Introduction to Molecular Biology

Content

- Cells and organisms
- Molecules of life (Biomolecules)
- Central dogma of molecular biology
- Genes and gene expression

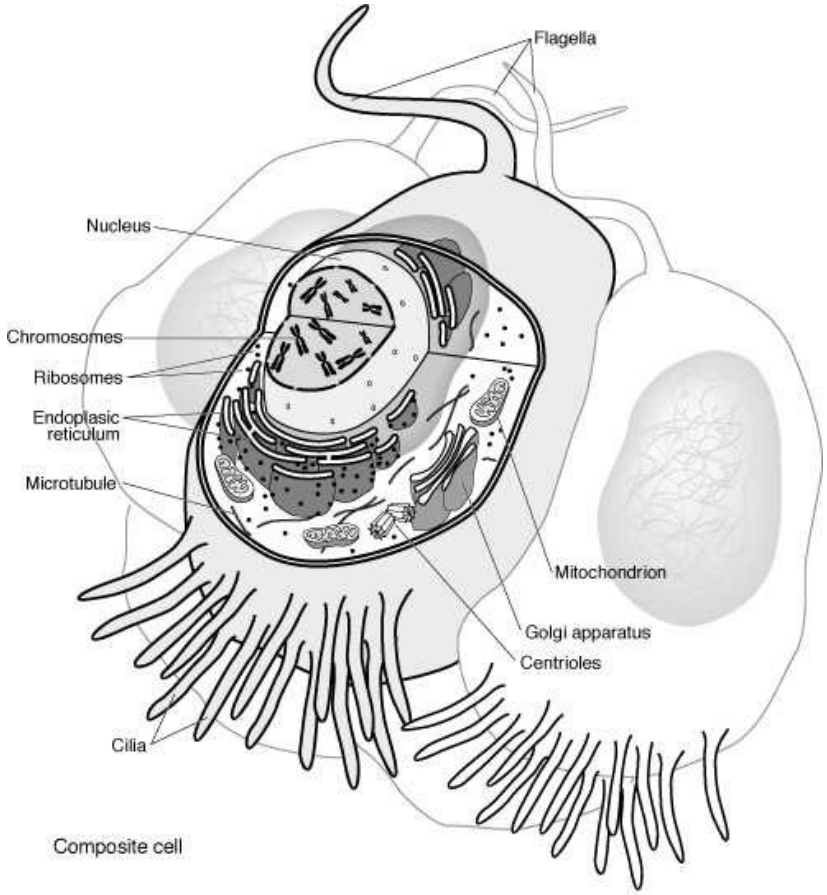
@: Most pictures have been freely obtained from:
http://www.accessexcellence.org/

Cells & organisms

Cells and organisms

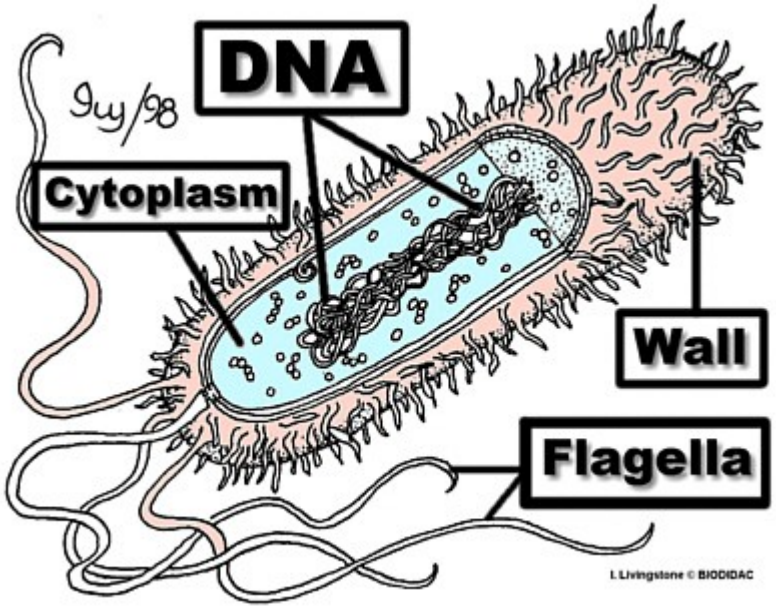
- Organisms
  - Unicellular: One single cell (or simpler)
    - Archaea
    - Prokaryotes: Bacteria, Yeast
    - Eukaryote: Protozoos
  - Pluricellular: Eukaryote cells
    - Different organitation levels (e.g. tissues)
    - Diversity in number, type and syze
    - Viruses are not properly organisms

Eukaryotes



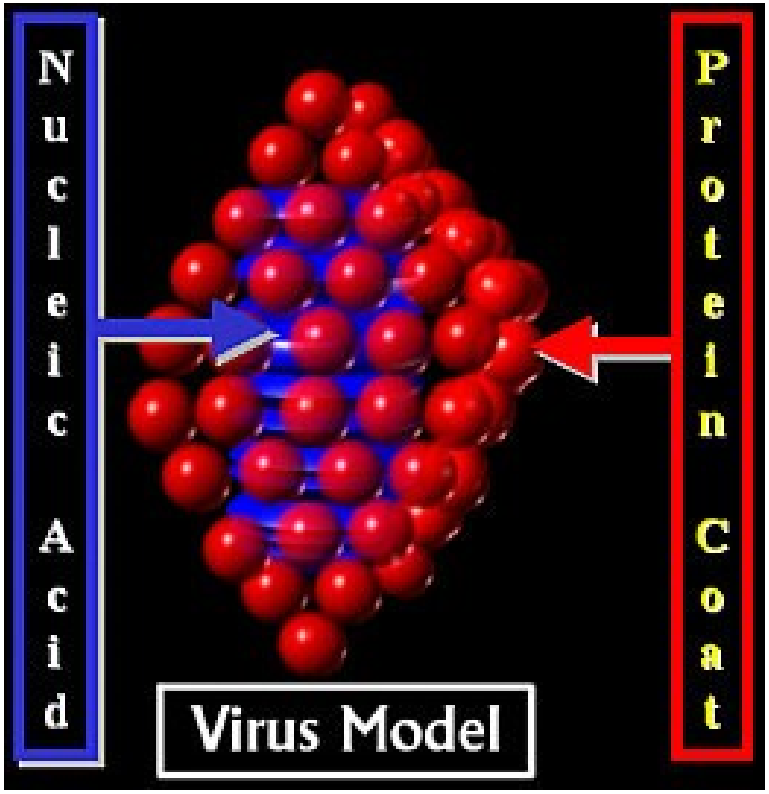
- "Eu" good,
  "Karyo" nut or kernel →
- Presence of nucleous separated from del cytoplasm by the nucleous envelope.
- DNA: double-stranded, it is organized in chromosomes
- The cell contains other membrane-bound organelles
- Sexual reproduction is common

