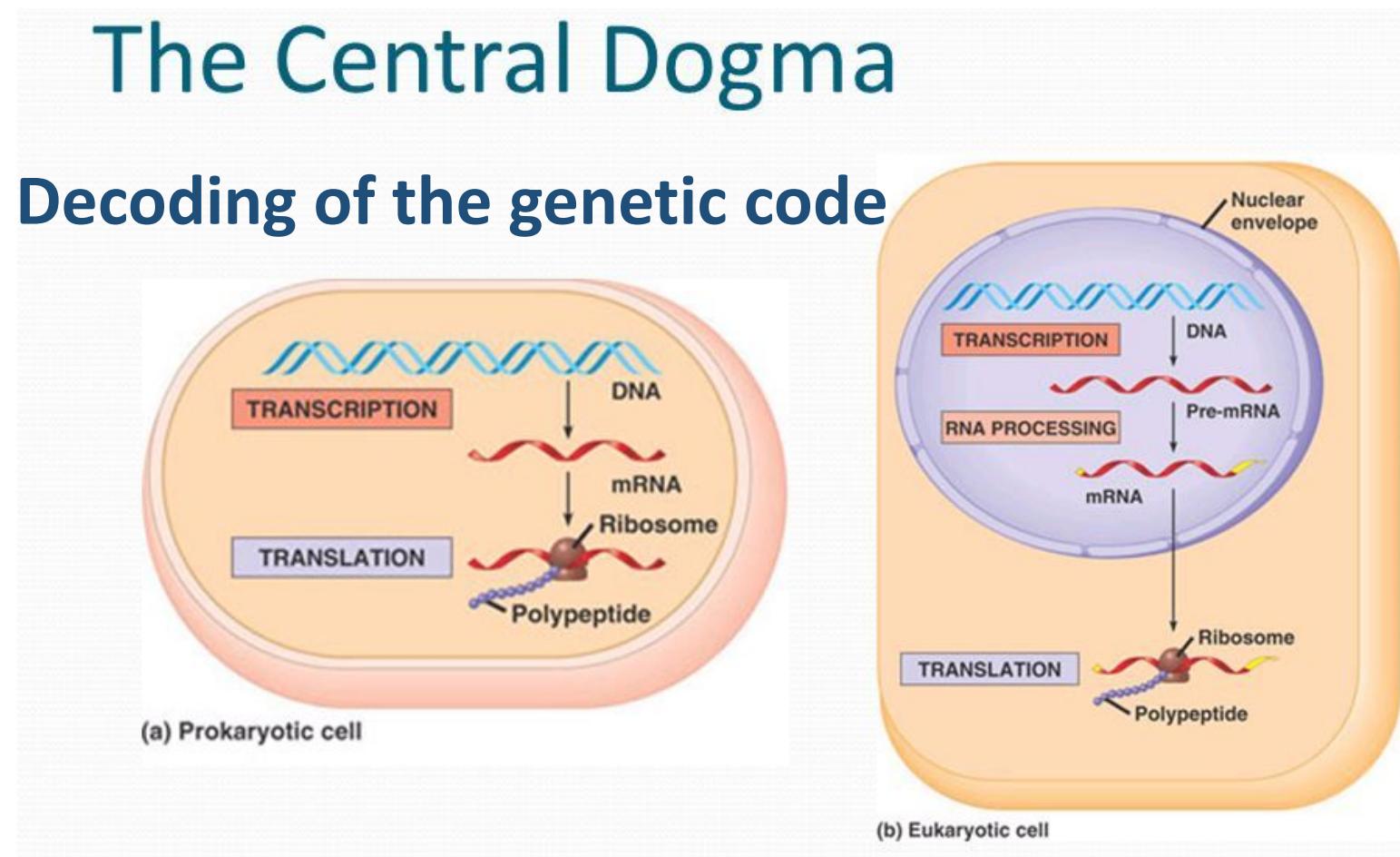
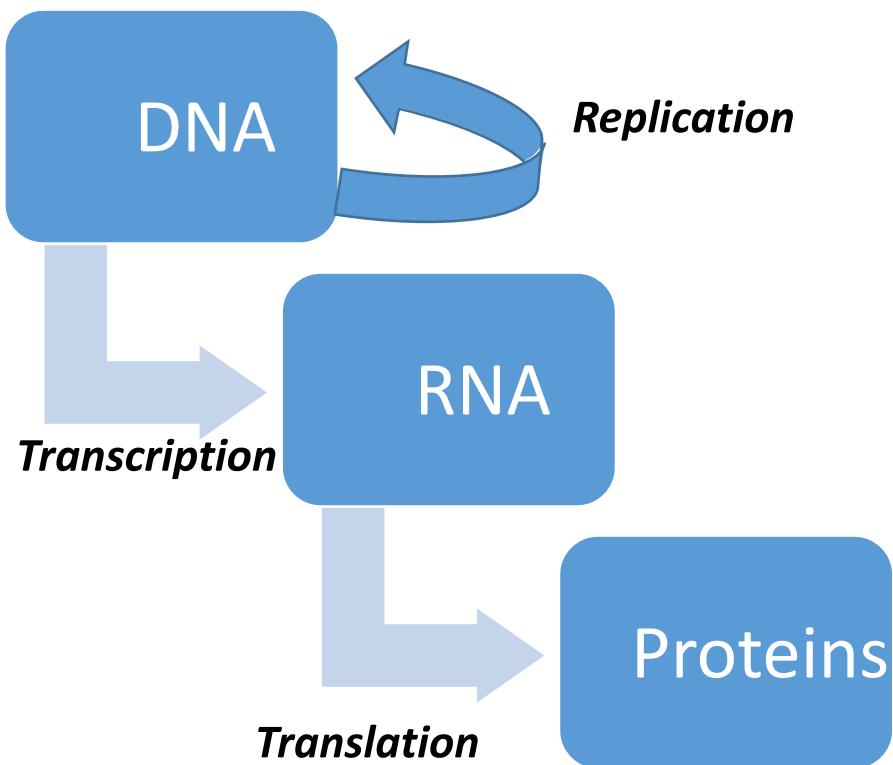


