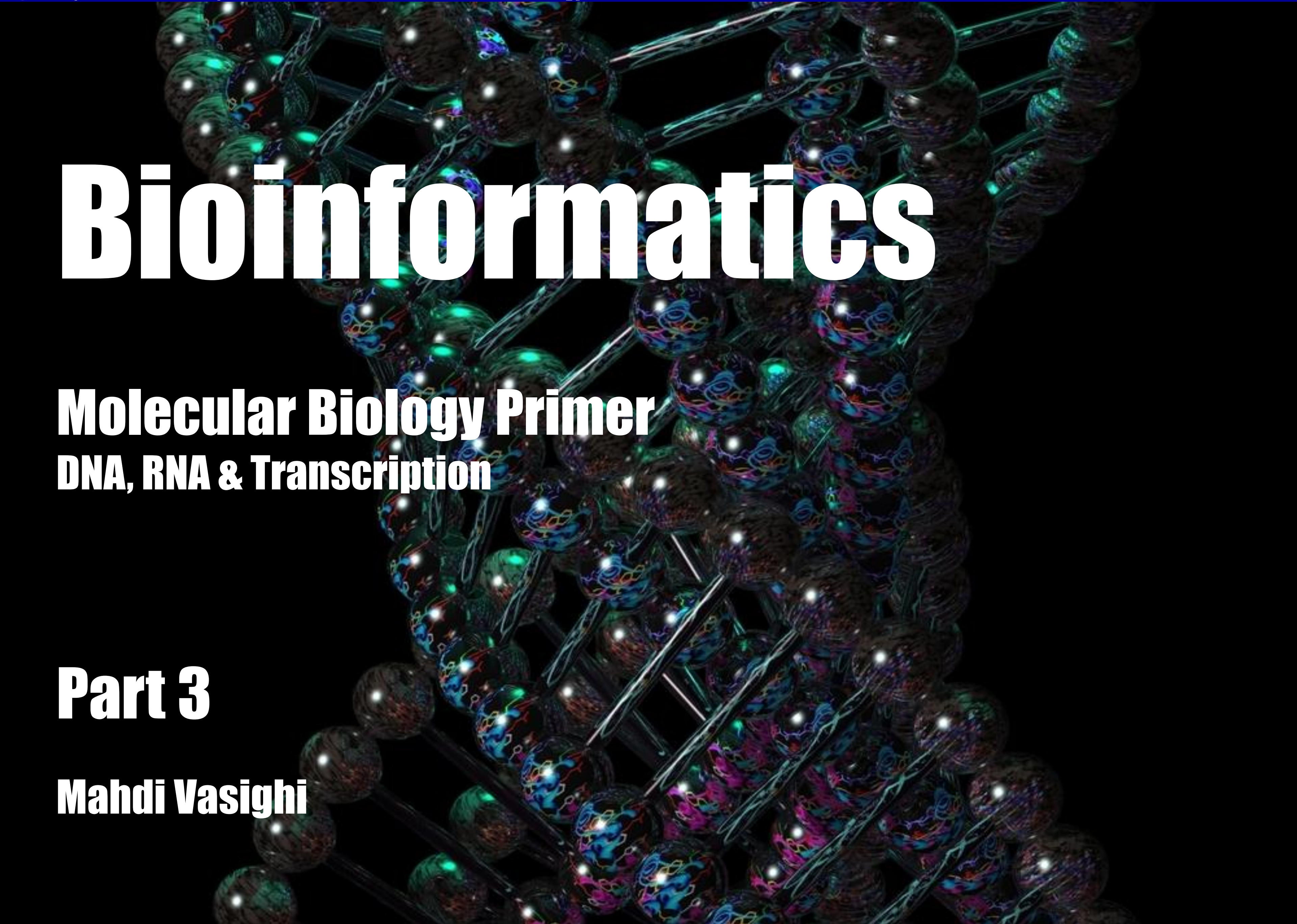


Bioinformatics

Molecular Biology Primer

DNA, RNA & Transcription

Part 3

Mahdi Vasighi

Weak forces and interactions

Ionic Interactions

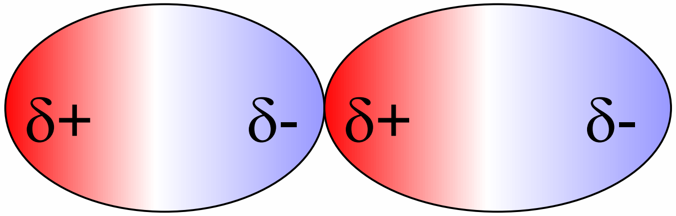
- result from the attraction of a positively charged ion (a cation) for a negatively charged ion (an anion).

Hydrogen bond

- interaction of a partially positively charged hydrogen atom in a molecular dipole (e.g., water) with unpaired electrons from another atom

Van der Waals forces

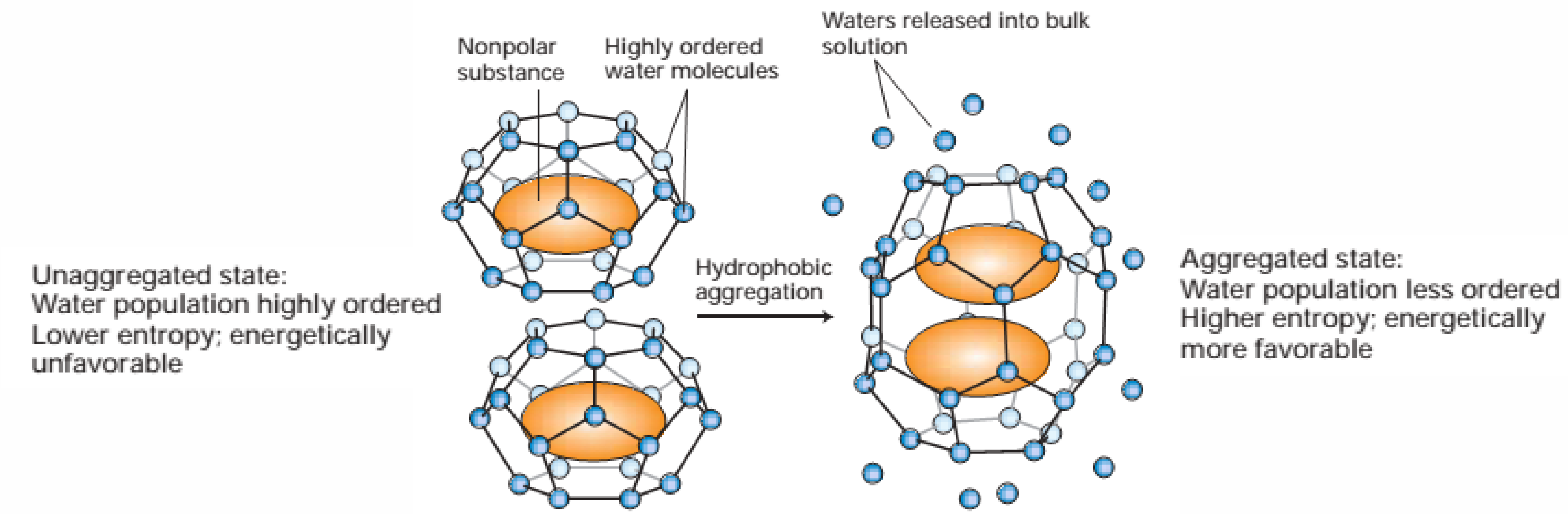
- two non-covalently bonded atoms are close enough together



