Lecture 8:

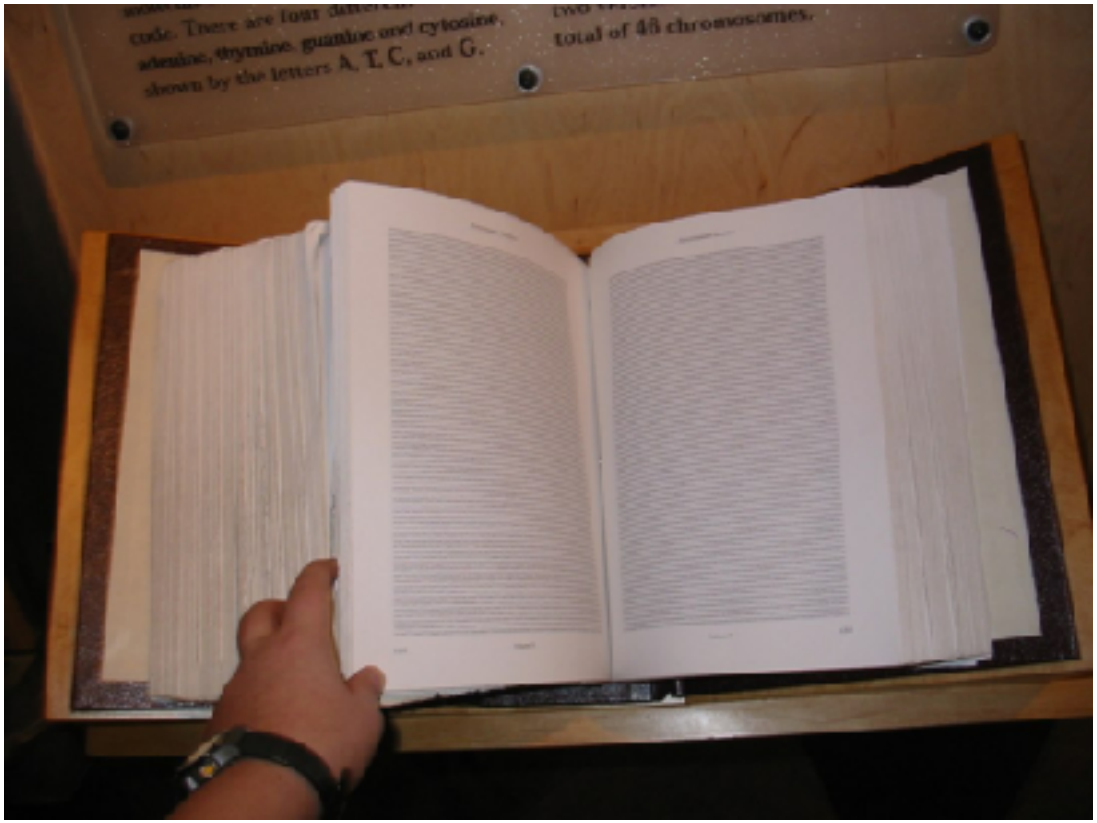
The chemical composition of the genetic material

Course 371

AIMS

- Introduce the chemical composition of nucleic acids
- Introduce the basic units of DNA and RNA (similarities and differences).
- Introduce the chemical bonds that links each chemical component of a nucleotide to one another.
- Go over the reasons for the reaction to take place as it does.

The genome in a cell?



The Wellcome collection in London.
The human genome printed using font size (5)!

The genome in a cell?

- If we print the genome using font size 12 and stretch the letter, it would go ~ from Kuwait to Spain!
- A lot of information. How is it packaged in a 100 trillion tiny little human cells (1-100 um)?

Nucleic acids

We have established that DNA is the genetic code.

What is it composed of?

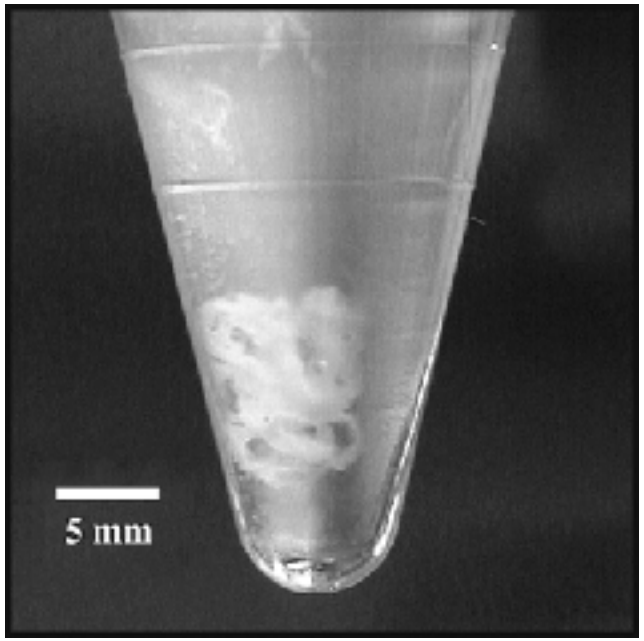
If DNA is the genetic code, what is RNA?

What's up with these weird names?

Nucleic acids

- DNA and RNA are organic compounds belong to a class called **Nucleic acids.**

- We will learn the similarities and differences between them.

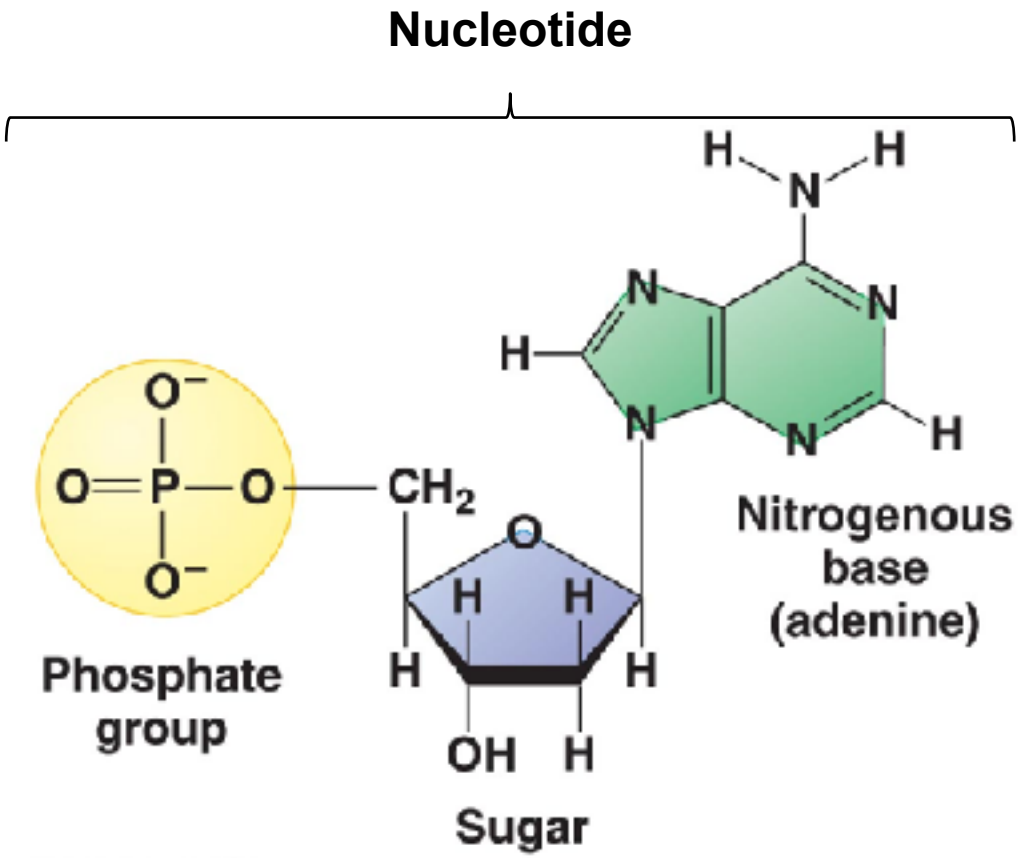


DNA and RNA chemical unit

- The chemical unit that makes nucleic acids (DNA and RNA) is called **Nucleotide.**

- A **nucleotide** is composed of:

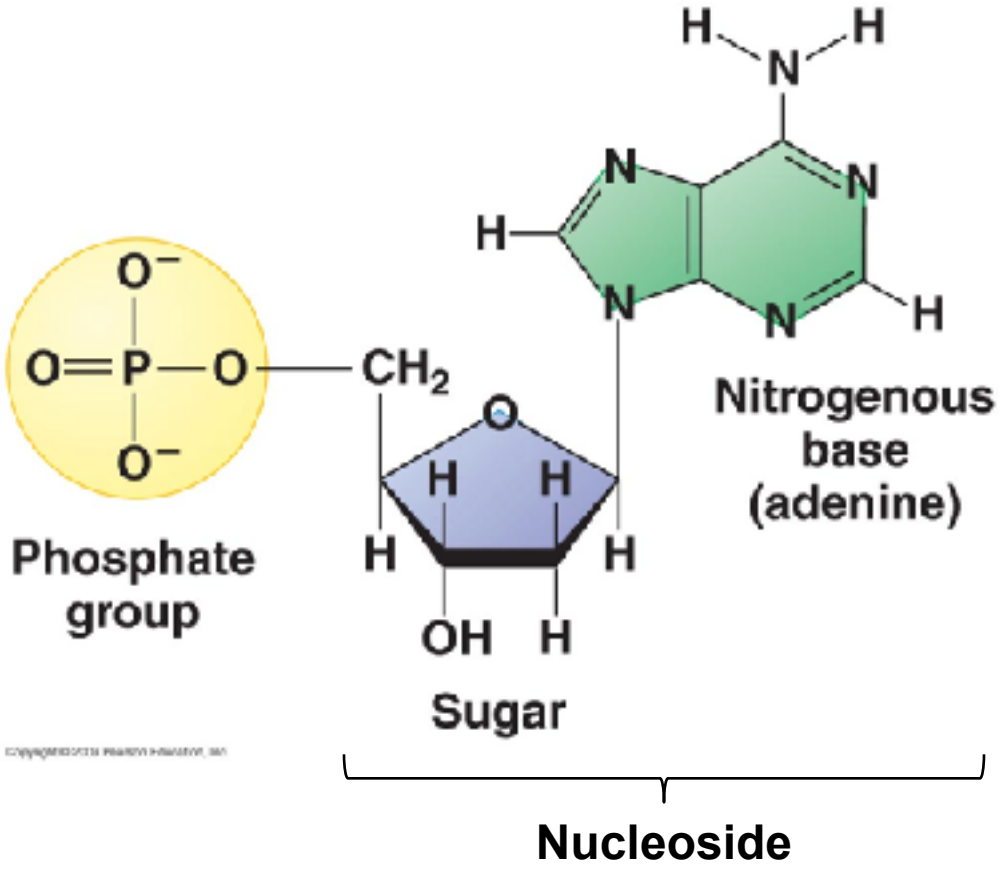
1. Sugar
2. Phosphate group
3. Nitrogenous base



DNA and RNA chemical unit

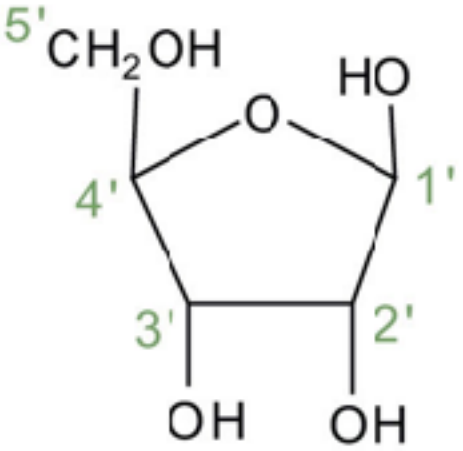
- A **nucleoside** is a part of the nucleotide and is composed of:

1. Sugar
2. Nitrogenous base

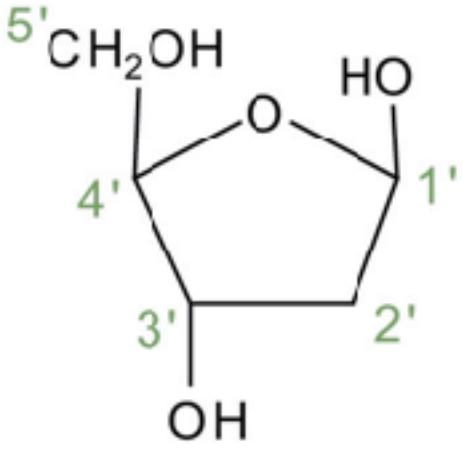


The sugar

- The sugar in DNA and RNA is **almost** the same.
- The sugar is a pentose (5 carbon sugar) – count them and know the carbon's numbers.

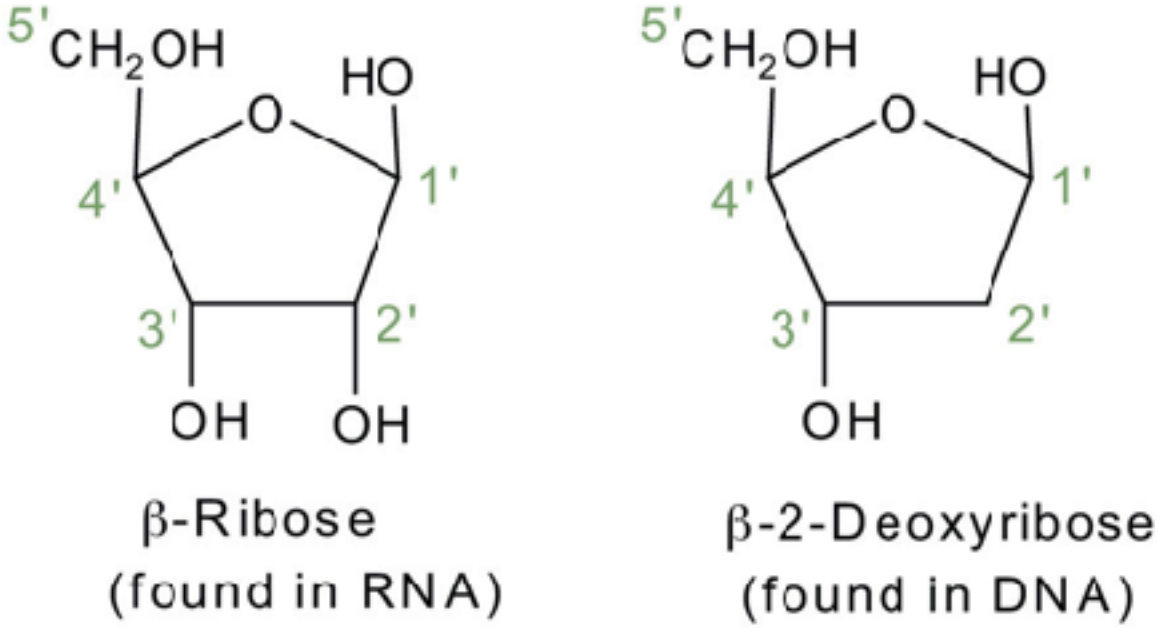


β-Ribose
(found in RNA)



β-2-Deoxyribose
(found in DNA)