Central dogma

- Replication
- Transcription
- Translation
- Splicing

Basic cellular mechanisms of life



Activity 1

- Calculate the total number of cells in a 50 kg person
- This is an approximate calculation for illustration purpose
- Cell dimension is 10 um in diameter for a sphere
- Assumptions

Assume the cell to be cubical in shape[although spherical is more appropriate]

For conversion use $1\text{dm}^3 = 1 \text{ l} = 1 \text{ kg}$.

Activity 1

- Q: How many cells are there approximately in an average 50 kg person?
- 10 microns diameter of a cell
- Volume = $10 \times 10 \times 10 \text{ um}^3 = 1 \text{ cell}$ [assuming it to be a cube]
- So in 1 mm^3 , there will be about 1 million cells [$1 \text{ um} \text{ is } 10^{-3} \text{ mm}$ or $1\text{mm} = 10^3 \text{ mm}$].
- In a dm^3 , there will be 10^{12} cells – 1 trillion
- $1 \text{ dm}^3 = 1\text{l} = 1\text{kg}$ [assumption]
- About 50 trillion cells.

Activity 2

- Calculate the length of the DNA
- Human DNA- $6.6 * 10^9$ bp
- Each base pair – 0.34 nm

Activity 2

- Calculate the length of the DNA
- Human DNA- $6.6 * 10^9$ bp
- Each base pair – 0.34 nm

About 2m long

- Amount of pressure and the level of packaging
- Compare the size to that of the cell **average is 6um in diameter!!!**