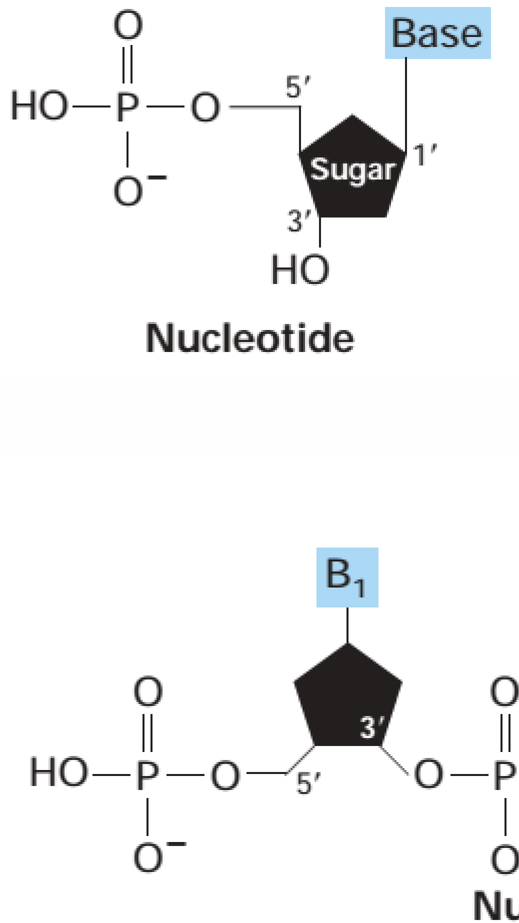
Weak forces and interactions

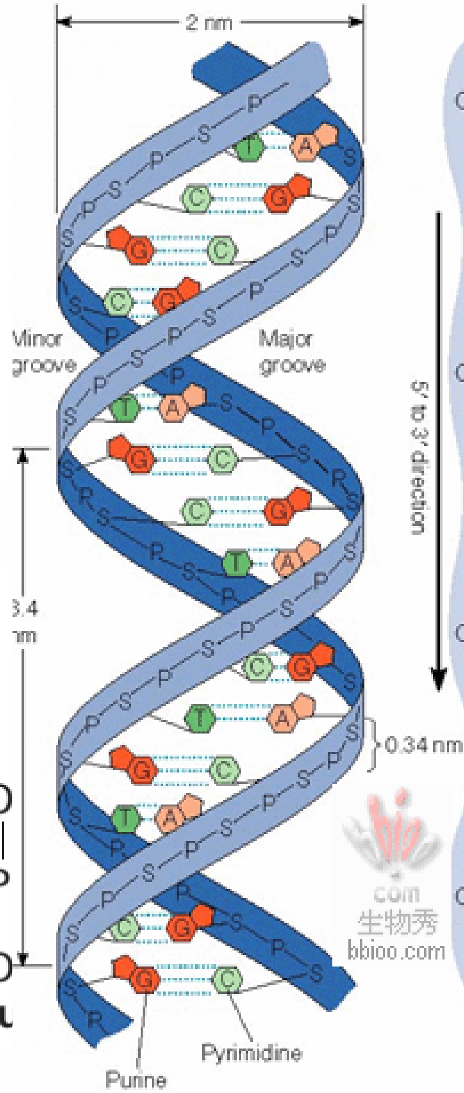
Hydrophobic Effect

- nonpolar molecules do not contain charged groups or become hydrated (hydrophobic)
- Nonpolar molecules or nonpolar portions of molecules tend to aggregate in water owing to a phenomenon called the **hydrophobic effect**.
- Because water molecules cannot form hydrogen bonds with nonpolar substances, they tend to form "cages"