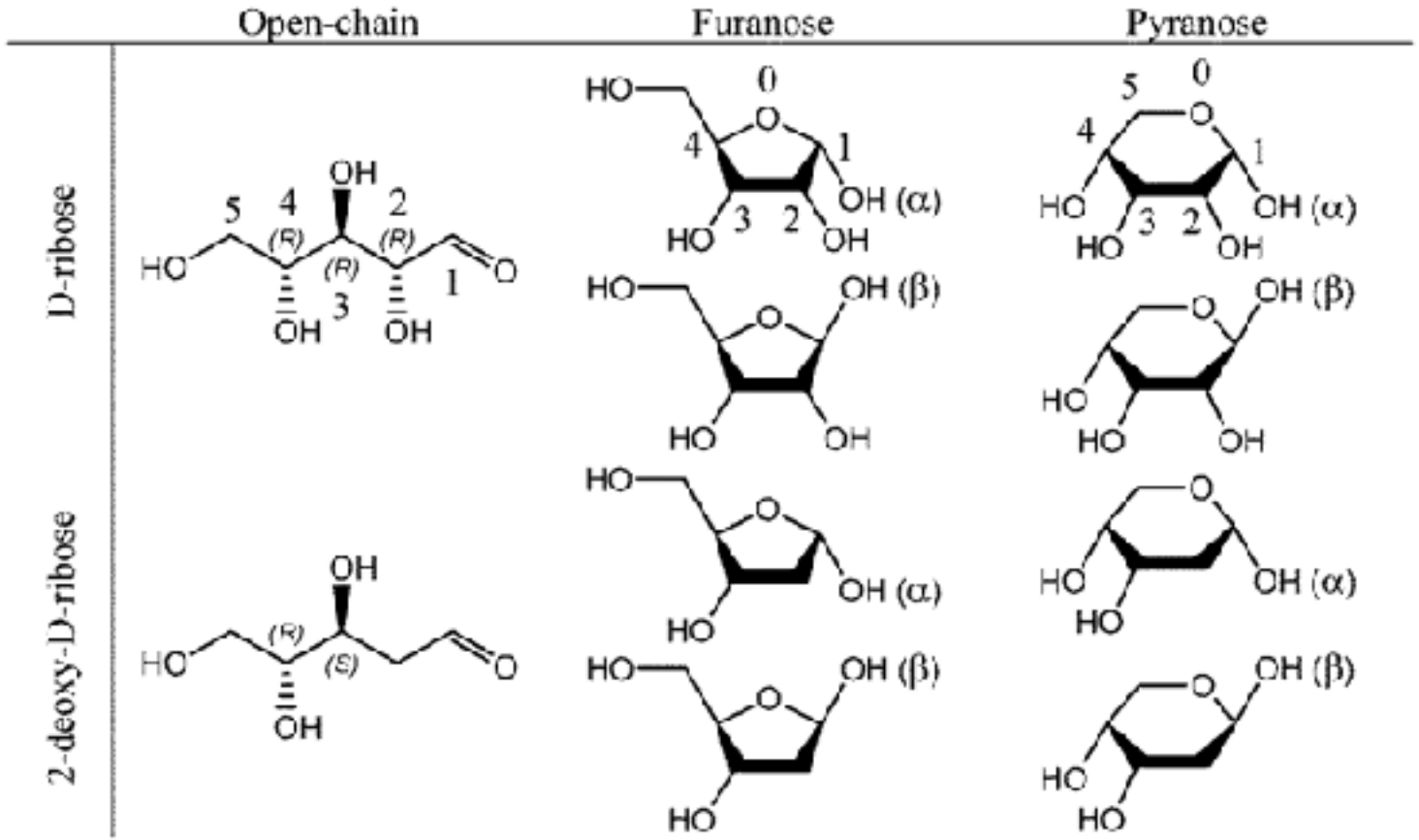
The sugar



- RNA's sugar is **ribose.** Hydroxyl group (OH) on most carbons.
- DNA's is **deoxy ribos.** 2-deoxy-ribose (with out OH on carbon #2)

The sugar

- The sugar in DNA and RNA is **Beta-furansoe**.
- 5 atoms ring.
- Position of the OH at carbon 1.



The sugar

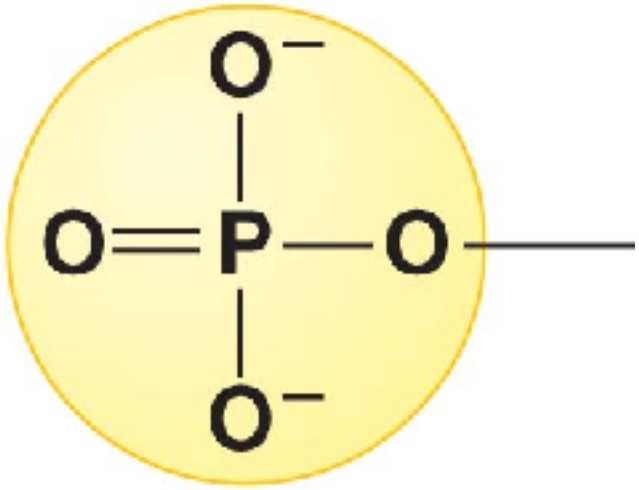
Why the carbons of the ribose sugar are numbered in the way shown earlier?

The sugar

Why is important to have the (R) group at carbon 1 to be in a Beta formation?

The phosphate group

- The phosphate group is attached to carbon #5 of the sugar.
- It is essential for the formation of DNA and RNA backbone and linking the nucleotides (we will see later).
- It is the reason for the negative charge of DNA and RNA.