Prokaryotes



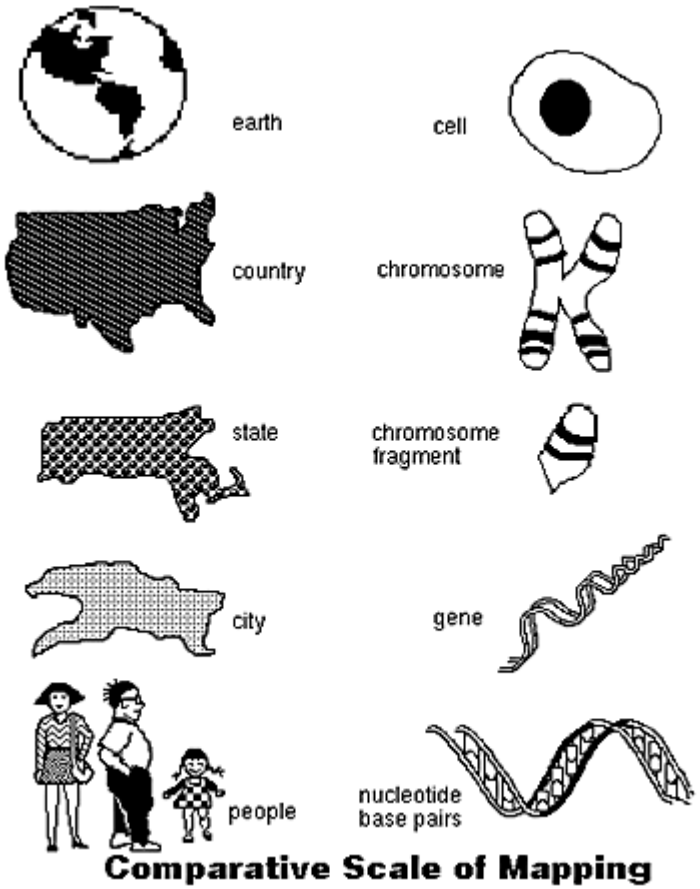
- Lack a cell nucleous
- DNA: circular single stranded
- Lack other membrane-bound organelles.
- Without sexual reproduction although there are genetic recombination

Viruses



- Contain nucleic acids and proteins but no other characteristics
- They use the cellular machinery of their hosts to replicate
- NO can replicate outside the host → NOT living beings

Cellular components to scale



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Biomolecules

Key biomolecules

- The basic components of biological systems are
  - Sugars (carbohydrates)
  - Fats (lipids)
  - Nucleic acids
  - Proteins
- Sugars and lipids have no important role regarding “biological information”→ Not discussed here

Nucleic acids and proteins

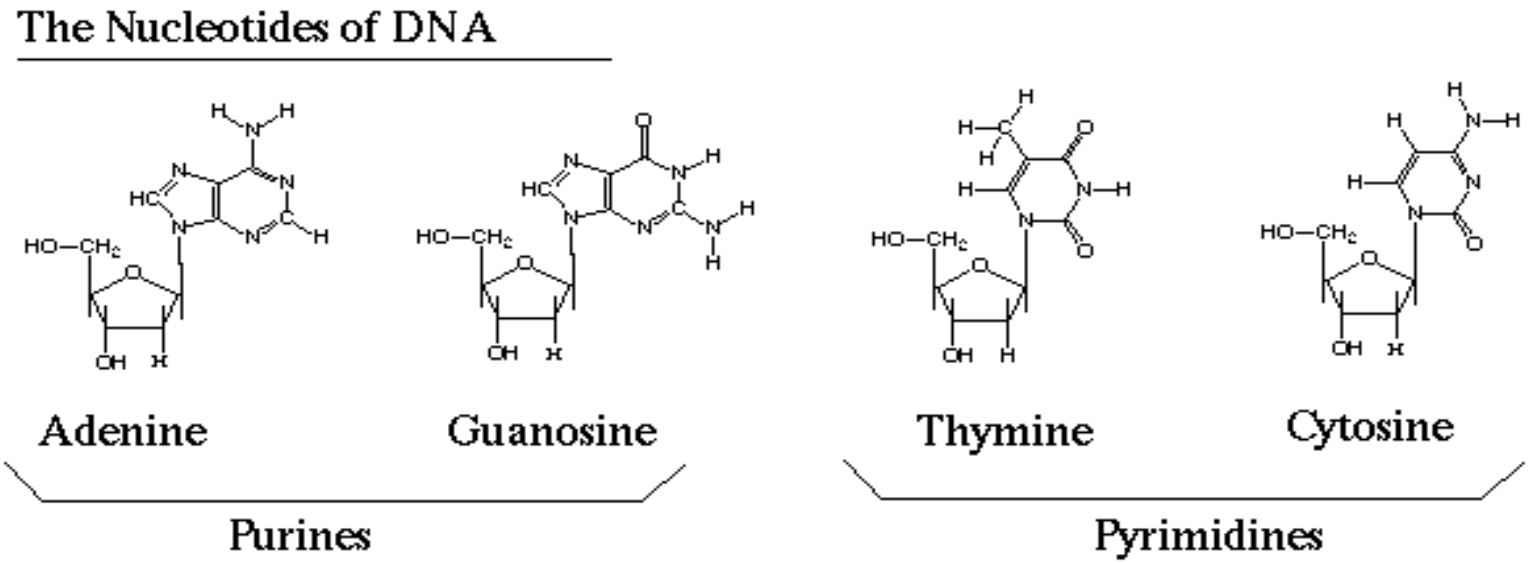
- Molecules that contain and transport information are
  - DNA (4 different nucleotides)
    - Contains encoded biological information
  - RNA (4 different nucleotides)
    - Carries information from DNA to proteins
  - Proteins (20 different amino acids)
    - Function and structure of living beings