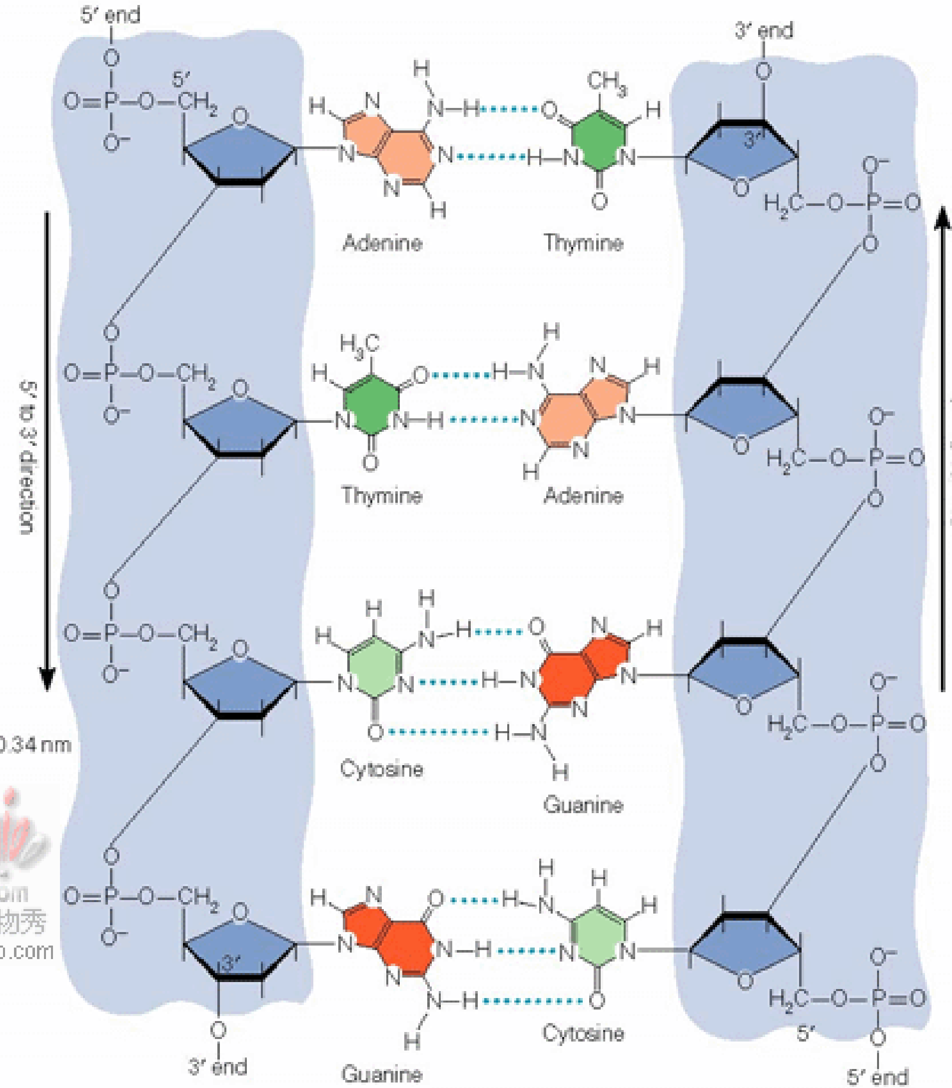


Deoxyribonucleic Acid : DNA





a) Double helix



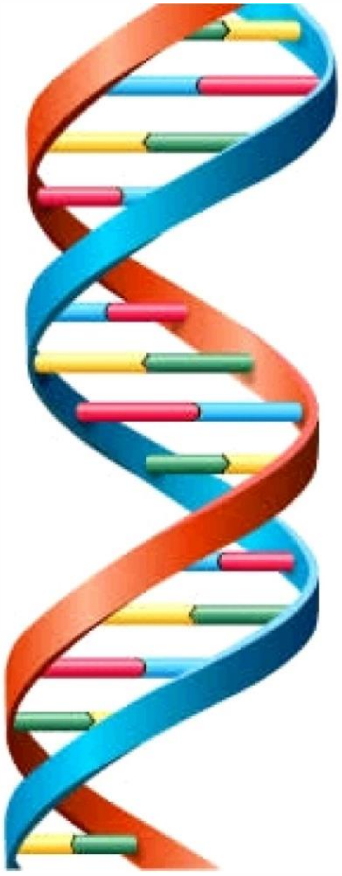
(b) Antiparallel orientation of strands

Deoxyribonucleic Acid : DNA

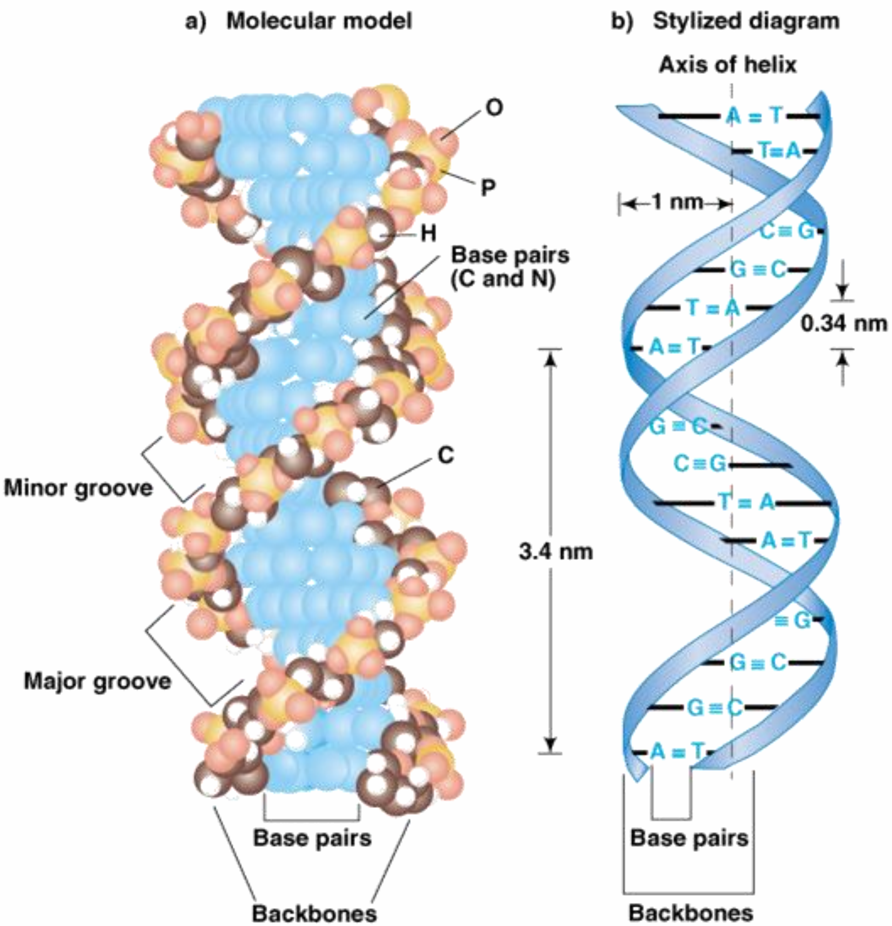
What Causes the Double Helix to Twist?

Imagine that you have two thin strands, each about 3.25 feet long, Now imagine fitting that thread into a water-filled container a few micrometers in diameter.

- **Size**: The space constraints require twisting to make the DNA more compact, and chemistry explains how the twisting happens.
- **Chemistry:** sugar and phosphate are both hydrophilic, or water-loving, while the bases are hydrophobic, or water-fearing.
- **Structure:** The spiral shape discourages water from flowing between them, and at the same time leaves room for the atoms of each chemical ingredient to fit without overlapping or interfering.
- **Stacking:** The stacking force attracts the bases above or below each other on the same strand.



Deoxyribonucleic Acid : DNA



DNA structure contains:

- major groove
- minor groove.

Given the difference in widths of the major groove and minor groove, many proteins which bind to DNA do so through the wider major groove.

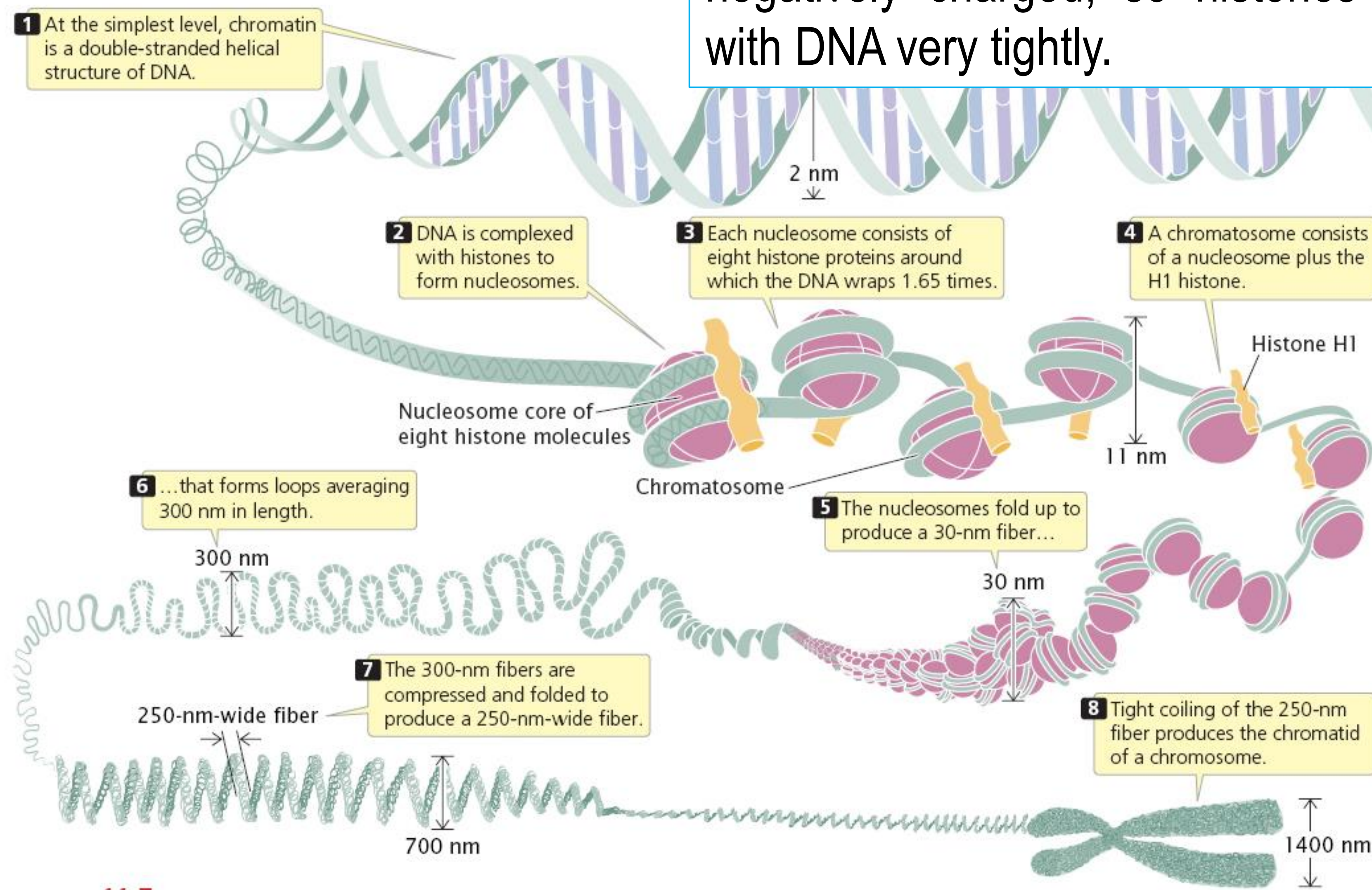
DNA Packaging

Each of us has enough DNA to reach from here to the sun and back, more than 300 times. How is all of that DNA packaged so tightly into chromosomes and squeezed into a tiny nucleus?