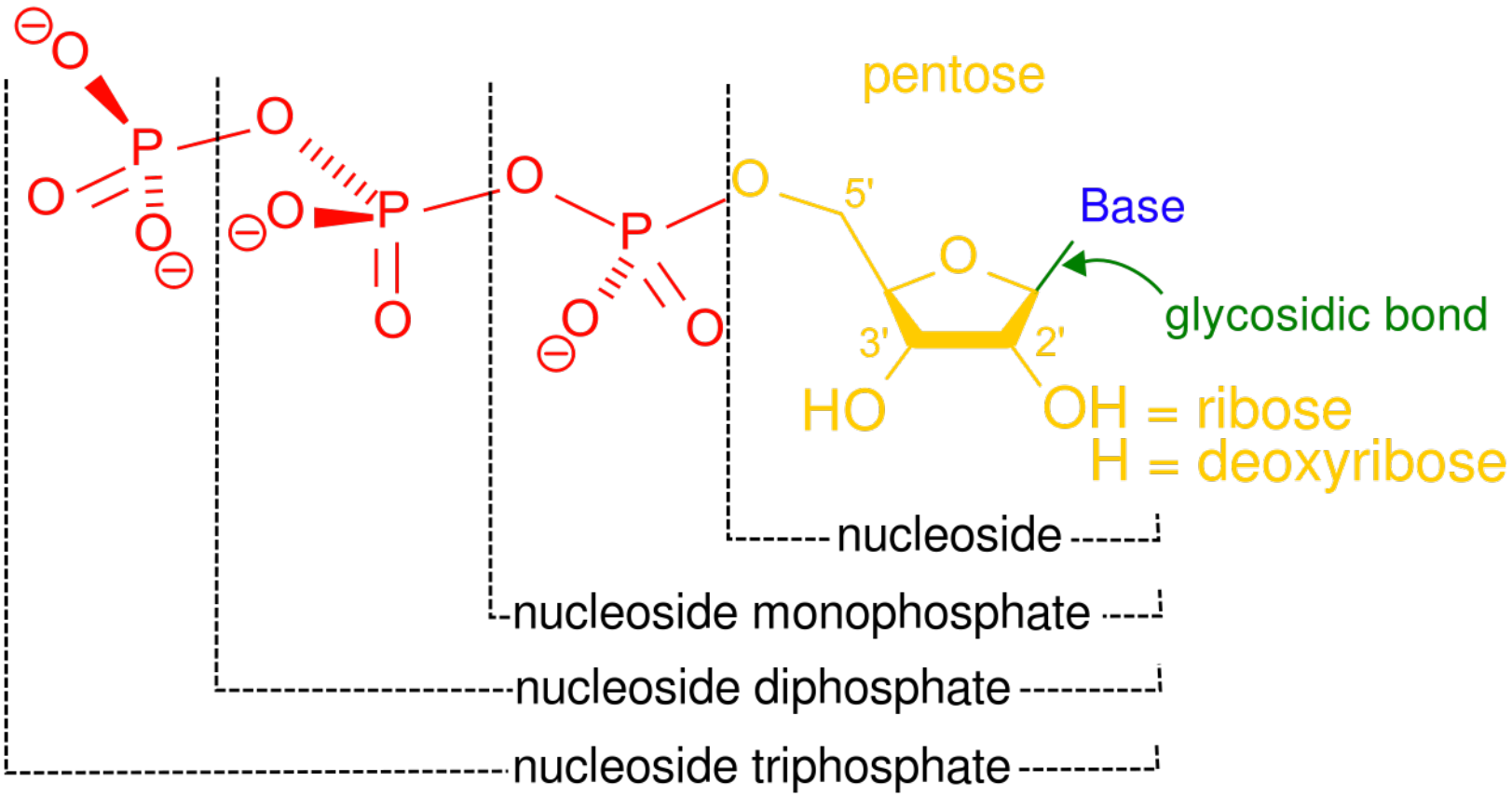


The phosphate group

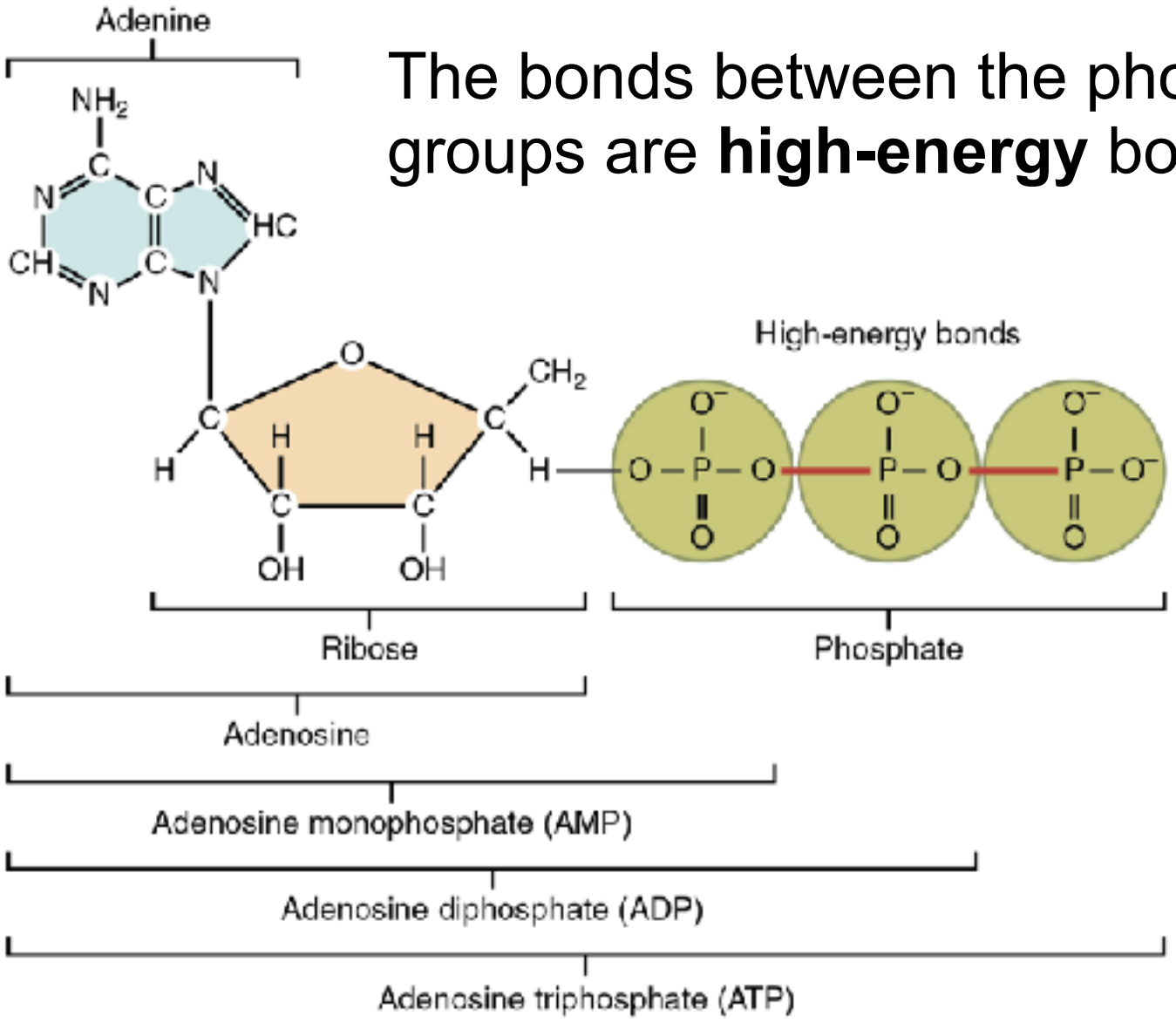
Which one is carbon #5 on the sugar?

The phosphate group

- A number of phosphate groups can be attached to carbon 5 of the sugar.
- NTPs? dNTPs?



DNA and RNA chemical unit



The bonds between the phosphate groups are **high-energy** bonds.

