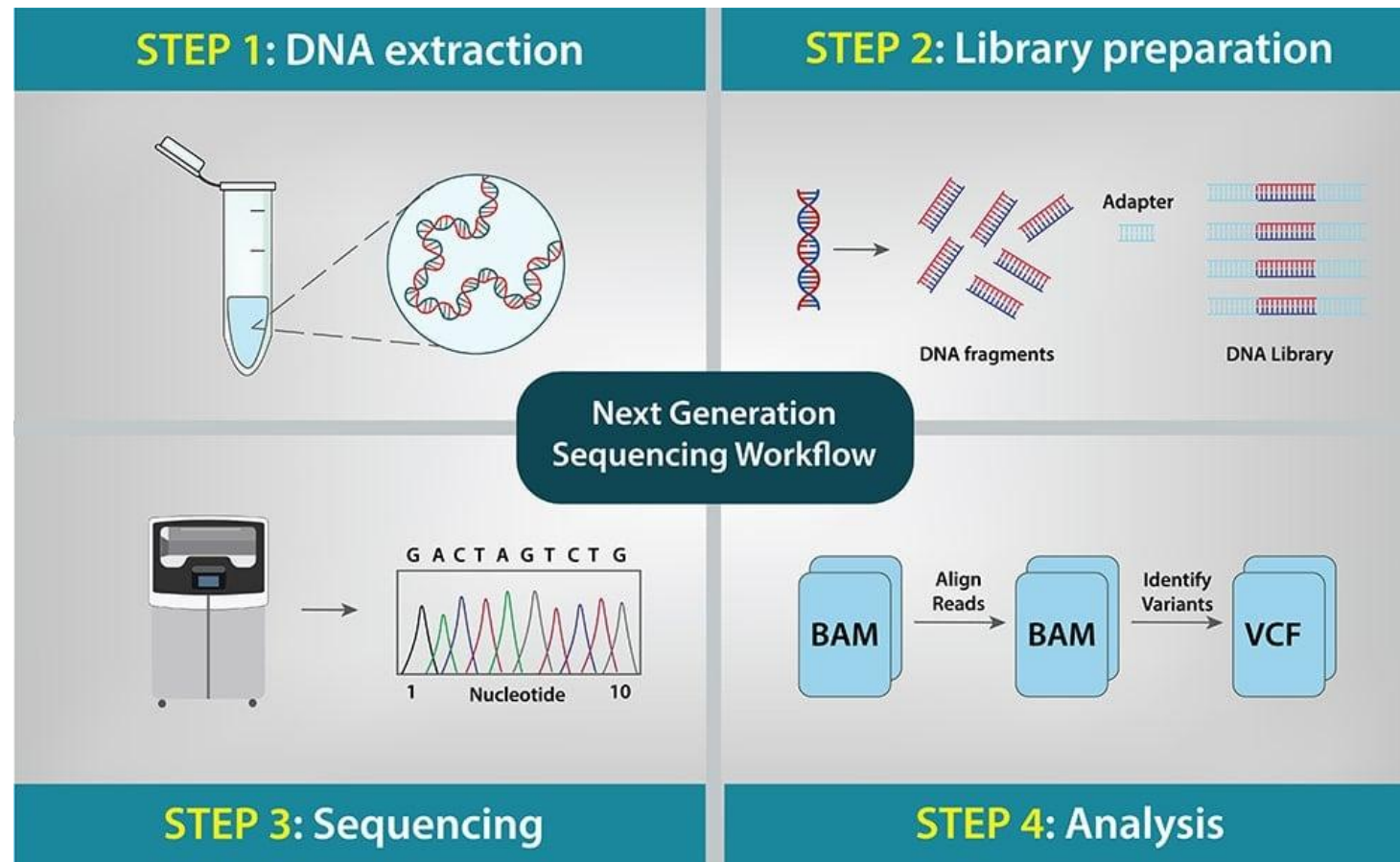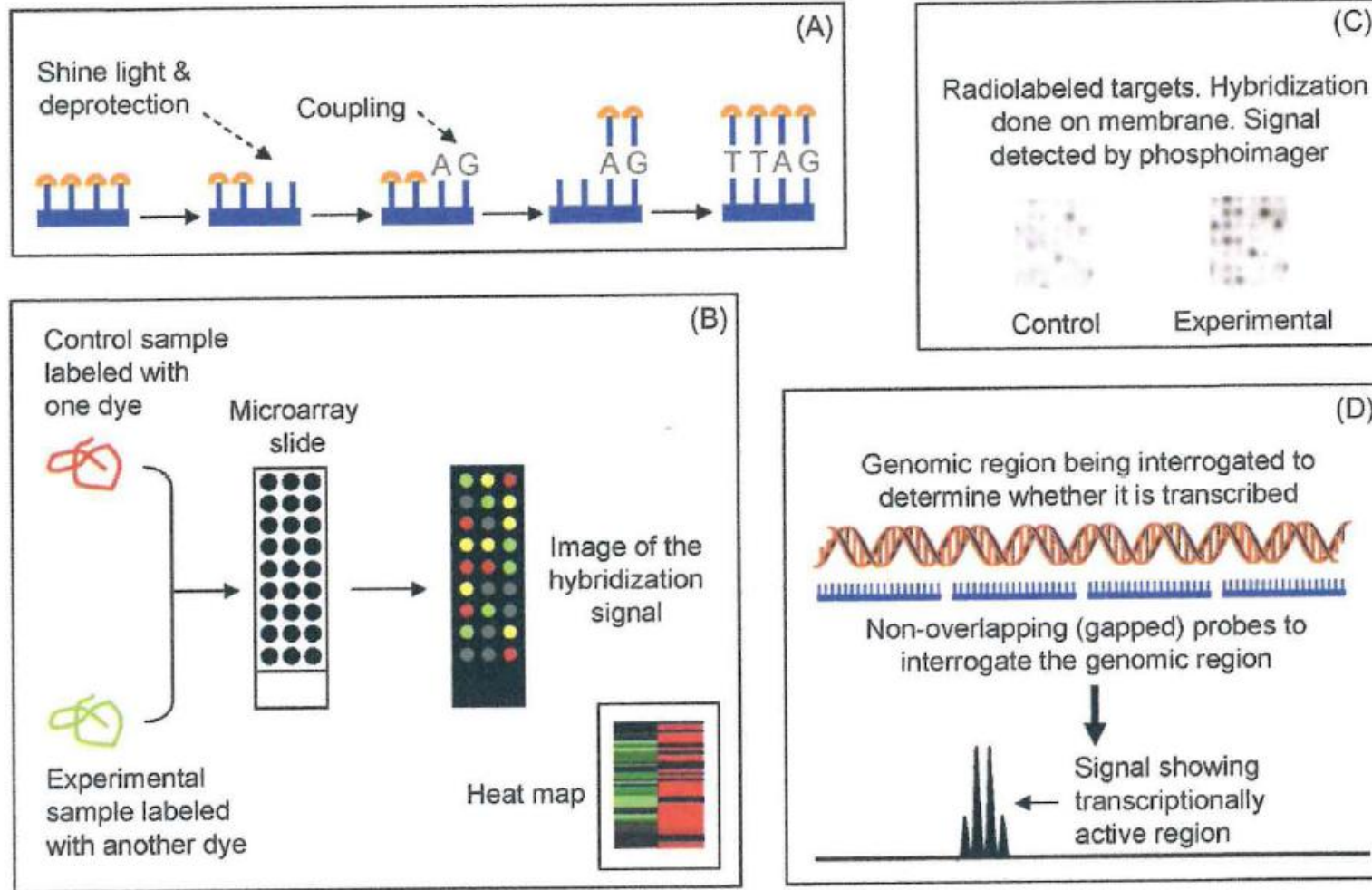
Roche 454 sequencing