- Human genome contains approximately 6 billion base pairs of DNA per cell.
- Each base pair is around 0.34 nanometers long
- Each cell therefore contains about 2 meters of DNA.
- The human body contains about 50 trillion cells
- Certain proteins compact chromosomal DNA into the microscopic space of the eukaryotic nucleus. These proteins are called **histones.**

DNA Packaging

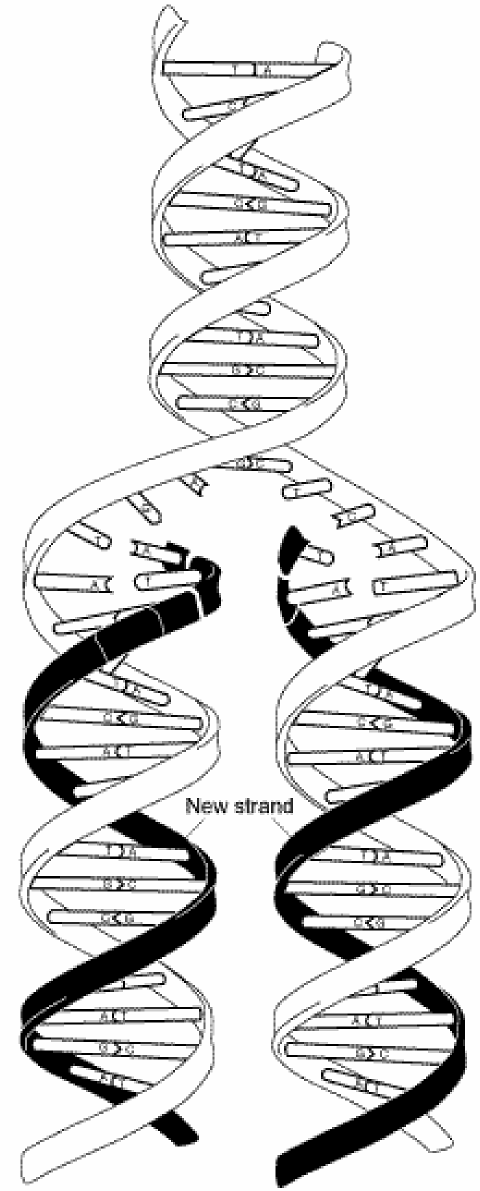
- **Histones** are a family of small, positively charged proteins. DNA is negatively charged, so histones bind with DNA very tightly.



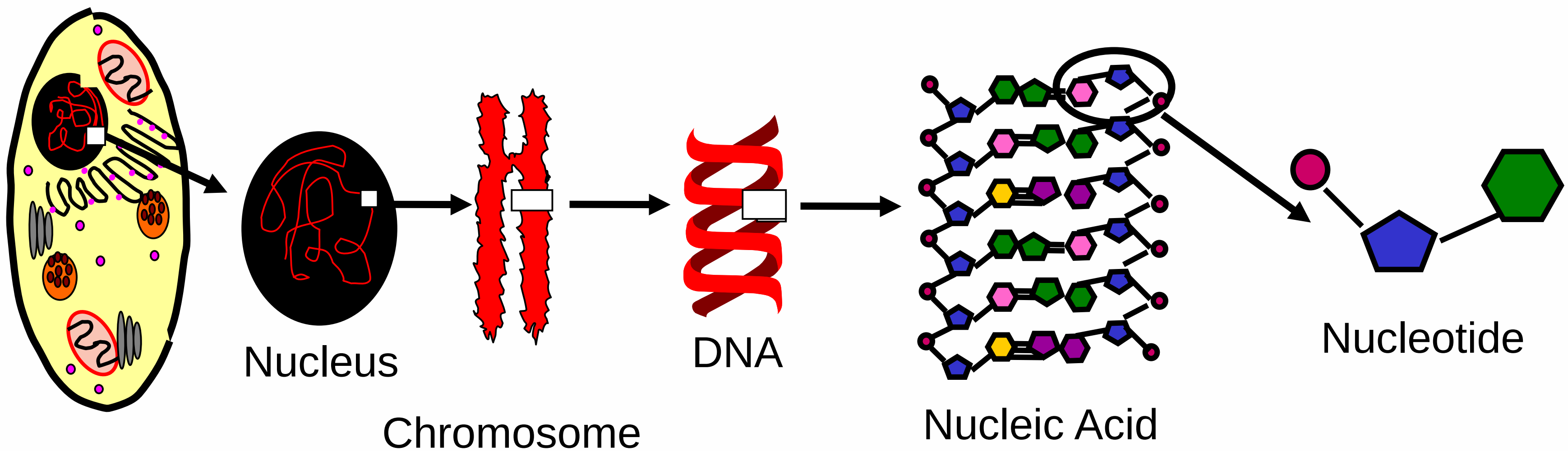
DNA Replication

DNA replication is a biological process that occurs in all living organisms and copies their DNA; it is the basis for biological inheritance. The process starts with one double-stranded DNA molecule and produces two identical copies of the molecule.

- A number of proteins are associated and assist in the initiation and continuation of DNA replication.



How does DNA control cell functions



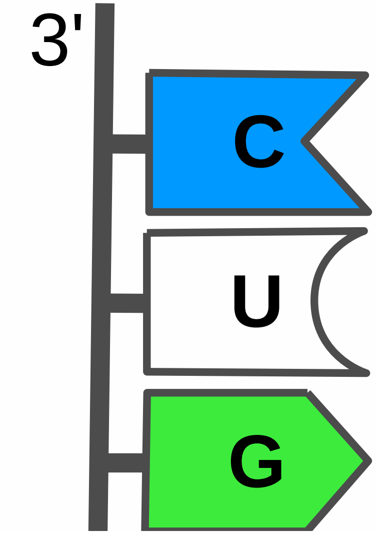
DNA stays in nucleus. A **messenger** is needed to control things!

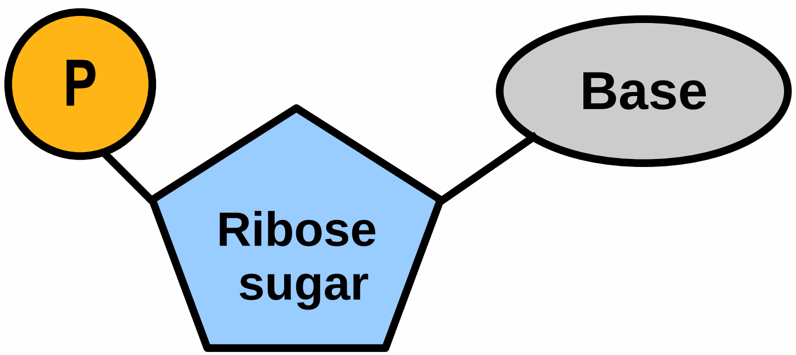
Ribonucleic Acid (RNA)

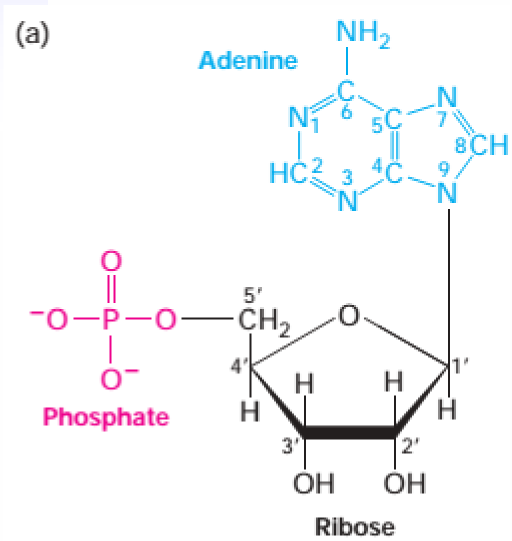
RNA is made up of a long chain of components called nucleotides. Each nucleotide consists of

- a nitrogenous base,
- a ribose sugar, and
- a phosphate group.