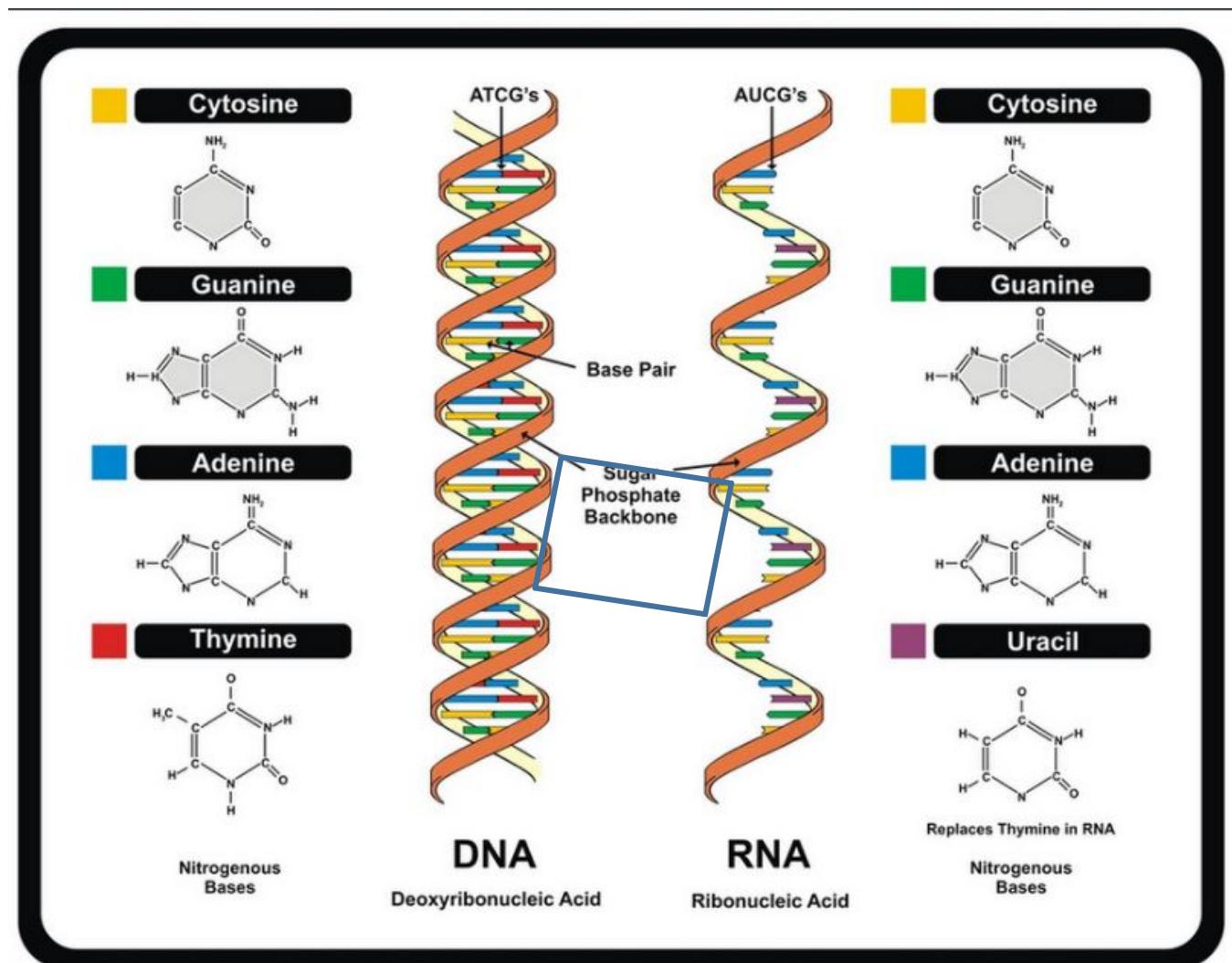
- DNA is just a fine, spiral coiled thread in the nucleus of every living cell.
- The human genome, encoded as DNA, contains 23 chromosome pairs, which is like 500 thousand to 2.5 million nucleotide pairs.
- What if it were to be stretched or coiled? Every human being has about ten trillion cells in their body. If all DNA cells are stretched, they can go as far as 744 million miles. Now the moon is only about 2,50,000 and the Sun is 93,000,000 miles away.