The nucleotide bases

Nitrogenous bases

Small bases

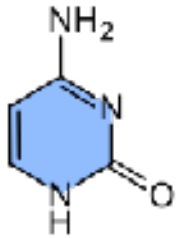
Large bases

Pyrimidines
One ring

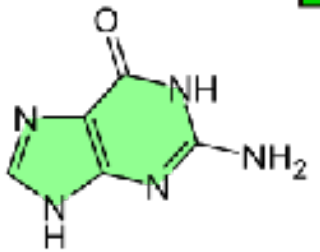
Purines
Two rings

Found in DNA and RNA

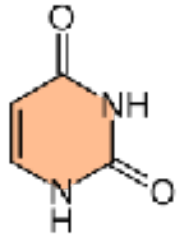
Cytosine **C**



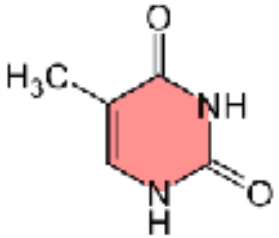
Guanine **G**



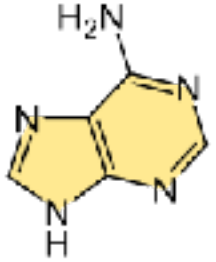
Uracil **U**



Thymine **T**



Adenine **A**

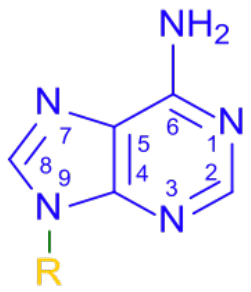


Found in RNA

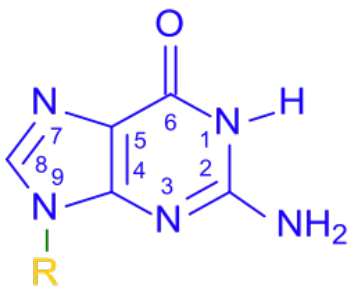
Found in DNA

The nucleotide bases

Purines

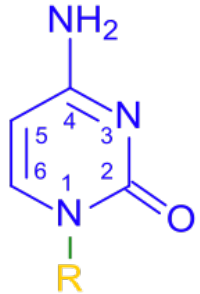


Adenine

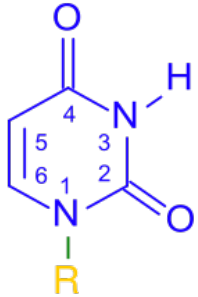


Guanine

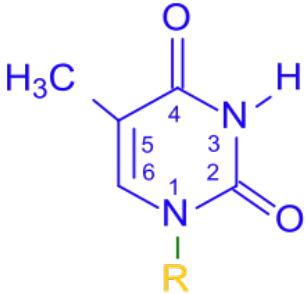
Pyrimidines



Cytosine



Uracil



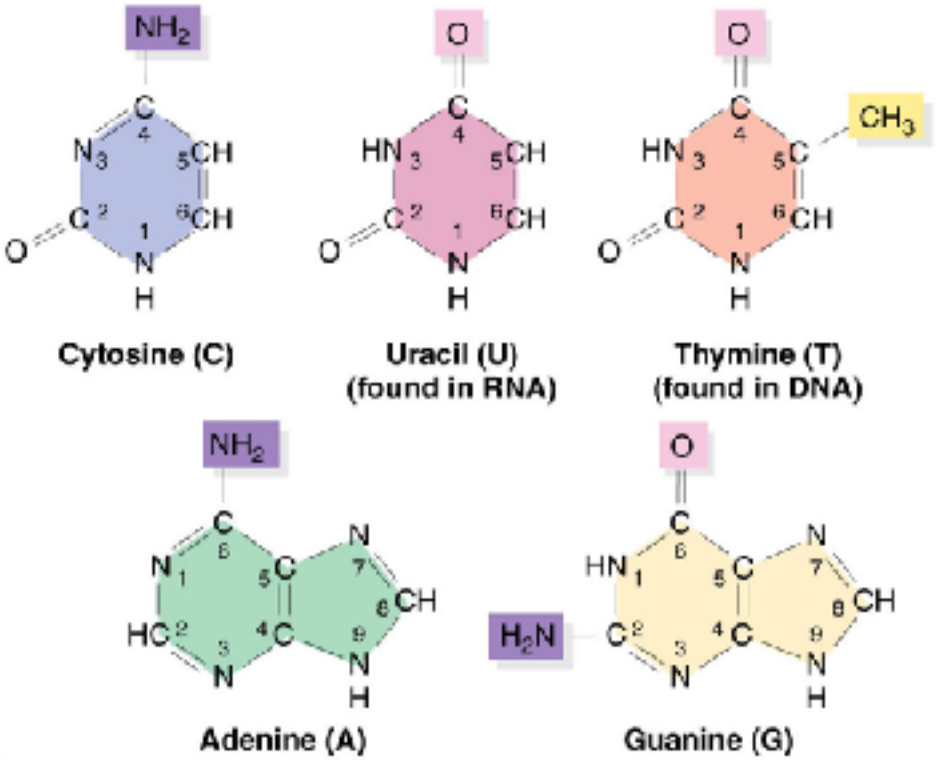
Thymine

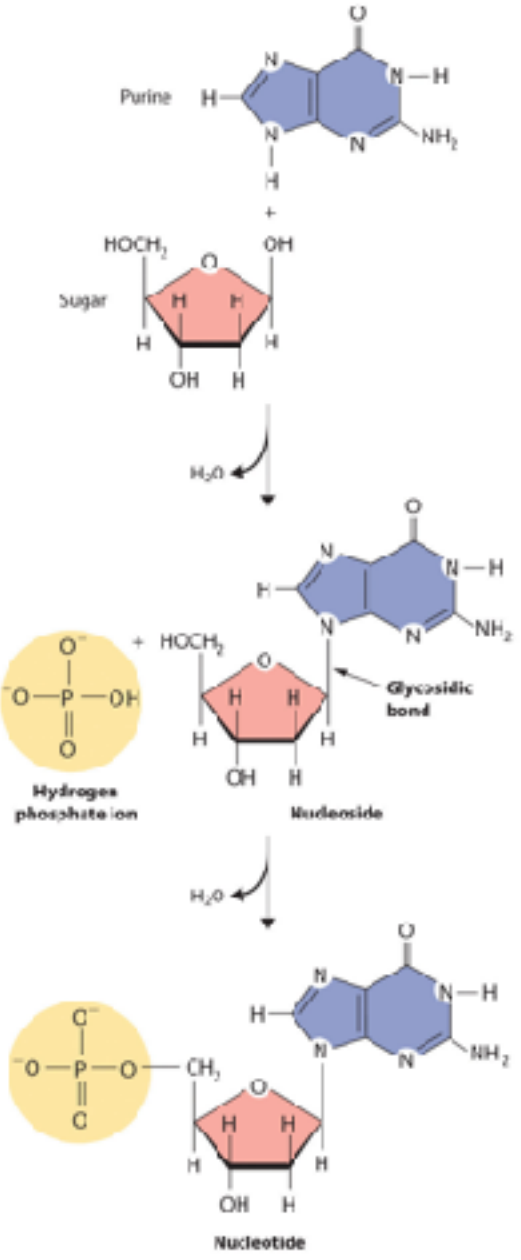
- The purines get attached to the sugar by a bond between N9 and C1.
- The pyrimidine get attached to the sugar by a bond between N1 and C1.

The nucleotide bases

Why N9 in purines forms a bond with the sugar and N1 of pyrimidine?

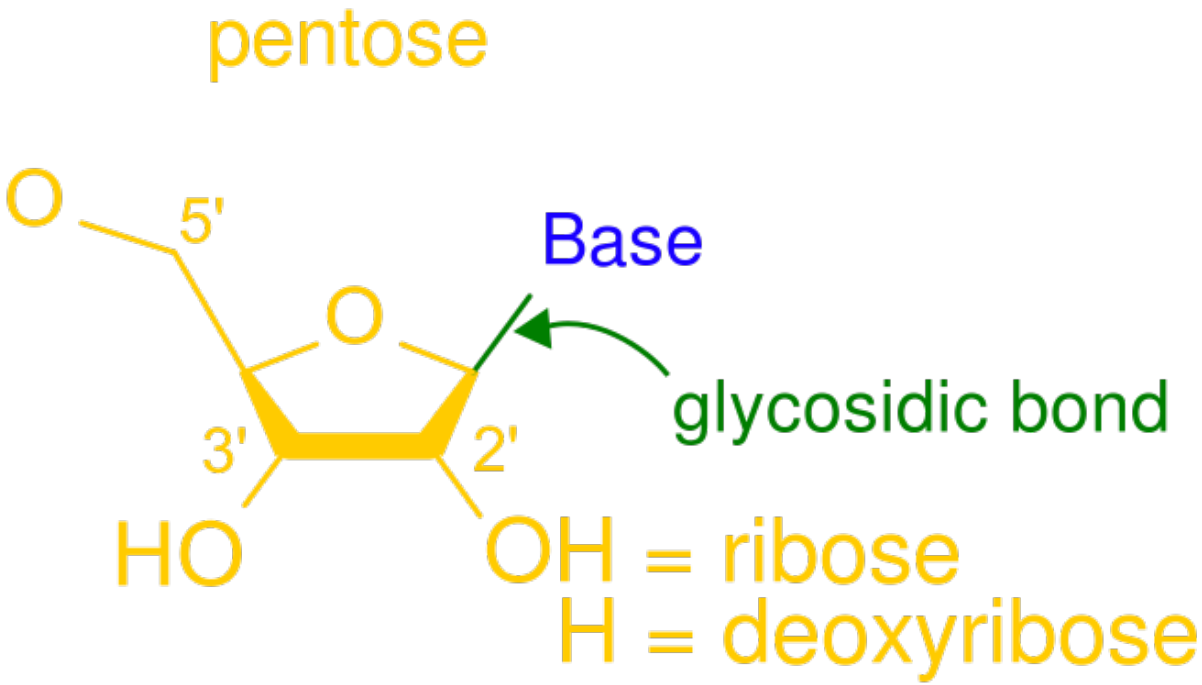
The nucleotide bases



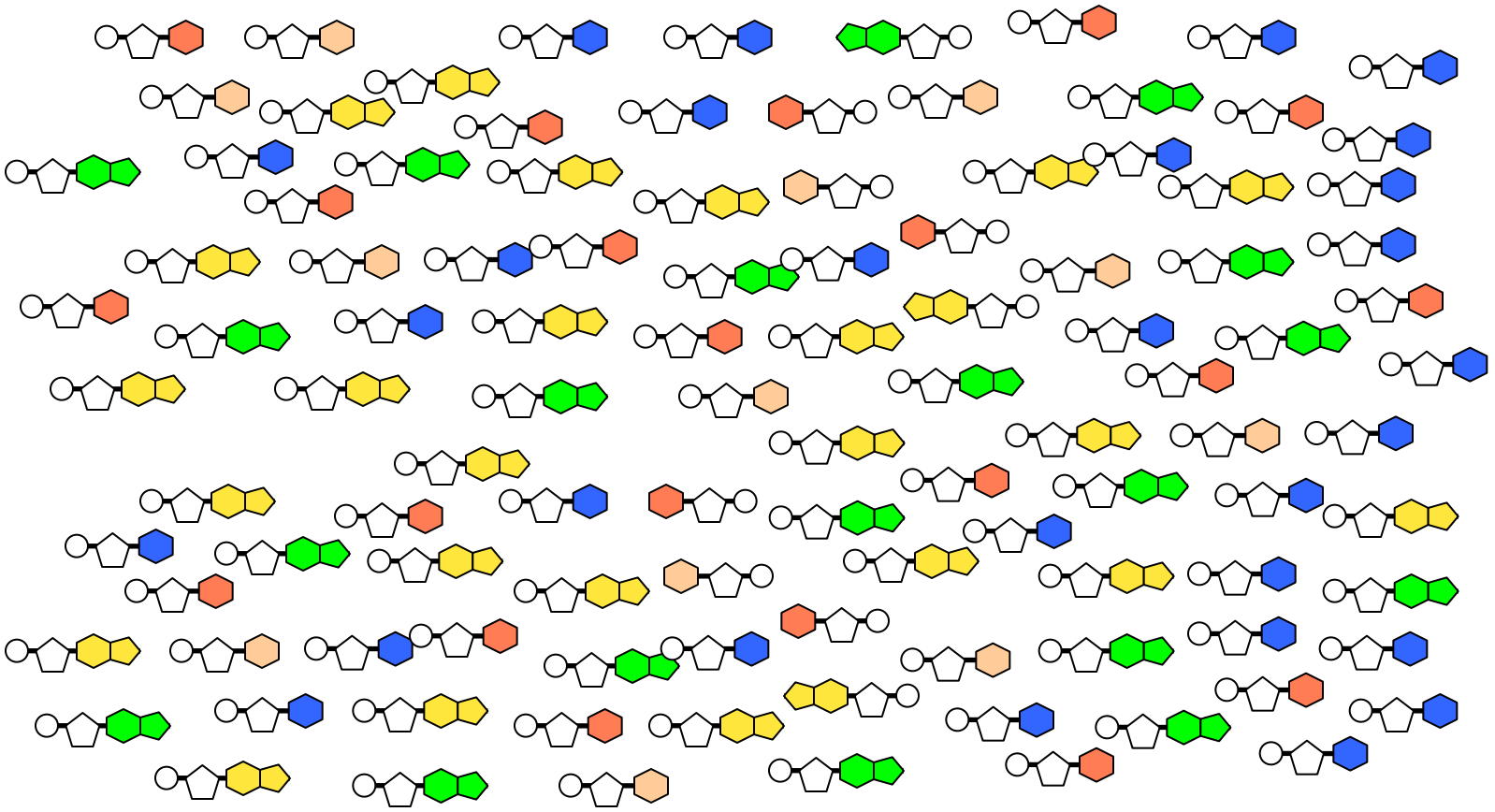


The nucleotide bases

- The bond linking the base to the sugar is a **glycosidic bond**.
- Glycosidic bonds link a sugar to another group.