Nucleotides

- Basic components of nucleic acids
- Consisting of
  - A sugar (Ribose or Deoxyribose)
  - A nitrogen base
  - A phosphate group
- In biological parlance we speak of "bases" instead of nucleotides to describe a string (3000bp = 3000 bp)

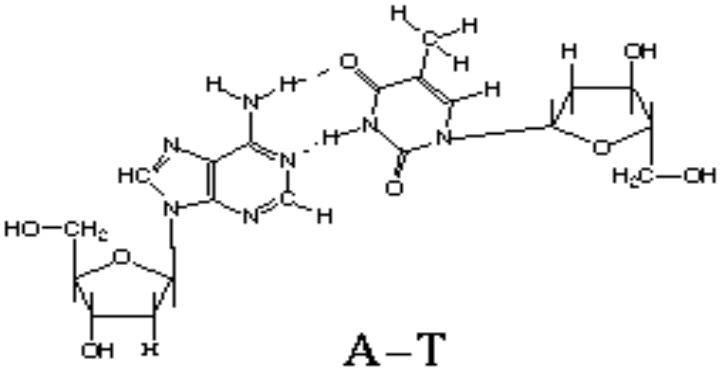
DNA nucleotides

Deoxyribonucleic Acid (DNA) contains four nucleotide bases.



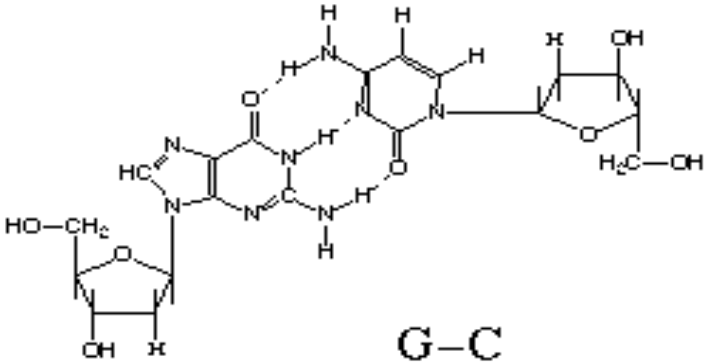
The pairing between complementary bases

DNA Basepairs



A–T

Adenosine–Thymidine
(Adenine–Thymine)



G–C

Guanosine–Cytidine
(Guanine–Cytosine)

The primary structure of DNA

- Sequence of nuceotides
- Forms an unbranched polymer
- Organized in a double-stranded

```
atgaatcgta ggggtttgaa cgctggcaat
acgatgactt ctcaagcgaa cattgacgac
ggcagctgga aggcggtctc cgagggcgga
```

DNA vs RNA

- DNA is organized into a complementary double helix. RNA does not.
- One of the four bases are different
  - DNA→ A, C, G, T
  - RNA → A, C, G, U
- Differ from the nucleotide sugar
  - DNA→ Deoxyribose
  - ARN → Ribose

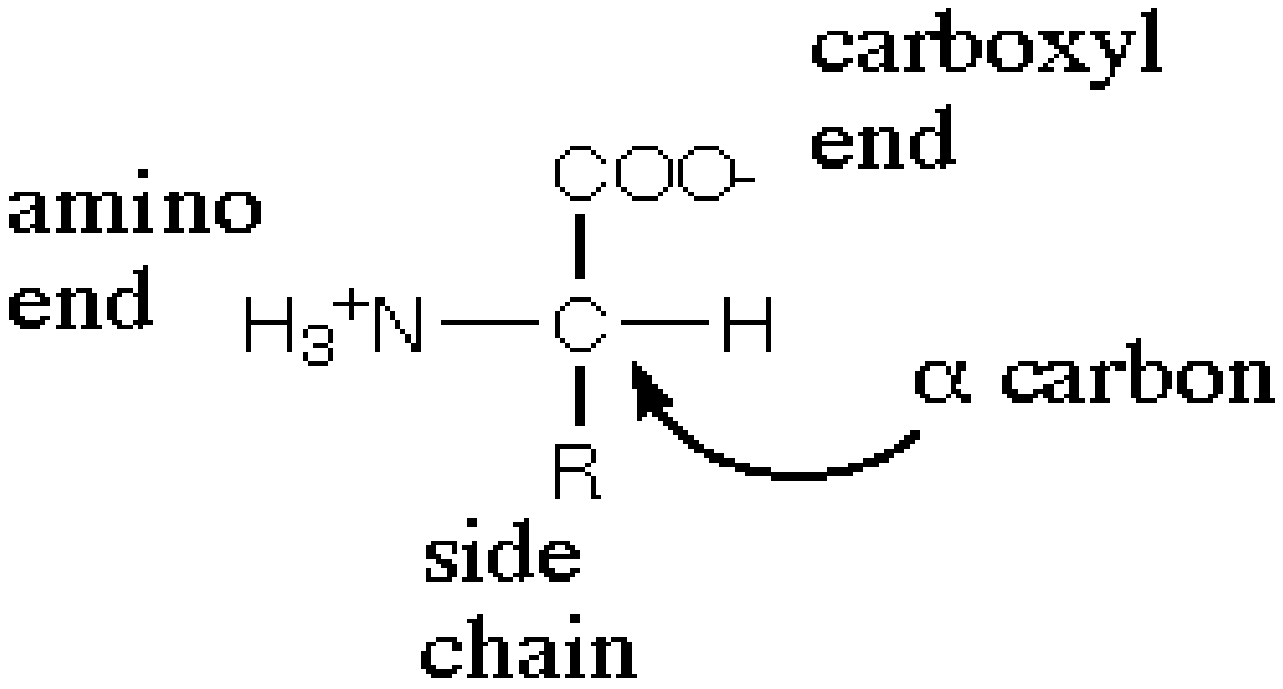
DNA strands sense

- Each DNA strand has a polarity:
  - The strand begins with the 1st nucleotide 5'-hydroxyl (or 5'-phospho) group, and
  - Ends with the last nucleotide 3'-hydroxyl group
  - The strand goes 5' to 3' ("*Five prime to three prime*")
- The two DNA strands are antiparallel
  - One goes 5' → 3' and the other goesy 3' → 5'.