Structure of DNA/ RNA

1. Double helix
2. Consists of 4 base pairs

Sugar- Phosphate backbone

Colored blocks are the bases.
There are 2 strands of the backbone
that runs in opposite direction
The bases on the 2 strands base pair



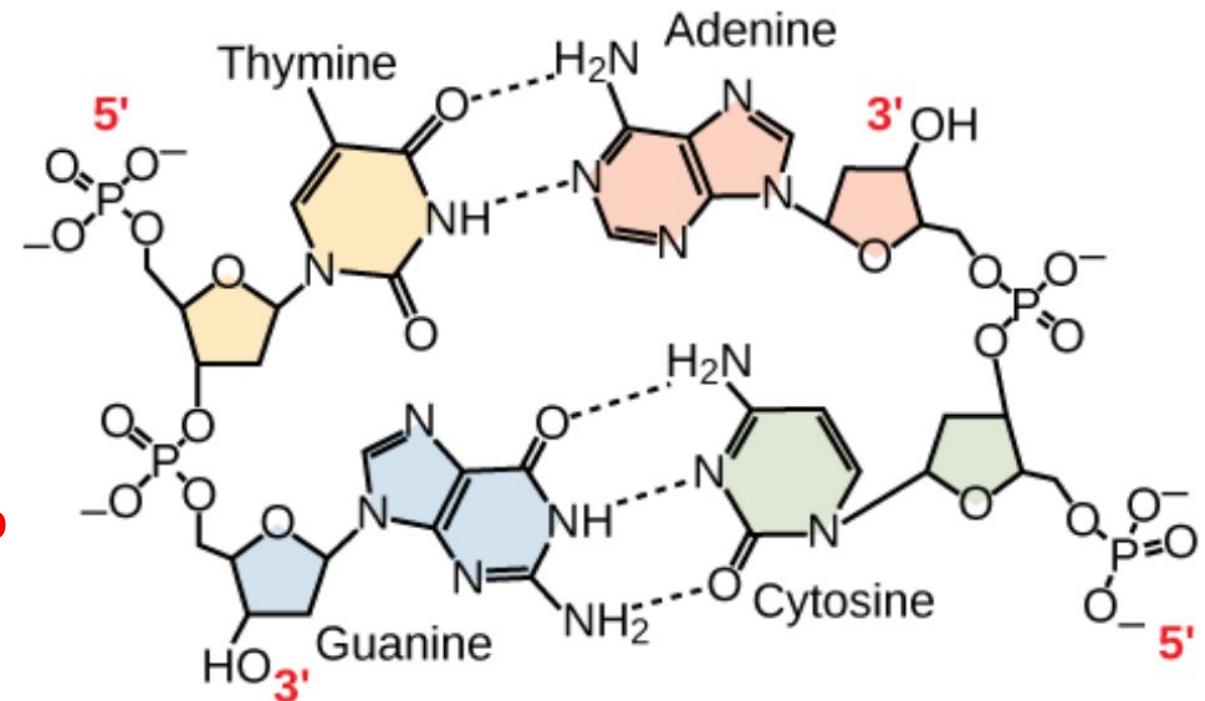
The rules pertaining to the basic DNA structure

- There are 4 bases- Adenine [A], Guanine[G], Thymine [T], Cytosine [C].
- A pairs with T [2 H-bonds]
- G pairs with C [3 H-bonds]

Note!!!

The 2 strands are anti-parallel to each other.