Nucleotides

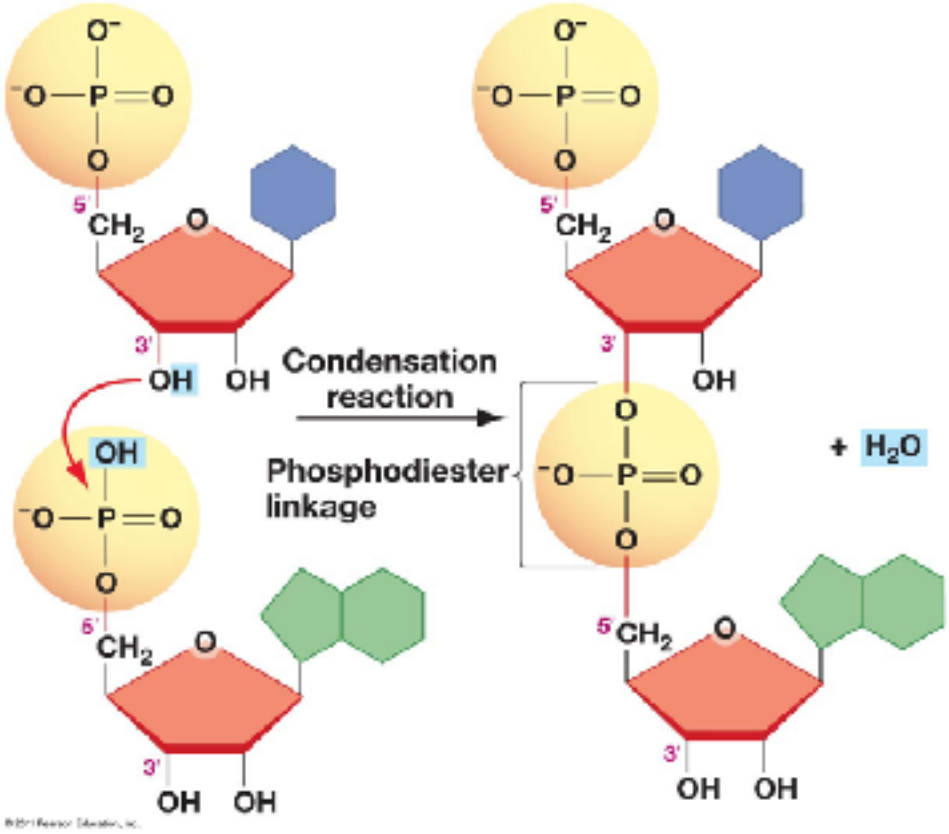


There are millions/billions of nucleotides in one genome.

How are they linked and connected?

Nucleotide linking

- Nucleotides are linked via **phosphodiester bond.**
- A covalent bond links the phosphate group of one nucleotide to the 3’ carbon of the sugar of another.



Nucleotide linking

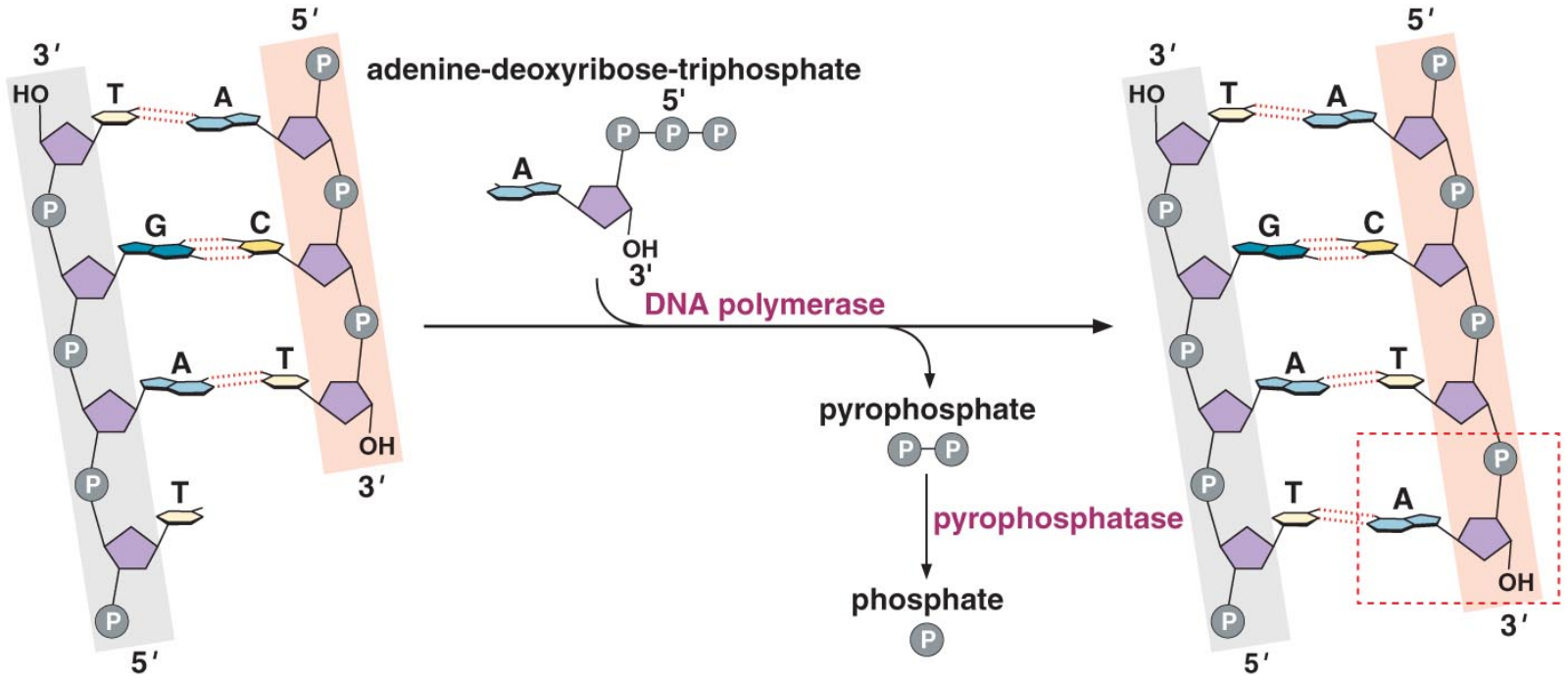
- Linking two nucleotides requires 3’ OH on the sugar of one nucleotide and a nucleoside triphosphate.
- The energy of the phosphate bonds is used to carry out the reaction favorably.
- The result is a two nucleotides linked by a phosphodiester bond and a pyrophosphate and water as side products.

What is pyrophosphate?