Illumina Solexa sequencing

ABI SOLiD sequencing

HD oligonucleotide-based array
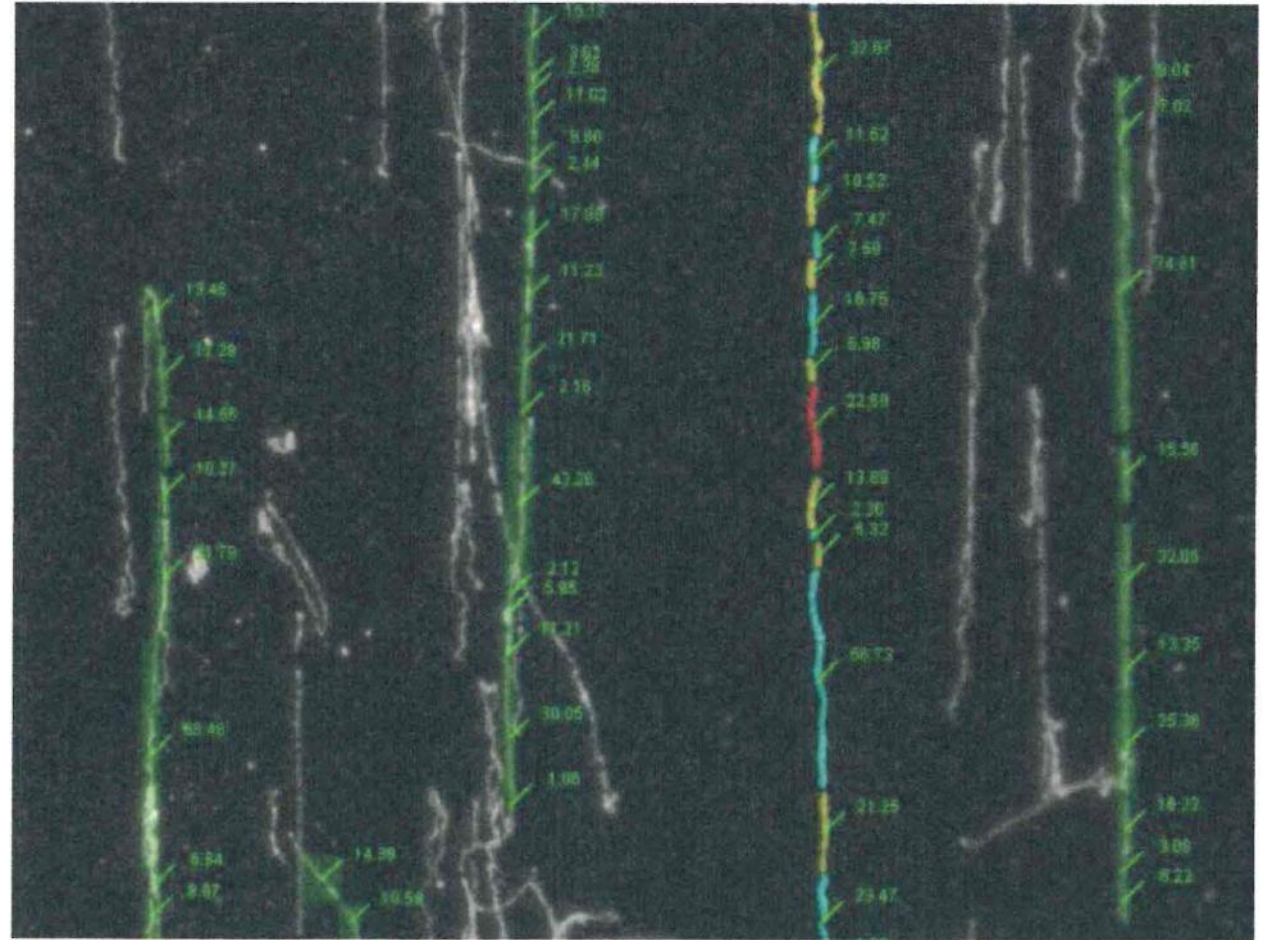