Observe the sugar-Phosphate backbone to understand

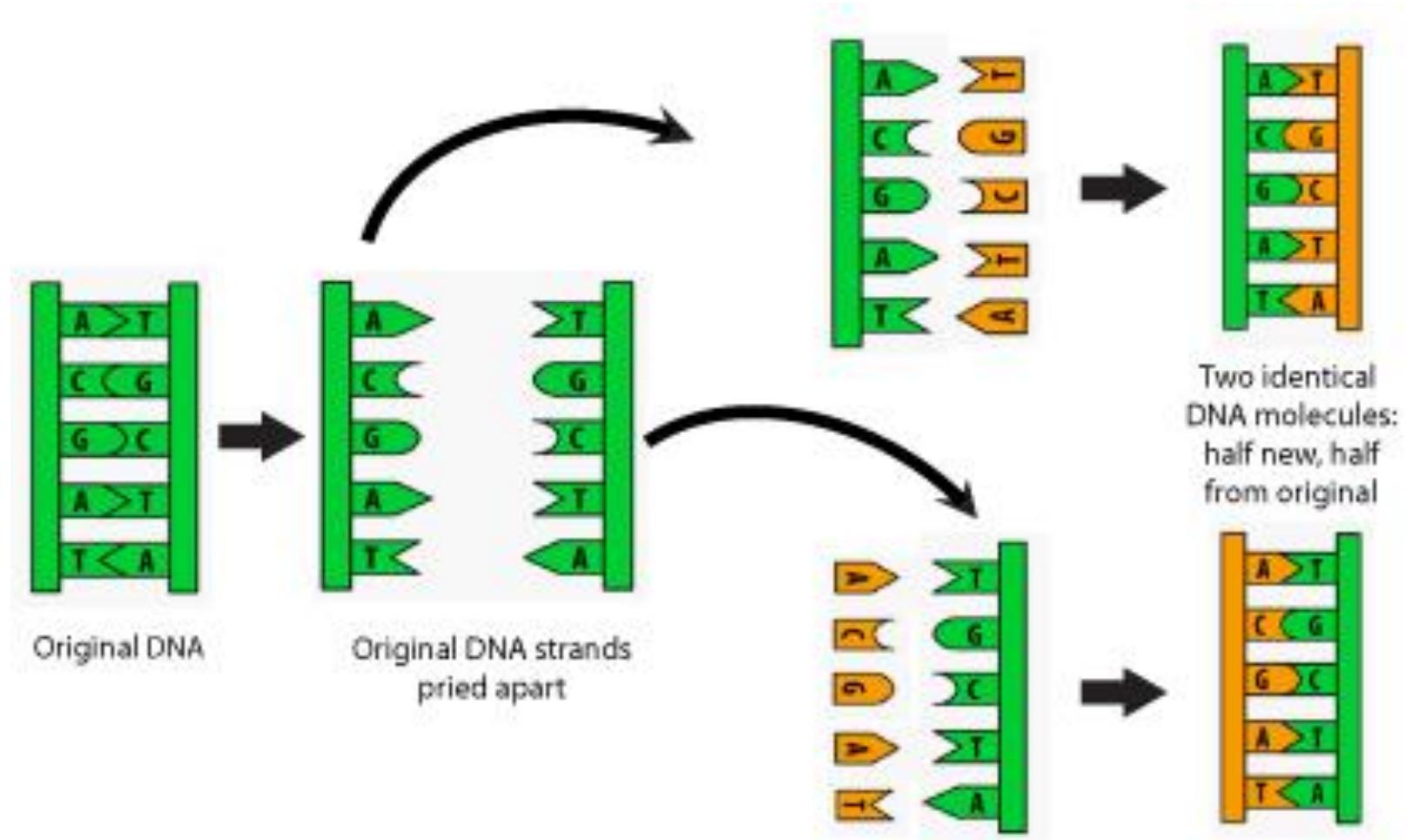


Other terminologies- Complementary strands

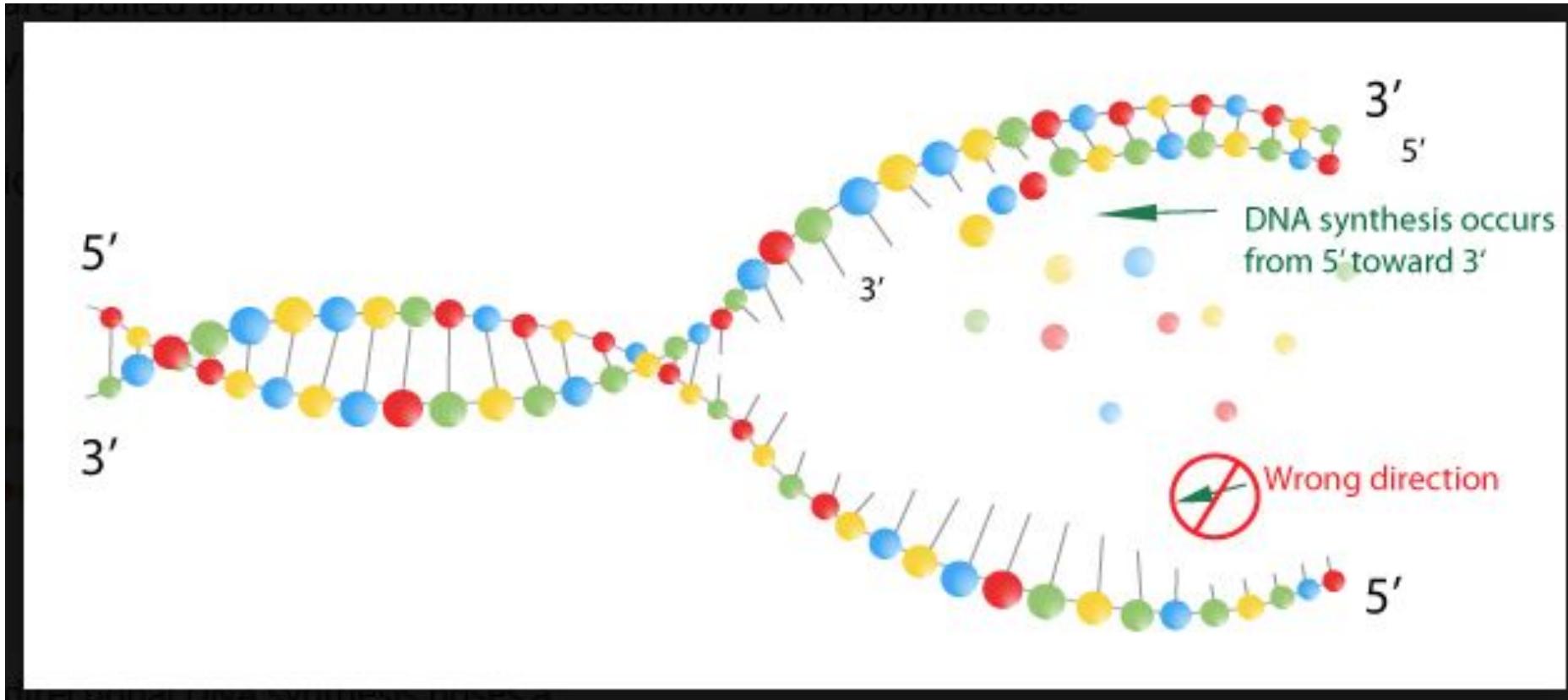
Replication- Making copies of DNA

Simple steps

1. Helicases-
Unwinds DNA
2. Polymerases-
Creates
Complementary
strand



Replication – More details pertaining to directionality



DNA to mRNA

5' TAC GCT GCT AGC TAG TCA 3'
3' 5' ??

3' ATG CGA CGA TCG ATC AGT 5'
5' UAC GCU GCU AGC UAG UCA 3'

5' TAC GCT GCT AGC TAG TCA 3'
3' ATG CGA CGA TCG ATC AGT 5'

Activity

- 5' TGG CCA TGC GCA AGC TGG TGC GCT CAG 3'
- 3' TGG CCA TGC GCA ACC TGG TGC GCT CAG 5'

Activity

Speed and Precision of DNA replication

- Polymerase 700 bp per sec
- Errors 1 in 10^7 nucleotides
- With proof-reading 1 in 10^9 nucleotides
- ATCTCTAGCTAGCTAGCTAGCTAGCTAGCAT

Genome

- The full genetic information of an organism
 - Contains all chromosomes
 - Comprises the coding & non-coding sequence data of the organism
 - Coding sequence data → part of the genome that encodes proteins
 - Non-coding (in earlier days: junk) DNA → part of the genome that does not encode proteins but still has a function
 - The function of non-coding DNA is only partially known
 - Non-coding DNA regulates protein processes