Nucleotide linking

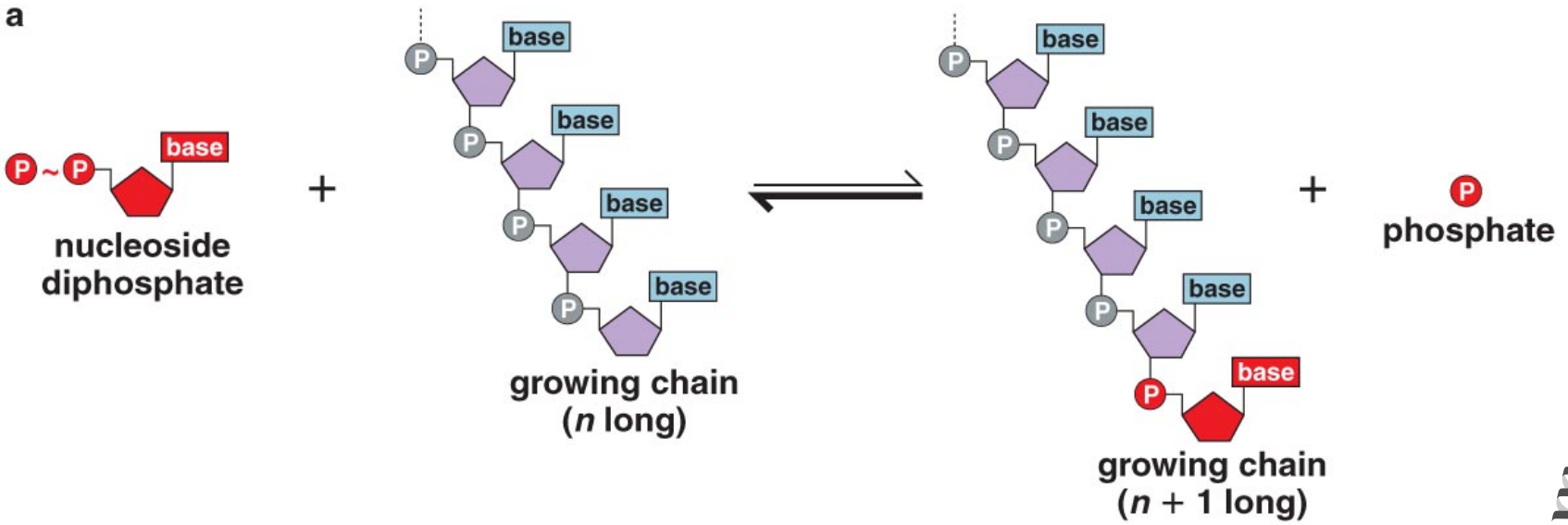
- Pyrophosphate breaks down into inorganic phosphates.

Why a nucleoside triphosphate is needed and not nucleoside diphosphate?



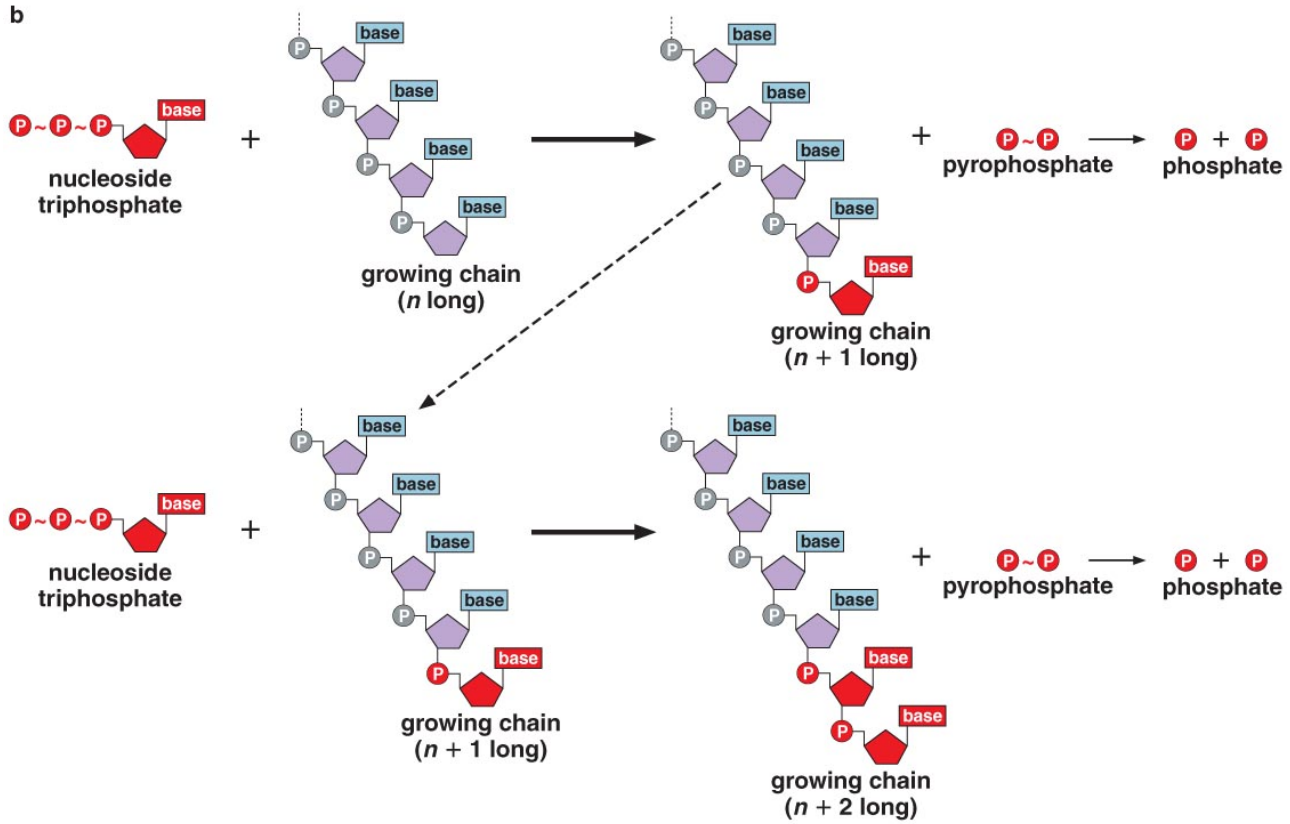
Nucleotide linking

- Using a nucleoside diphosphate to link nucleotides is not an energetically favored reaction.
- The phosphate by product favors the reaction in the opposite direction.



Nucleotide linking

- Using nucleoside triphosphate results in linking nucleotides and a pyrophosphate
- The reaction is favored in the direction of linking nucleotides



Nucleotide linking

Table 10.2 Standard Gibbs free energies of hydrolysis for ATP, AMP, and pyrophosphate

Reactants and products	$\Delta G^{\circ\prime}_{hydrolysis}$ (kJ mol^{-1})
$ATP + H_2O \rightarrow ADP + P_i + H^{\oplus}$	−32
$ATP + H_2O \rightarrow AMP + PP_i + H^{\oplus}$	−45
$AMP + H_2O \rightarrow Adenosine + P_i + H^{\oplus}$	−13
$PP_i + H_2O \rightarrow 2P_i$	−29

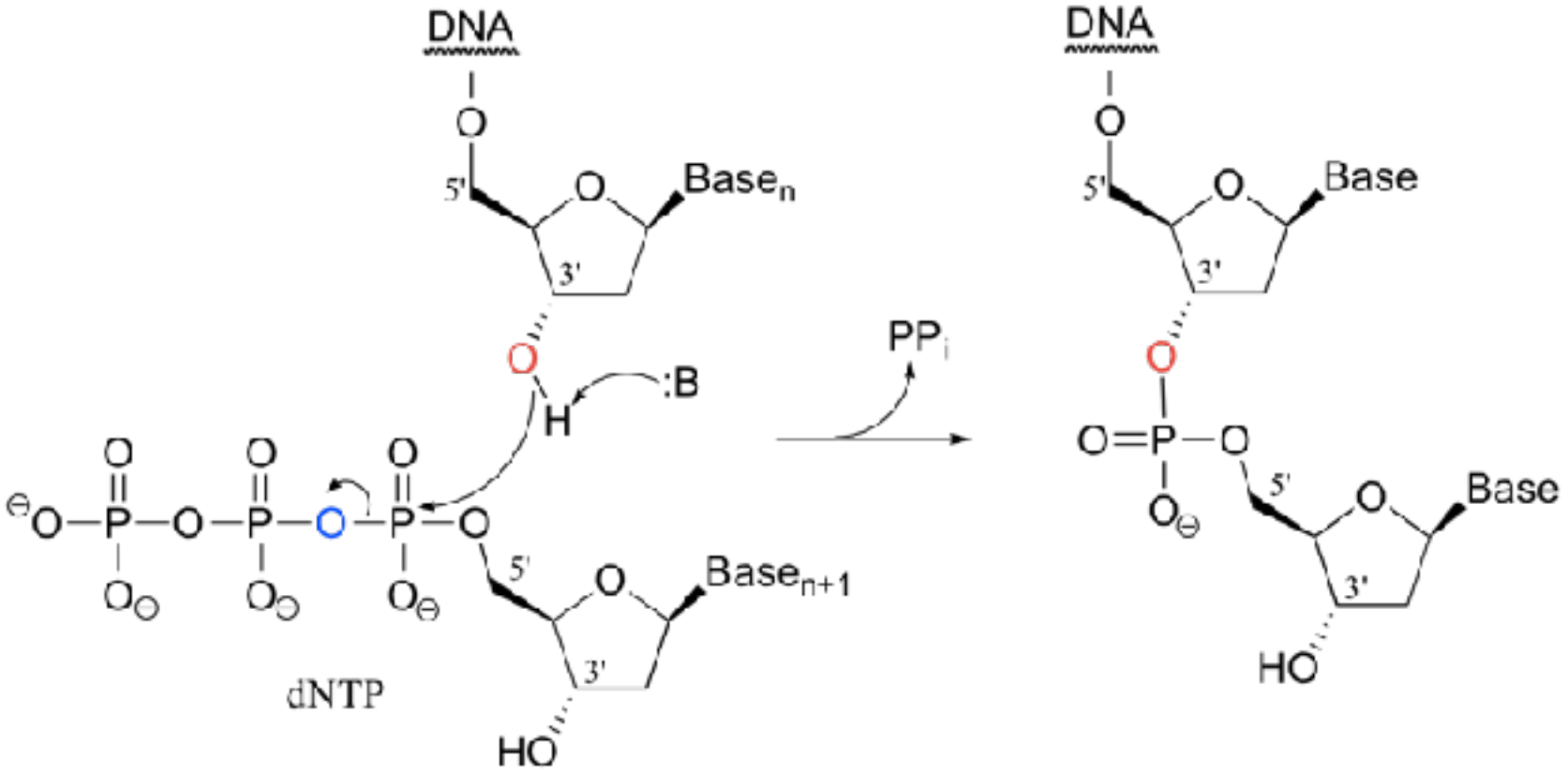
P_i(inorganic phosphate) = $HPO_4^{(2-)}$