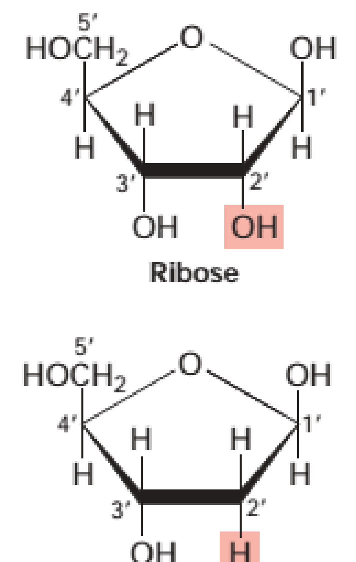
Adenine
Uracil
Guanine
Cytosine







Adenosine 5′-monophosphate (AMP)



Ribose

2-Deoxyribose

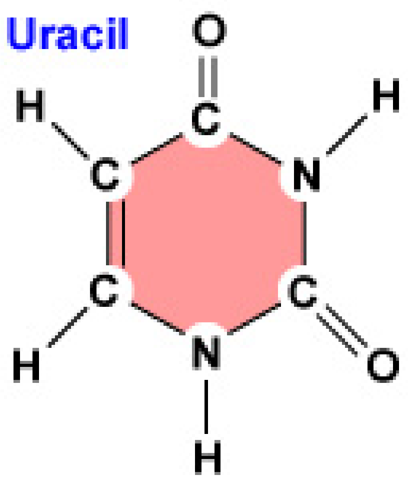
Ribonucleic Acid (RNA)

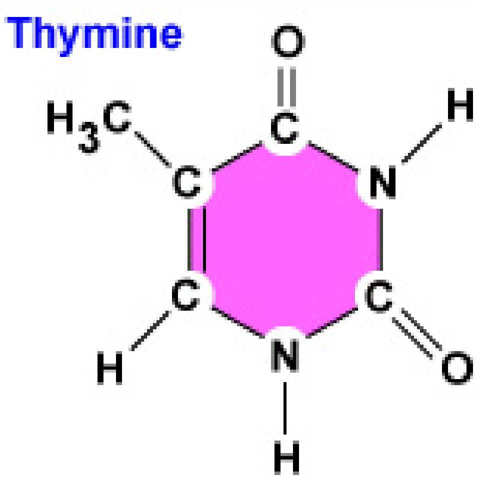
RNA

- Single strand
- Ribose sugar
- Uracil replaces Thymine!
- Found in nucleus & Cytoplasm

DNA

- Double Helix
- Deoxyribose sugar
- Adenine pairs with Thymine
- Found in nucleus

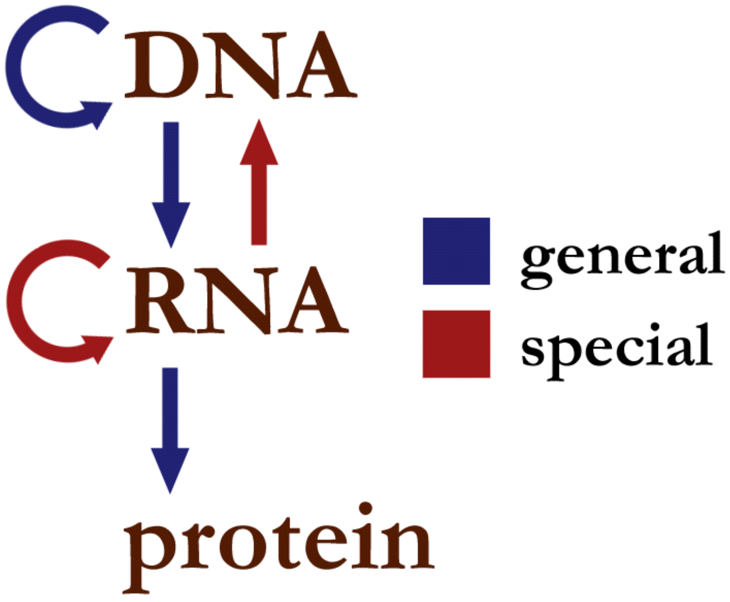




Central dogma of molecular biology

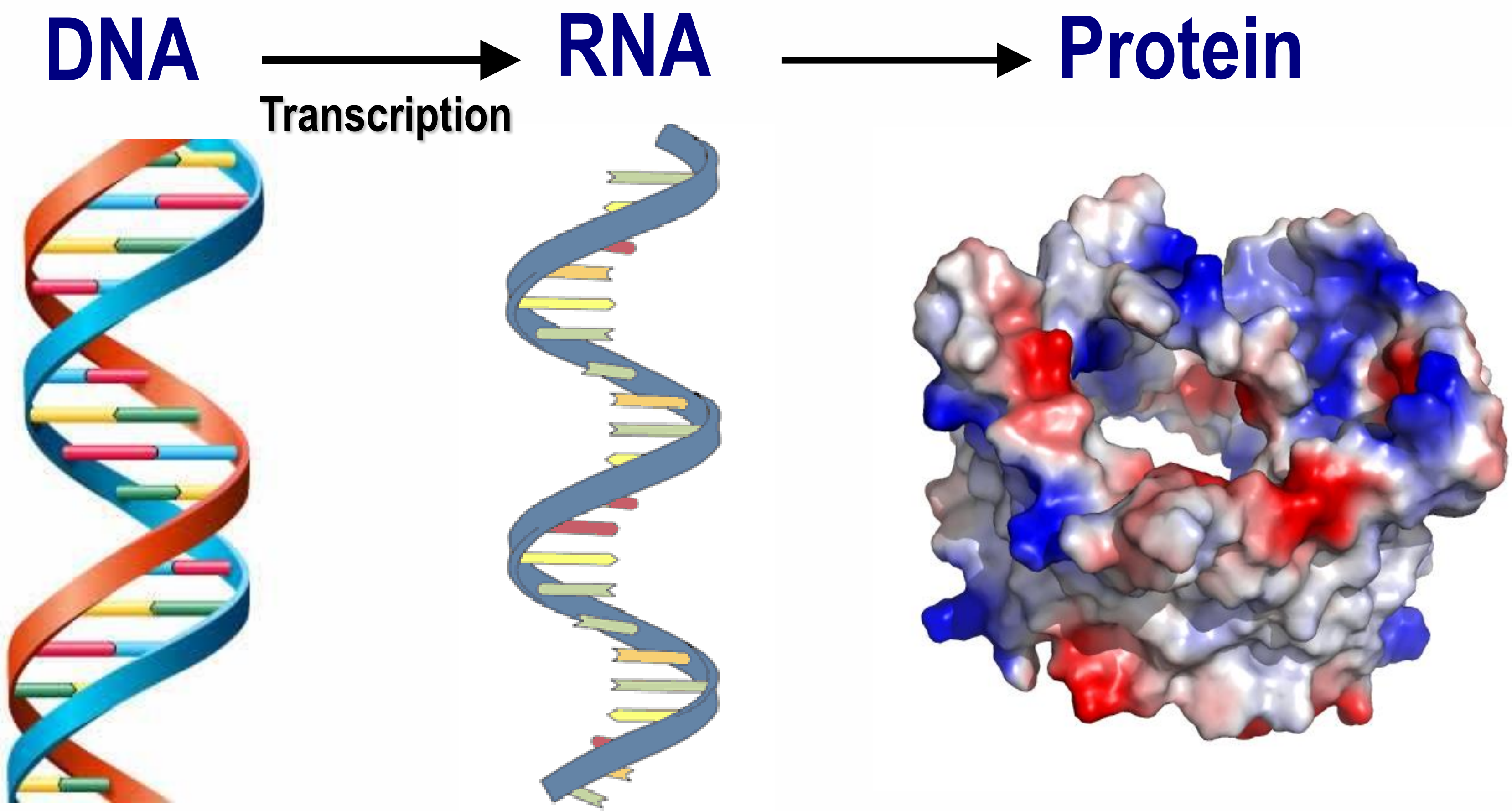
The central dogma of molecular biology deals with the detailed residue-by-residue transfer of sequential information. It states that such information cannot be transferred back from protein to either protein or nucleic acid.

There are 3 major classes of biopolymers: DNA and RNA (both nucleic acids), and protein.