Difference between individuals

- Roughly only 0.1% of the 3 billion nucleotide human genome (or 3 million bases) are different
- Still, this leaves room for roughly 4 3,000,000 different genomes, and is for all intents and purposes an endless diversity between any two individuals.
- While specific individuals of the species may differ in some bases, the basic long DNA sequence is roughly the same in all members of the species. Of course, this handful of differences is critically important, and the large Human Diversity Project is underway to understand how various individuals differ. This will hopefully identify the mutations responsible for a number of genetic diseases

Difference between species

- The human genome - about 3 billion bases
- The fly genome has a scant 140 million bases.
- However, an analysis of the genomic sequences for two vastly different organisms (fruit flies and humans) has revealed that many genes in humans and flies are similar.
- As many as 99% of all human genes are conserved across all mammals!
- Some human genes show strong similarity across not only mammals and flies but also across worms, plants, and (worse yet) deadly bacteria. A species, then, is a collection of individuals whose genomes are “compatible,” in the sense of mating.

Evolution and Natural selection

- Some process must exist that generates new species from old ones. This process is called evolution.
- The theory that all living things have evolved through a process of incremental change over millions of years has been at the heart of biology since the publication in 1859 of Charles Darwin's On the Origin of Species.
- Filtering of mutations is called natural selection

Model Organism

- A species that is extensively studied/sequenced to understand particular biological phenomena, with the expectation that discoveries made for the model organism will provide insight into the workings of other organisms.
- Selection criteria:
 - easy experimental manipulation
 - ease of genetic manipulation
 - easy to grow
 - short life-cycle/generation times
 - easy to extract DNA data
 - Economical importance → rice
- Often researchers reverse-engineer organisms
- Full list of model organisms:
<http://www.life.umd.edu/labs/mount/Models.html>

Some Model Organisms

- *Escherichia coli*

gut bacterium → can cause food poisoning, grows fast, inexpensive to cultivate



- *Drosophila Melanogaster*

fruit fly → breeds quickly



- *Arabidopsis Thaliana*

flowering plant → small genome

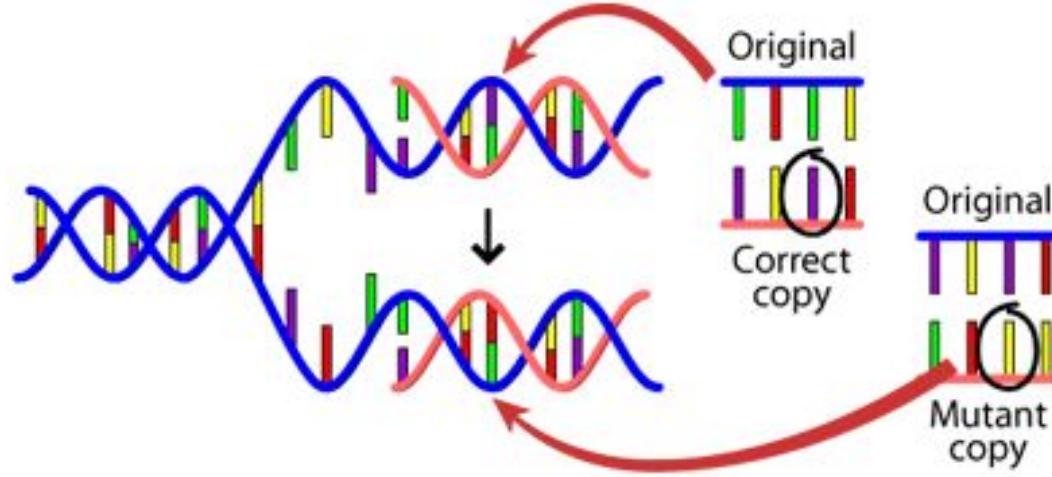


Types of mutations

- Substitution- Exchanges one base for another
- Insertion- Insertion of extra base pairs
- Deletion- Deletion of a base pair or sections of DNA
- Frame shift- Insertions or deletions resulting in altered proteins due to a shift in the frames.
- There are other types but the above ones are the basic.