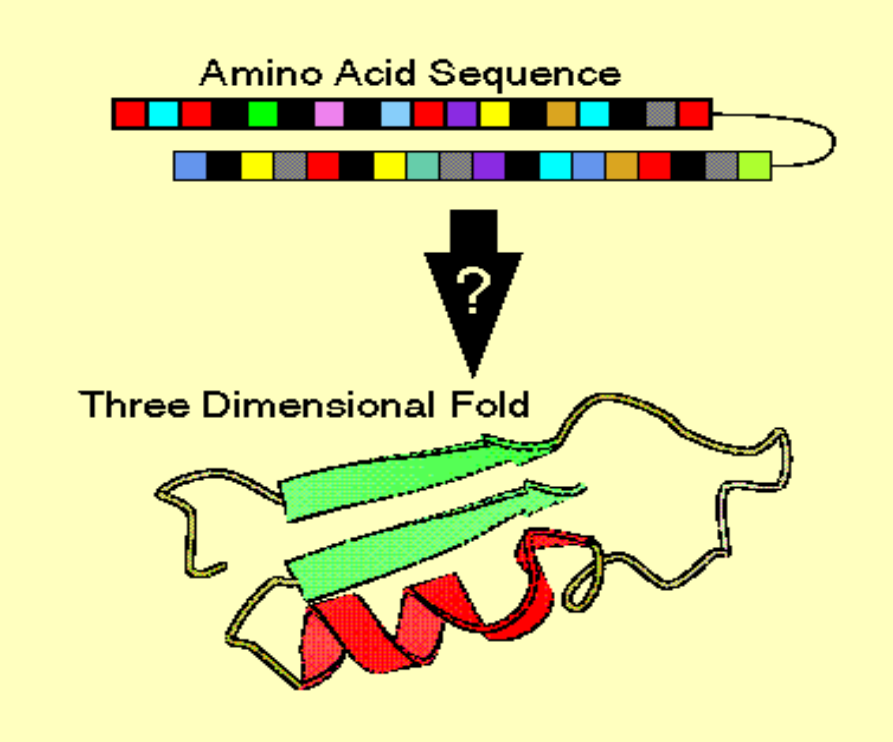
Proteins

- Amino acid sequence
- Forms an unbranched polymer
- There are 20 different amino acids (AA)
- The key function of proteins is in its three dimensional structure

Amino acids



Proteins “fold” into conformational structure

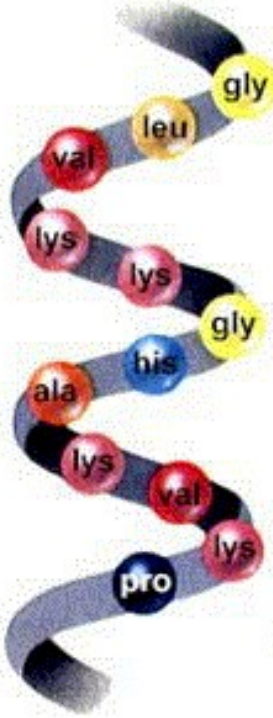


Protein's structure

Proteins fold into lowest to highest complexity level:

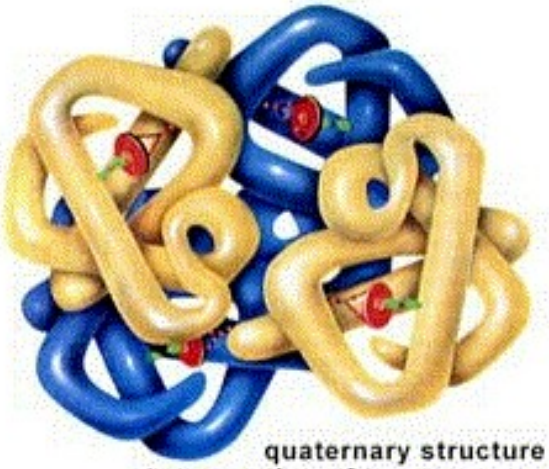
- Primary structure: amino acid sequence
- Secondary structure: regularly repeating local structures stabilized by hydrogen bonds.
- Tertiary structure: fold into 3-dimensional structures.
- Quaternary structure: structure formed by several protein molecules (protein complex).

primary structure
(amino acid sequence)



secondary structure
(α-helix)

tertiary structure
(folded individual peptide)



quaternary structure
(aggregation of two or more peptides)