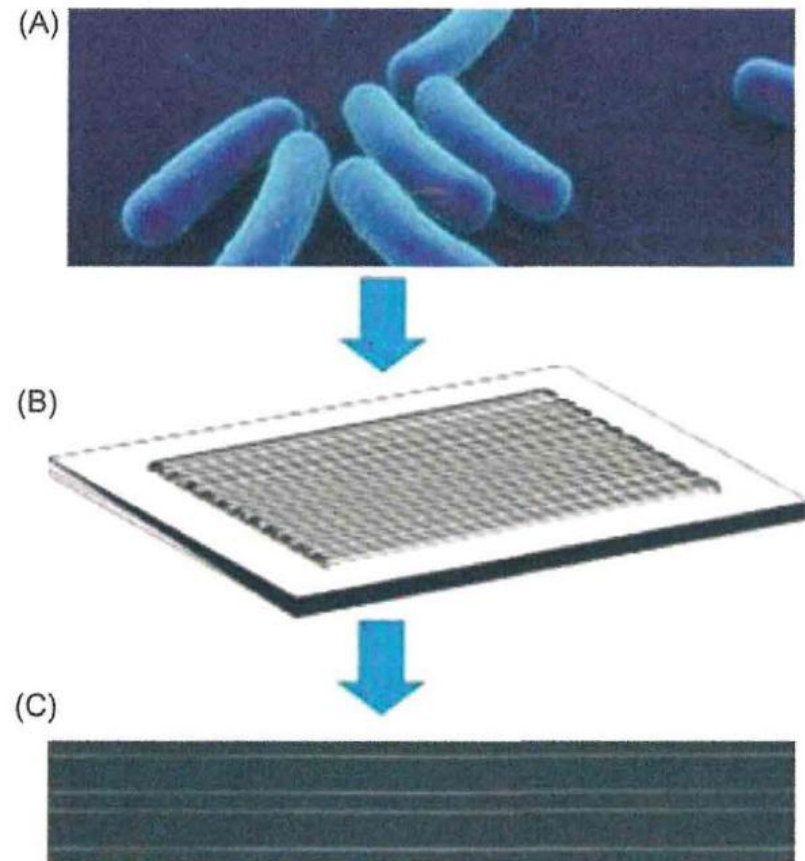
Optical mapping

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