General	Special	Unknown
DNA → DNA	RNA → DNA	protein → DNA
DNA → RNA	RNA → RNA	protein → RNA
RNA → protein	DNA → protein	protein → protein

Central dogma of molecular biology



Transcription

DNA ⟶ RNA

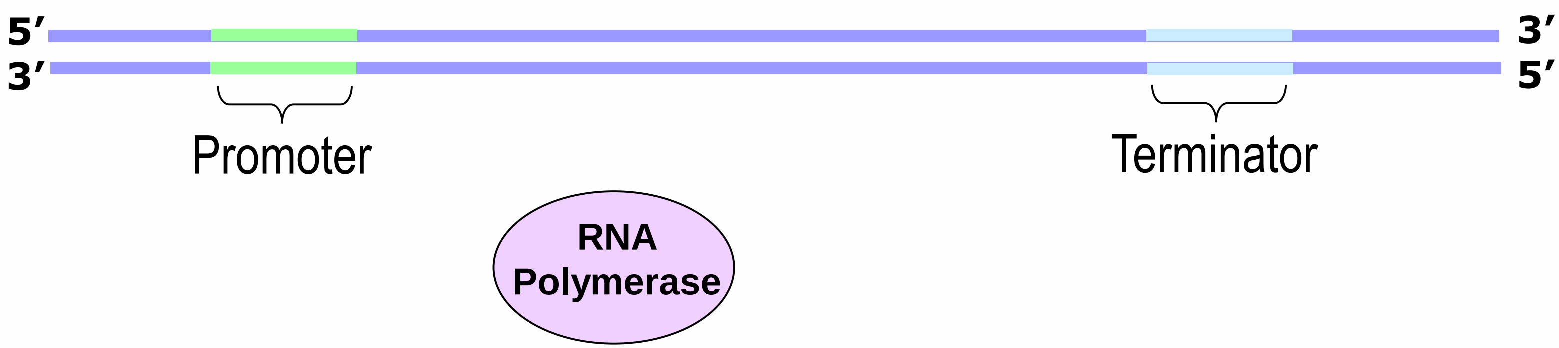
Transcription is the process of creating a complementary RNA copy of a sequence of DNA.

During transcription, a DNA sequence is read by RNA polymerase, which produces a complementary RNA strand.

Transcription can be explained easily in 4 steps.

Transcription

Step 1: RNA polymerase (RNAP) unwinds the DNA by breaking the hydrogen bonds between complementary nucleotides. (Binding RNA polymerase)



Promoters are regions of DNA that promote transcription and, in eukaryotes, are found at -30, -75, and -90 base pairs upstream from the transcription start site

RNAP is an enzyme that polymerizes ribonucleotides at the 3' end of an RNA transcript.

Transcription

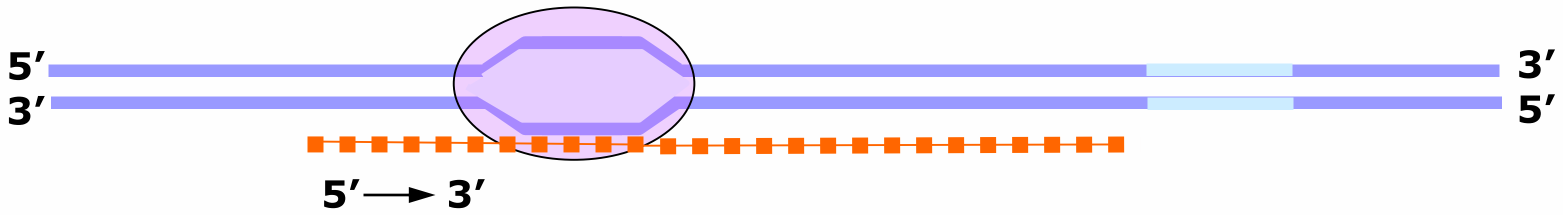
Step 1: RNA polymerase (RNAP) unwinds the DNA by breaking the hydrogen bonds between complementary nucleotides. (Binding RNA polymerase)

Transcription

Step 2: RNA nucleotides are paired with complementary DNA bases. (Initiation of RNA synthesis)

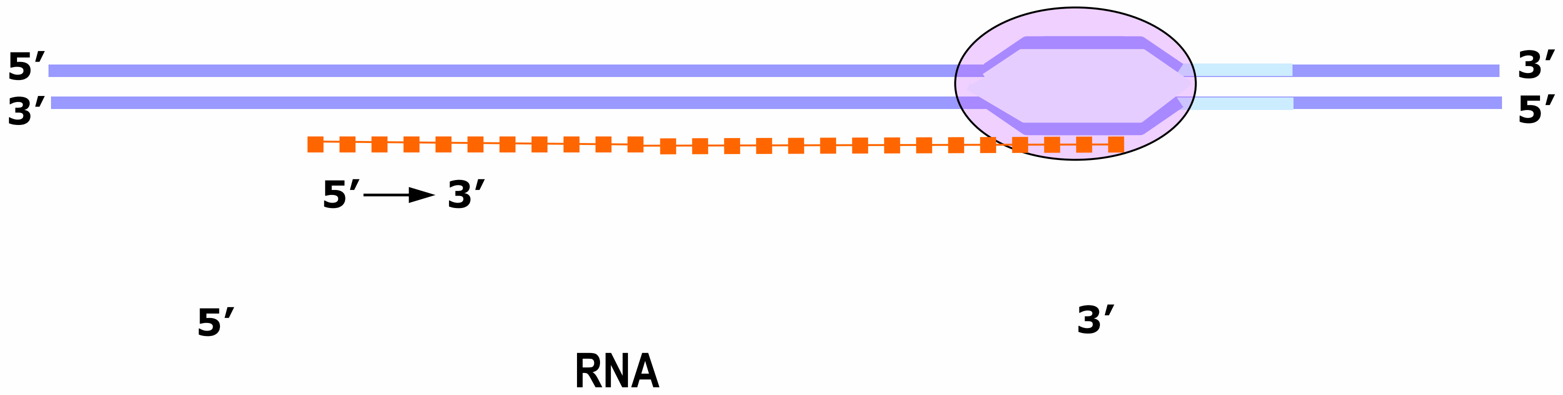
Transcription

Step 3: RNA sugar-phosphate backbone forms with assistance from RNA polymerase. (Elongation of RNA)