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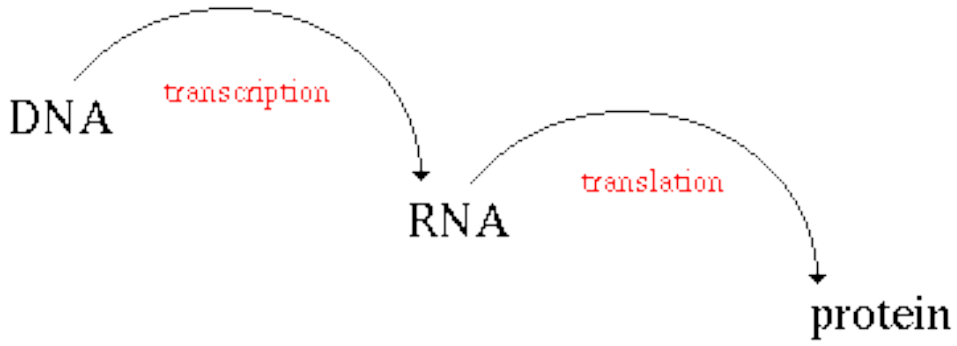
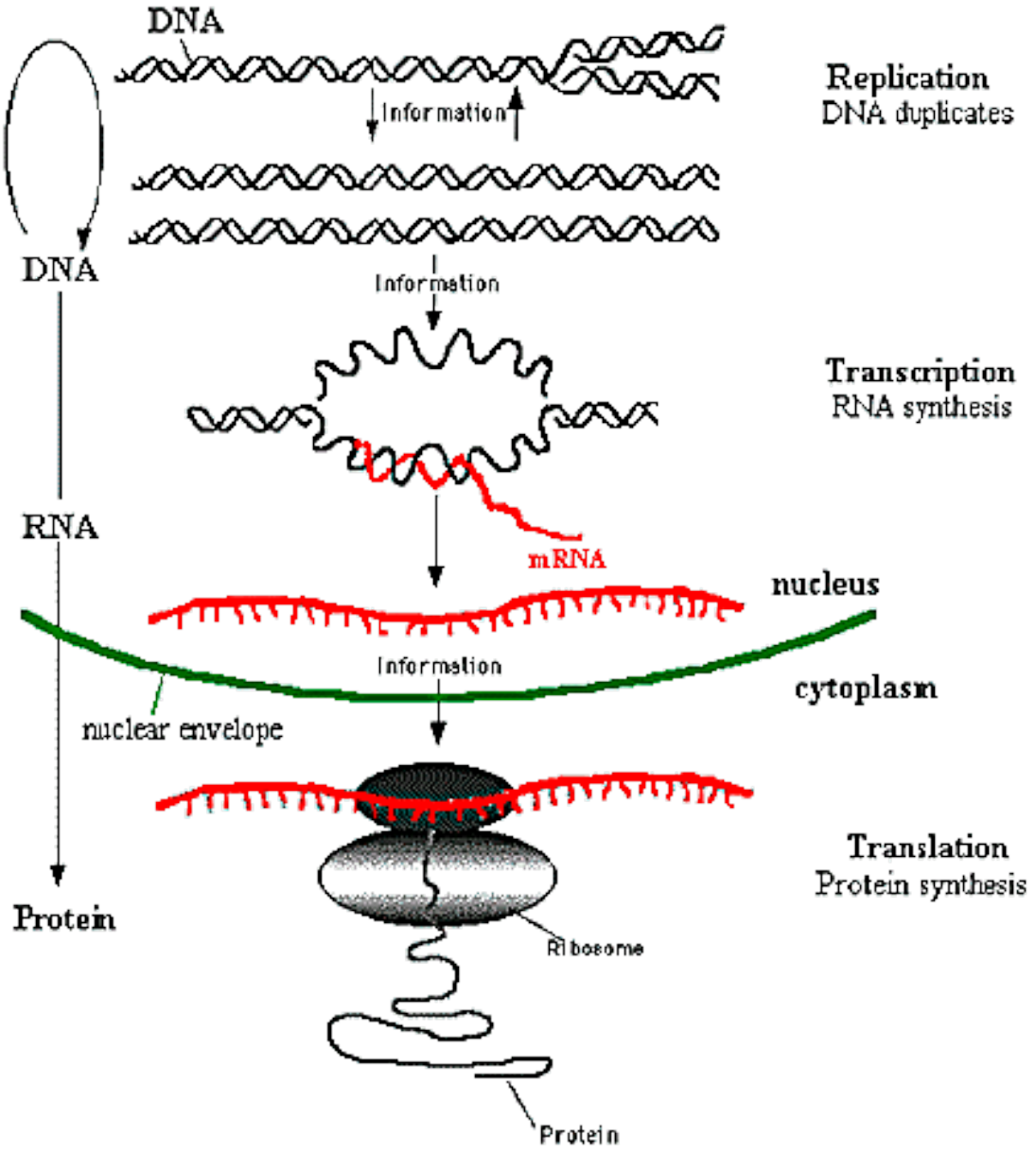
Central dogma of molecular biology

Central dogma of molecular biology

- *Central dogma of molecular biology* states that information encoded in DNA is transferred to proteins through RNA.

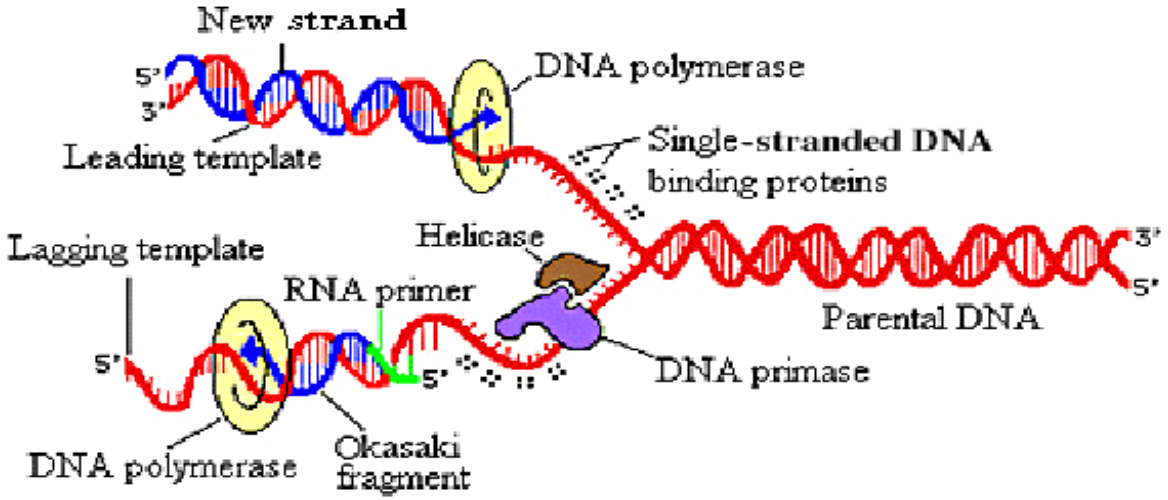



DNA
Information
Replication
DNA duplicates
DNA
Information
Transcription
RNA synthesis
RNA
mRNA
nucleus
Information
cytoplasm
nuclear envelope
Translation
Protein synthesis
Protein
Ribosome
Protein