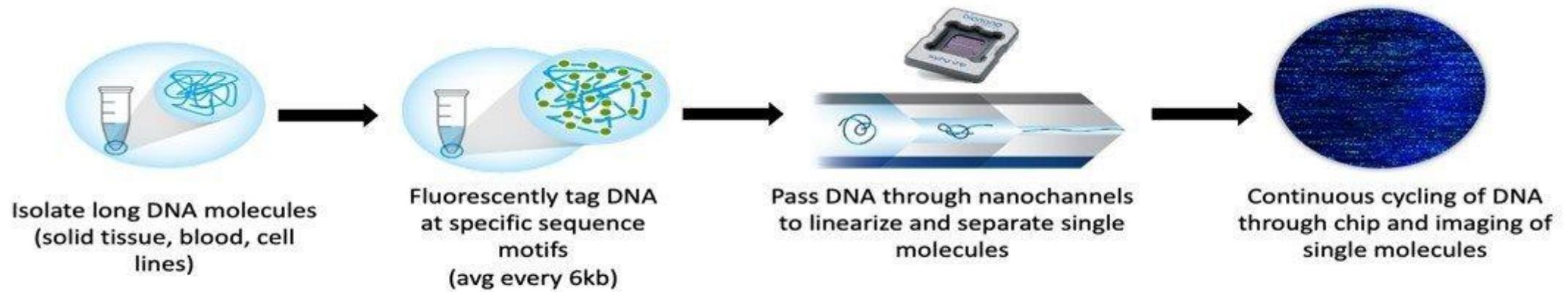
Optical mapping

- Thank you for your attention!

Questions?