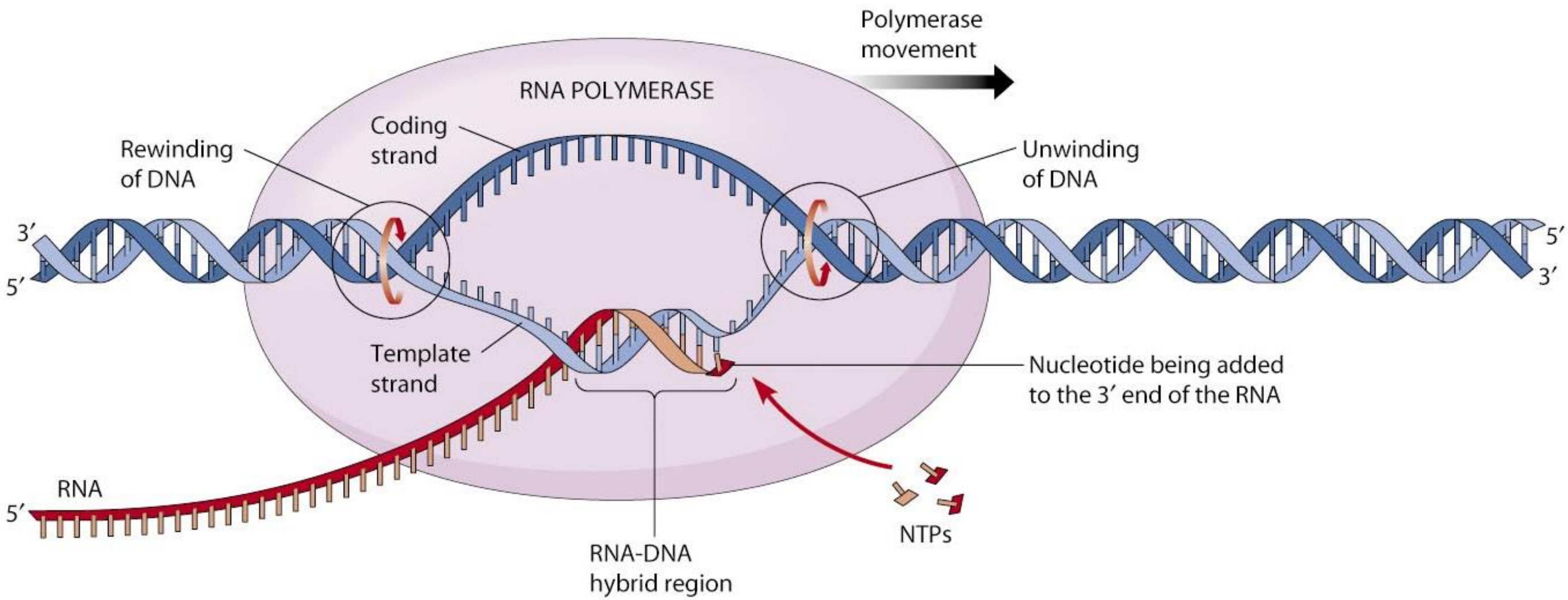


Transcription

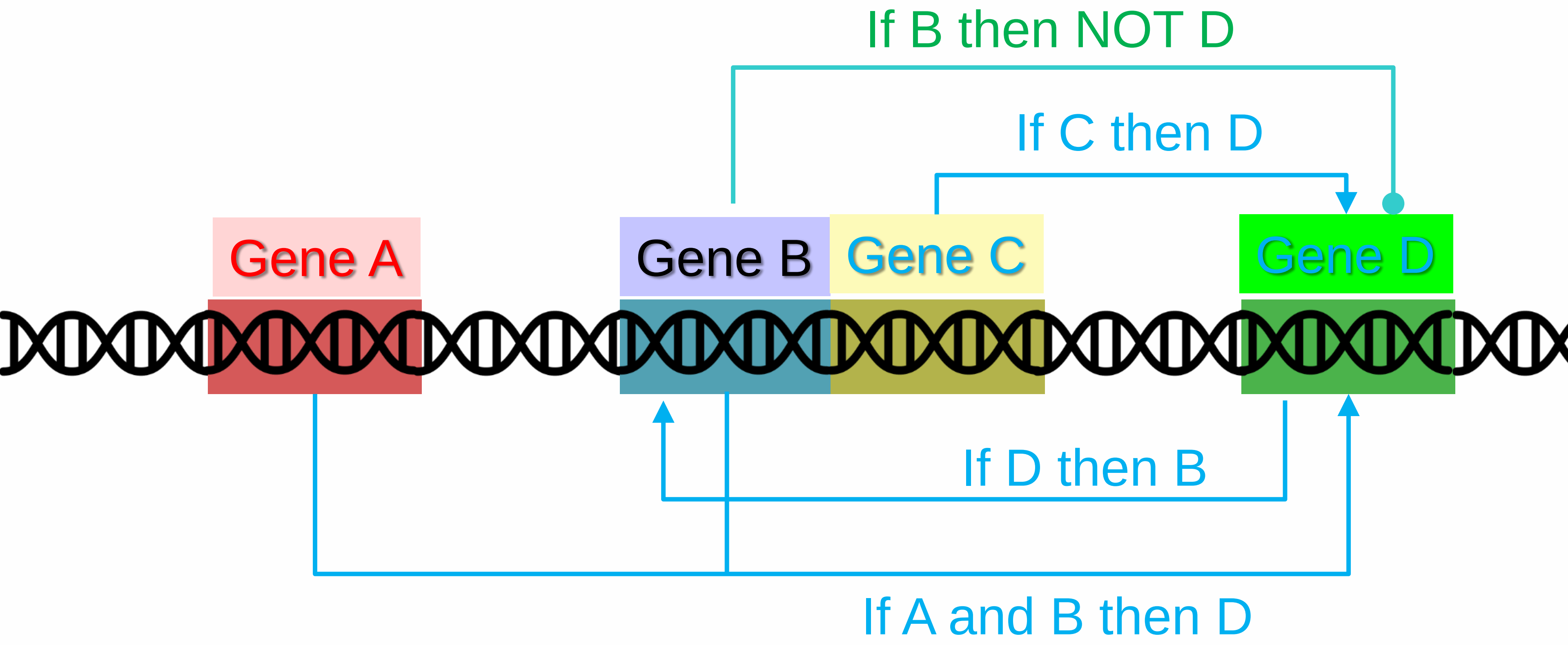
Step 4: RNA polymerase leaves DNA. RNA strand is released. DNA rewinds itself into the double helix. (Termination)



Transcription

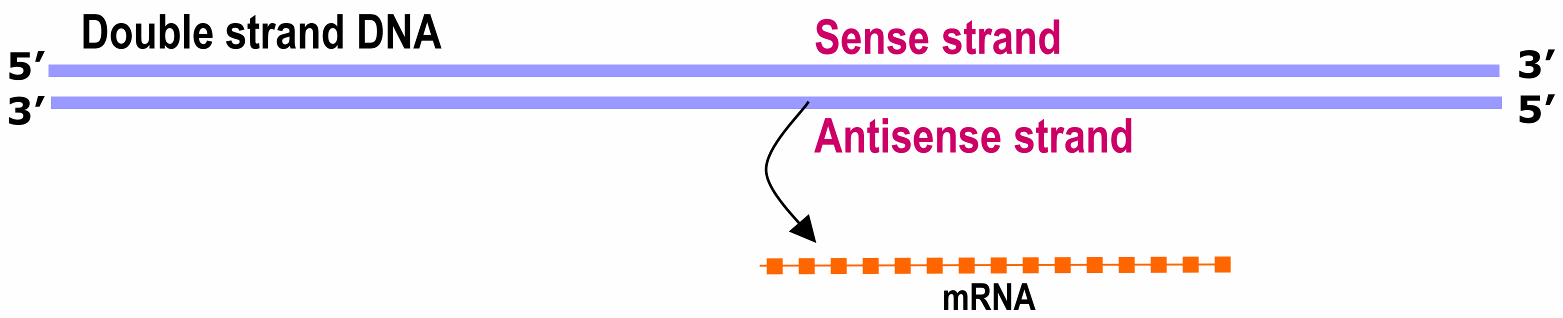


Transcription



Transcription

The two complementary strands of double-stranded DNA (dsDNA) are usually differentiated as the "sense" strand and the "antisense" strand. The DNA sense strand looks like the messenger RNA (mRNA).



It is ultimately the gene product, or mRNA, that dictates which strand of one segment of dsDNA we call sense or antisense.

Transcription

The two complementary strands of double-stranded DNA (dsDNA) are usually differentiated as the "sense" strand and the "antisense" strand. The DNA sense strand looks like the messenger RNA (mRNA).