From DNA to proteins

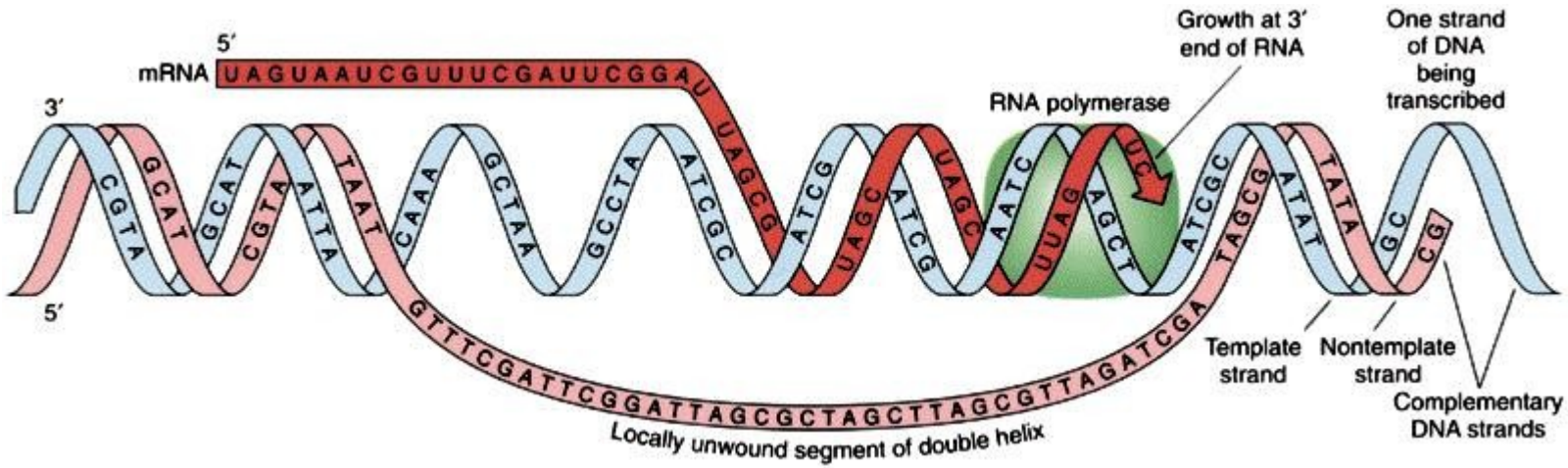
- DNA is replicated in a complex process involving many enzymes: replication replicación
- DNA is copied in a string of complementary messenger RNA (mRNA): transcription transcripción
- In eukaryotic cells, the mRNA is processed procesa eliminating coding fragments (“splicing”) and migrates from the nucleous to the cytoplasm.
- The mRNA carries coded information to ribosomes (ribosomal RNA) that "read" and perform protein synthesis: translation traslación

1. Replication

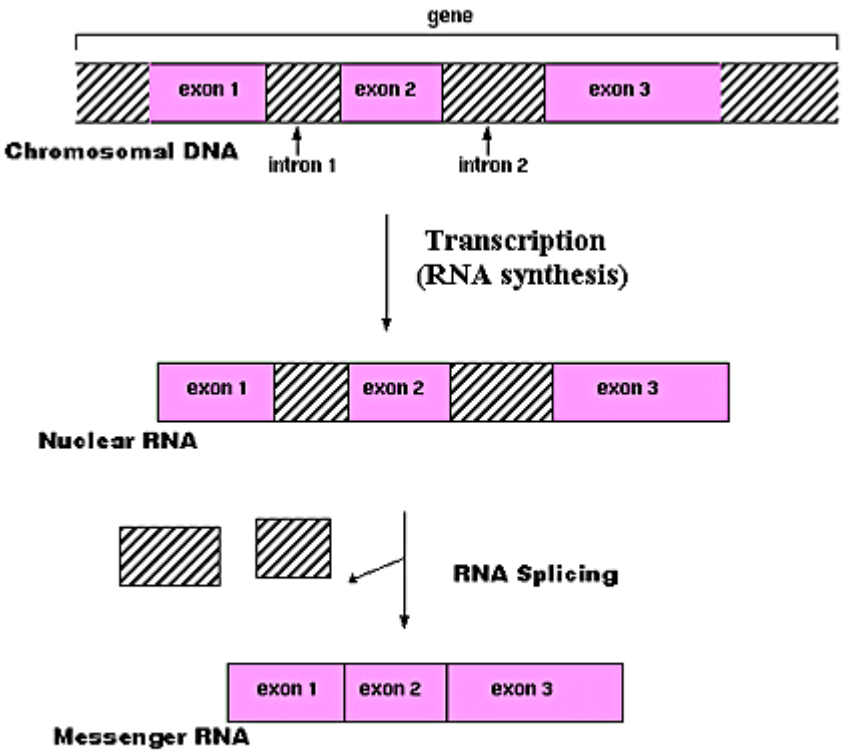


- Animations (1), (2), (3)