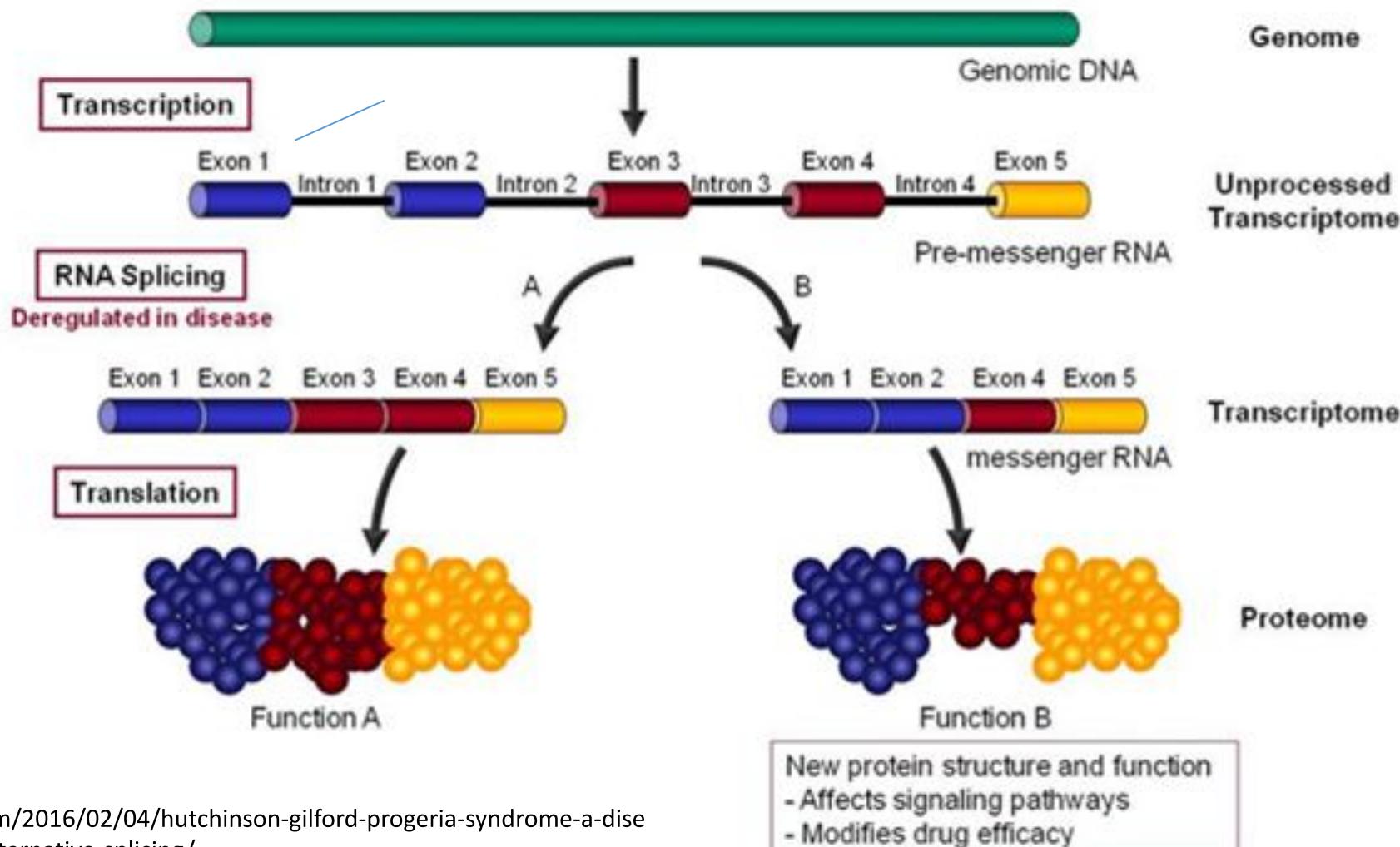
Causes of mutation

- DNA fails to copy accurately
- External influences can create mutations- harmful chemicals and radiation



- Cell can repair- But is not perfect

Hutchinson-Gilford Progeria Syndrome – a disease of accelerated aging due to Alternative Splicing



“HGPS is a major clue to solving the “puzzle of aging” and the molecular mechanisms here are relevant to normal aging. ”



<https://en.wikipedia.org/wiki/Progeria>