Sense	5′	T T A A C C G G A C G T A C G T T C C	3′
Anti-sense	3′	A A T T G G C C T G C A T C C A A G G	5′

↓ Transcription

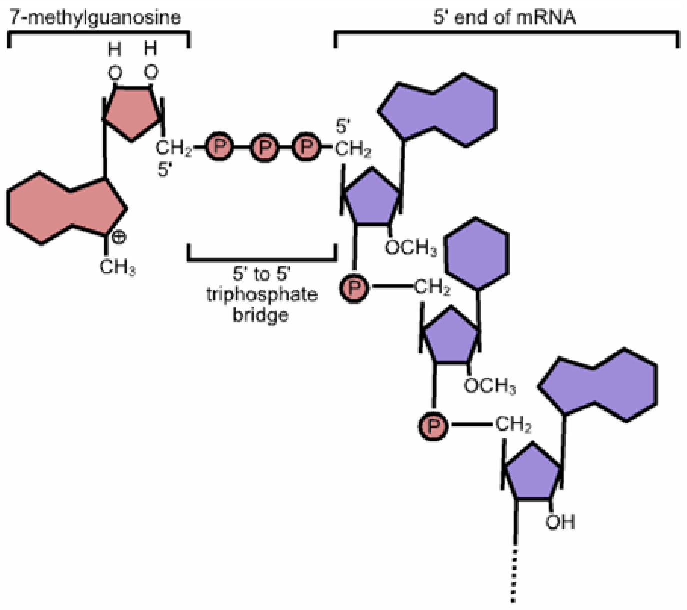
mRNA	5′	U U A A C C G G A C G U A G G U U C C	3′

Transcription

The brief existence of an mRNA molecule begins with transcription and ultimately ends in degradation.
During its life, an mRNA molecule may also be processed, edited, and transported prior to translation.

5' cap addition:

To give the mRNA stability, a 5 prime "cap" (a guanosine nucleotide methylated at the 7th position) is joined to the 1st nucleotide in an unusual "5 prime to 5 prime" linkage.



Transcription

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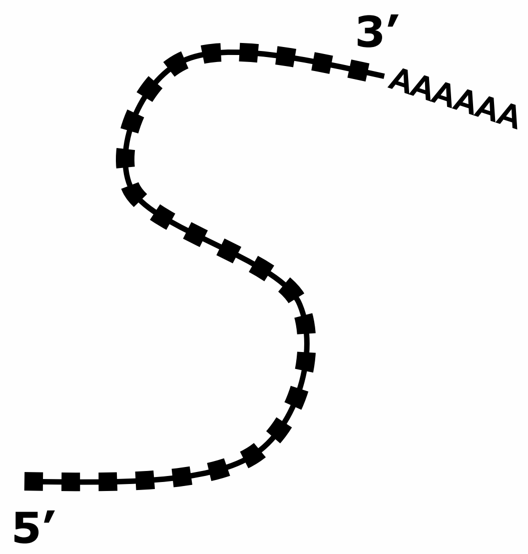
Addition of a poly-A tail (polyadenylation):
The poly(A) tail consists of multiple adenosine monophosphates; in other words, it is a stretch of RNA that has only adenine bases.

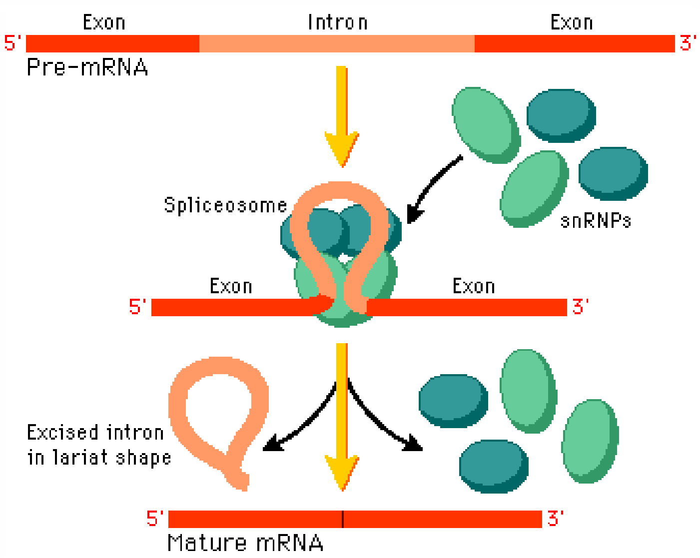


Transcription

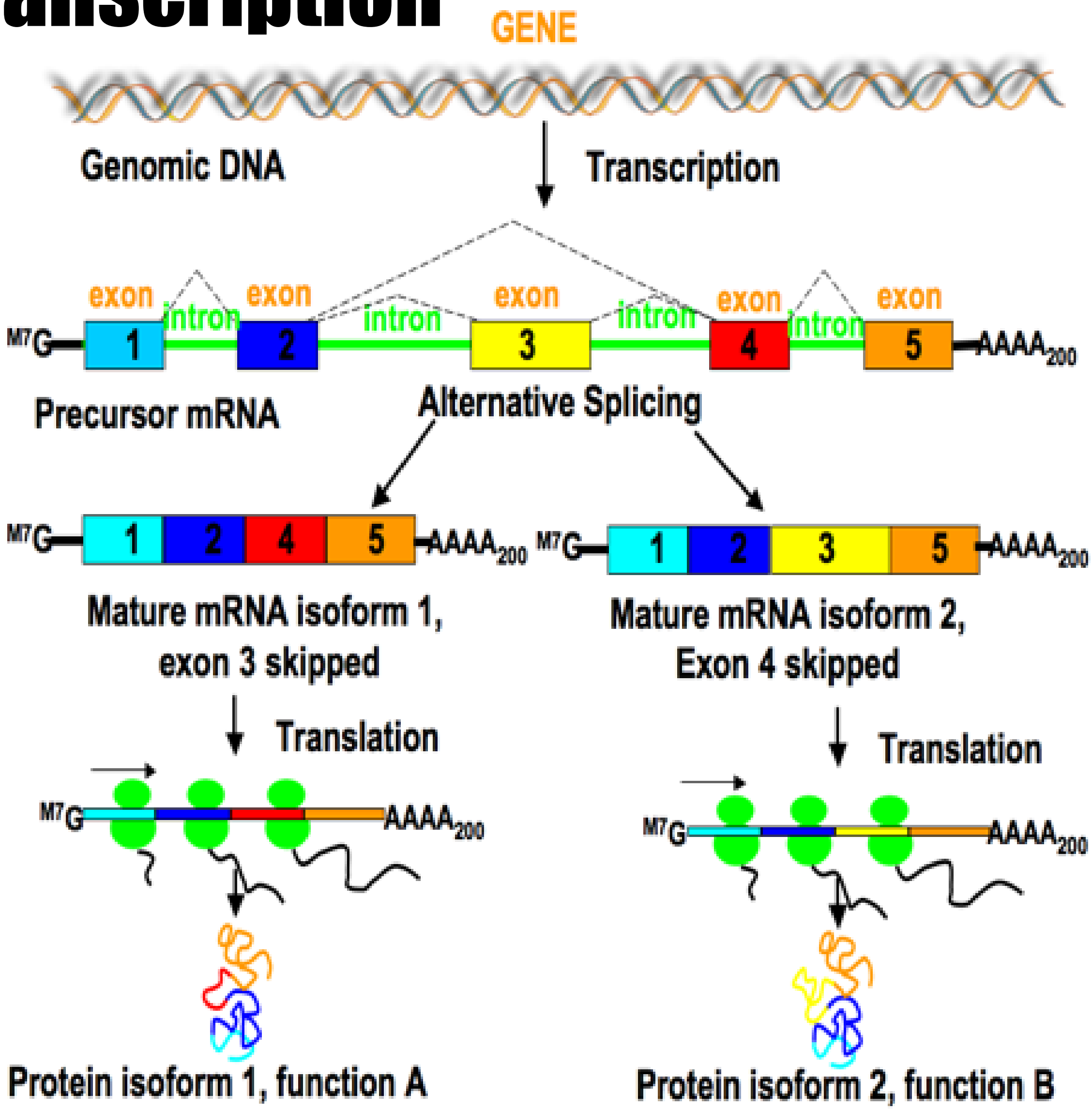
The brief existence of an mRNA molecule begins with transcription and ultimately ends in degradation.
During its life, an mRNA molecule may also be processed, edited, and transported prior to translation.

RNA splicing:

Splicing is the process by which pre-mRNA is modified to remove certain stretches of non-coding sequences called **introns**; the stretches that remain include protein-coding sequences and are called **exons**.



Transcription



http://bitesizebio.com/10148/what-is-alternative-splicing-and-why-is-it-important/