2. Transcription

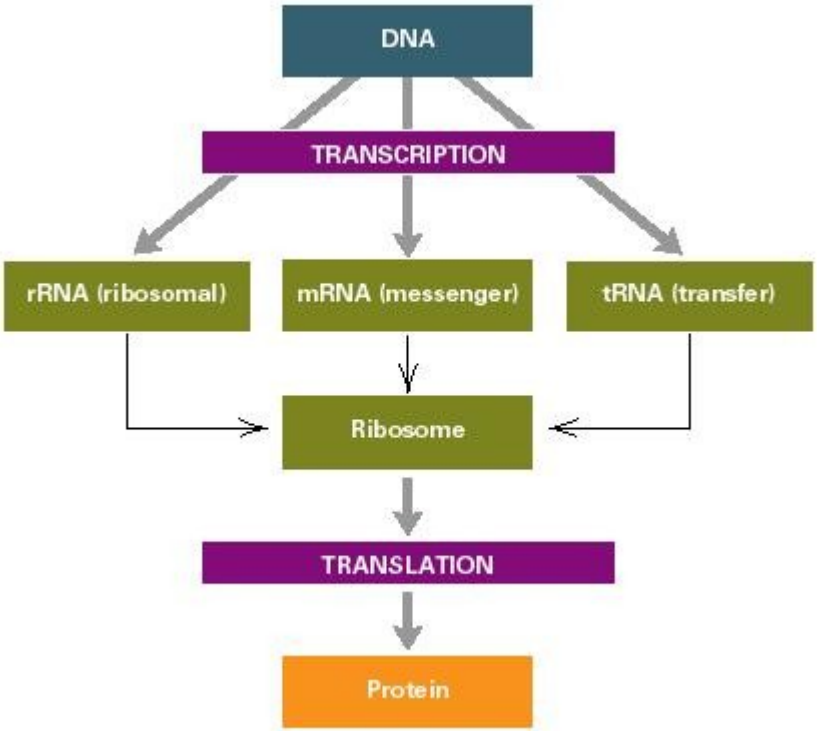


3. RNA processing or splicing

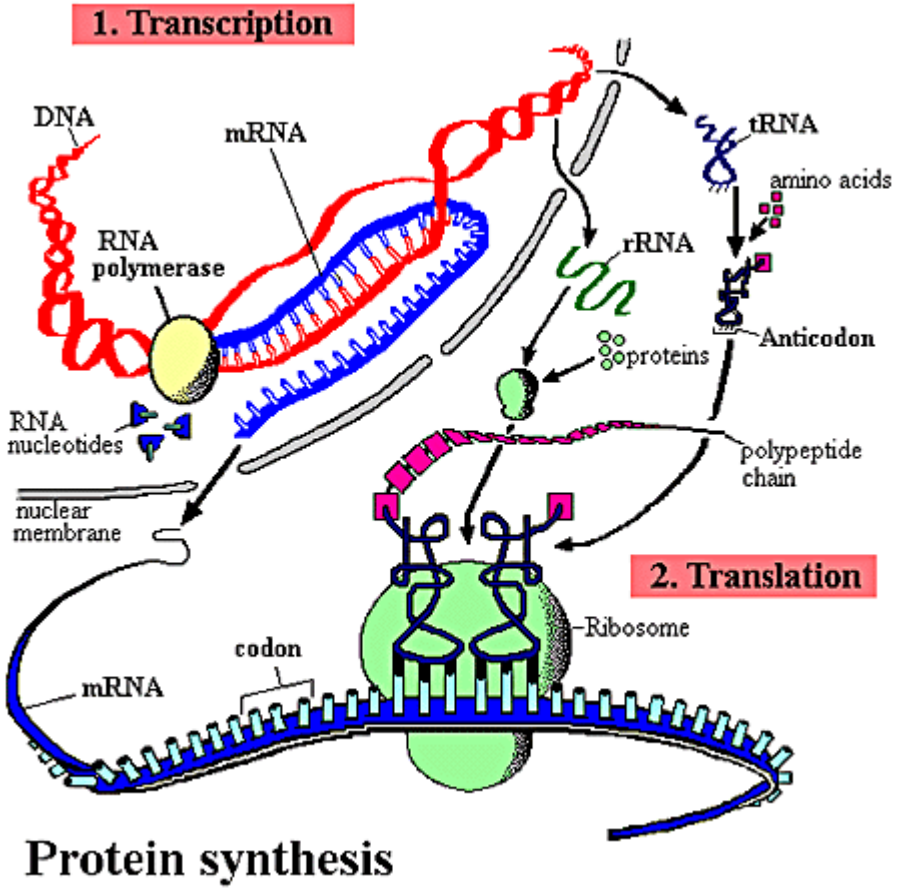


RNA synthesis and processing

1DNA vs. 3 RNA's



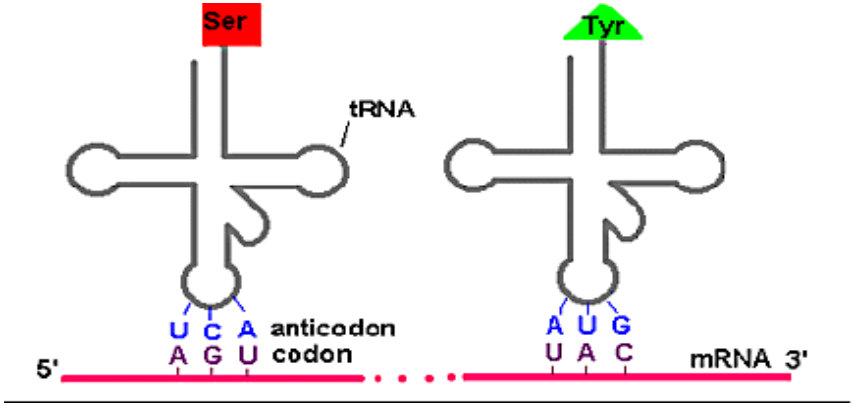
4. Protein synthesis



Protein synthesis

- The mRNA goes to the cytoplasm where it binds to ribosomes.
- Codon: mRNA information unit.
- The tRNA brings the complementary AA tRNA.
- The AA are bound to the protein to complete the sequence.
- Animations (1), (2)

4’ The genetic code



2nd base in codon

1st base in codon	U	C	A	G	3rd base in codon
U	Phe Phe Leu Leu	Ser Ser Ser Ser	Tyr Tyr STOP STOP	Cys Cys STOP Trp	U C A G
C	Leu Leu Leu Leu	Pro Pro Pro Pro	His His Gln Gln	Arg Arg Arg Arg	U C A G
A	Ile Ile Ile Met	Thr Thr Thr Thr	Asn Asn Lys Lys	Ser Ser Arg Arg	U C A G
G	Val Val Val Val	Ala Ala Ala Ala	Asp Asp Glu Glu	Gly Gly Gly Gly	U C A G

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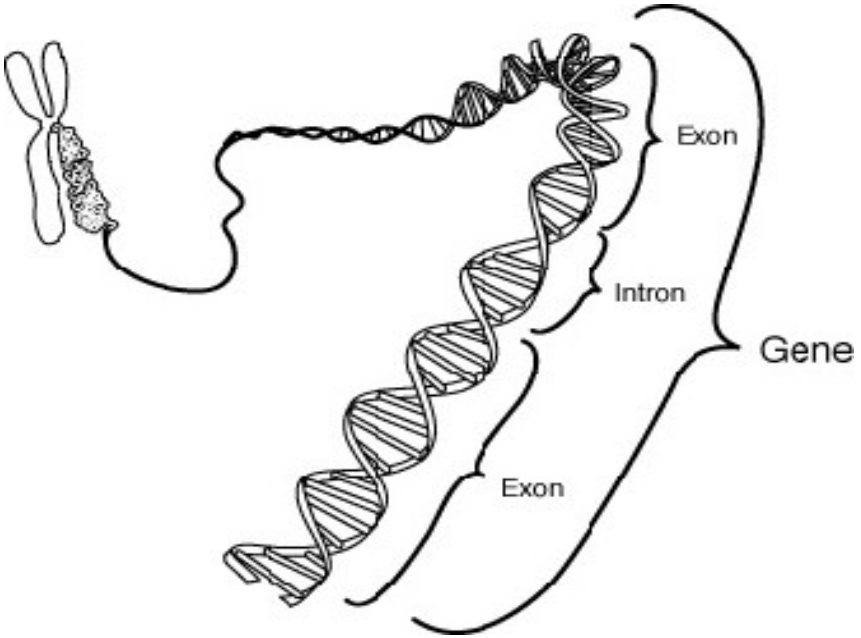
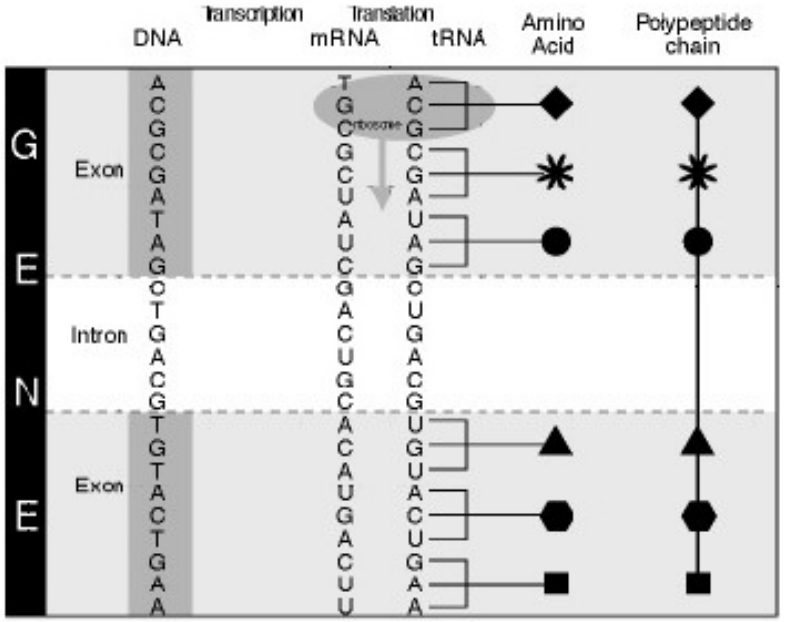
Genes and gene expression

What is a gene?

- It is the functional and physical unit of heredity transmitted from one generation to their offsprings.
- Genes are DNA fragments
- Most of the genes contain the necessary information for the synthesis of a specific protein.

Gene components





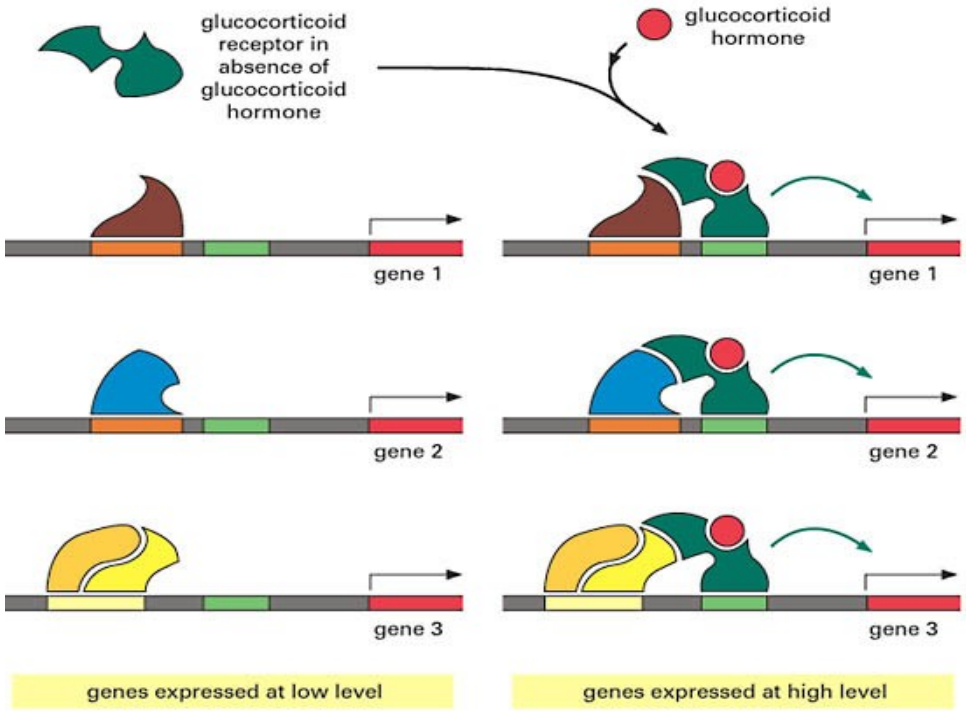
Regulation of gene expression

- Genes can be “turned on” or “off”.
- Each cell expresses (or active or "on") only a fraction of their genes.
- Remaining genes are repressed ("off").
- The process consisting in activate genes and suppress others is *gene regulation*.
- Gene regulation determines:
  - The appearance and different function of different cells types
  - The ability of some cells to react quickly to environmental changes

How genes are regulated?

- Gene regulation can occur at any point in the process of expression but often occurs during transcription.
- Environmental signs or other cells activate proteins called *transcription factor*.
- They bind to the *regulatory regions* of genes, increasing or decreasing the level of transcription→ They control the amount of gene product produced by the gene in every moment.

Example: Genes activation



- With no HGC (glucocorticoid hormone) genes are inactive
- In presence of HGC genes are activated and expressed (in block)

Mutations

- Mutations are genetic changes randomly produced or by the action of mutagens (chemicals, X rays, UV, etc.)
- Most are lethal because the original AA and nucleotides sequence is the product of millions of years of evolution
  - → Product of natural selection (or not...)

Mutations at the molecular level

- A mutation results in a change in the order of nucleotides in the genes
- Consider for example the peptide

```
Nucleotides TAC TTA {C}GA TAA TGC ATT
Codons mRNA-   AUG AAU {G}CU AUU ACG UAA
Sequence AA-   met asn  ala  ile thr stop
```

- We can change a nucleotide (eg. “C”→”G”) for another or delete it.

Point mutations

- Point mutation
  - Substitution of one nucleotide for another
  - It can be lethal or harmless (due to the degeneracy of the code)

```
Nucleotides TAC TTA {C}GA TAA TGC ATT
Substitution C→G   TAC TTA {G}GA TAA TGC ATT
Codons mRNA-   AUG AAU {C}CU AUU ACG UAA
New seq.    met asn  pro  ile thr stop
Original seq.  met asn  ala  ile thr stop
```

“Frameshift” mutation

- Change the reading frame
  - Deleting a nucleotide→ change in the grouping of codons

```
Nucleotides TAC TTA {C}GA TAA TGC ATT
C supression TAC TTA GA(T) AAT GCA TT?
Codons mRNA-   AUG AAU CU(A) UUA CGU UA?
New seq.     met asn  leu  arg lys ???
Original seq.  met asn  ala  ile thr stop
```