PP_i(pyrophosphate) = $HP_2O_7^{(3-)}$

High energy bonds and the free energy determines the reaction direction.

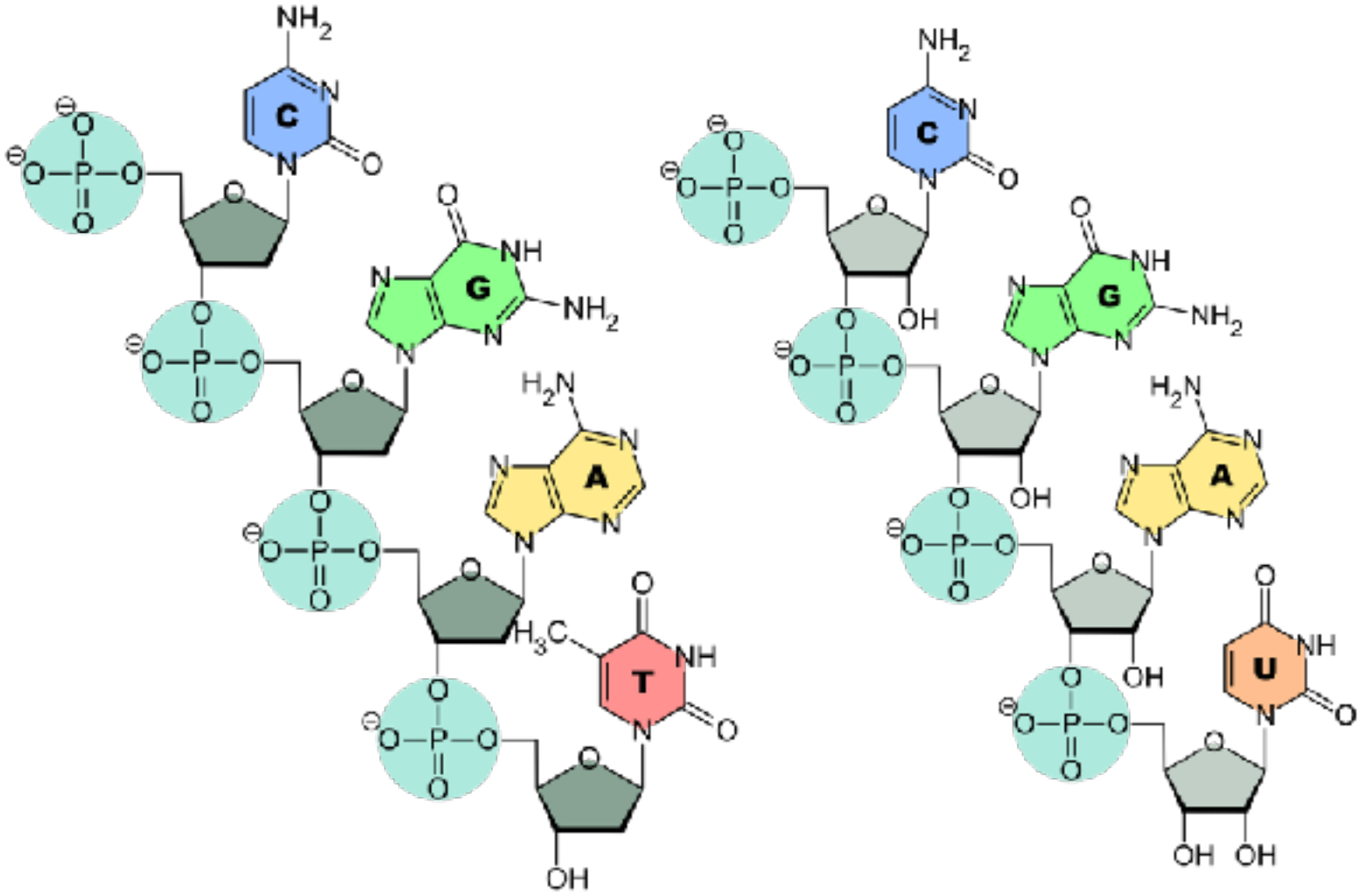
Nucleotide linking

Formation of phosphodiester bond



Nucleotide linking

The backbone of DNA/RNA is composed of sugar-phosphate-sugar-phosphate etc.



Nucleotide linking

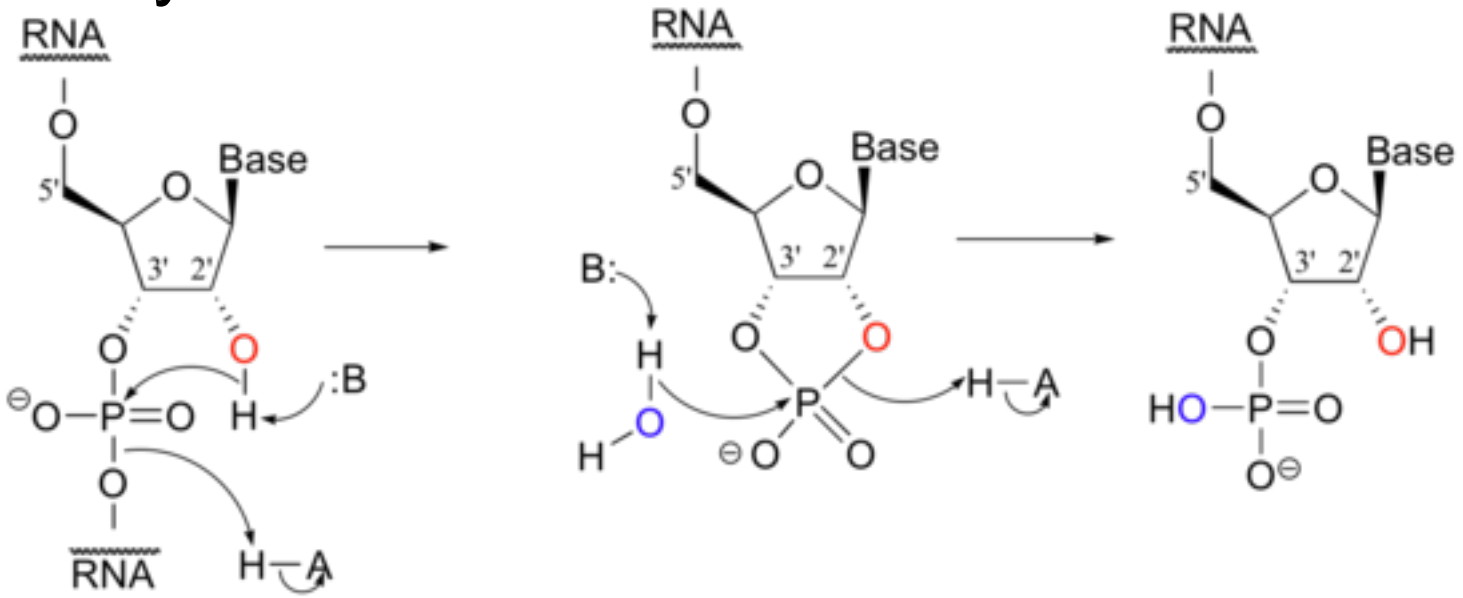
Is the reaction of linking two nucleotides via phosphodiester bond a spontaneous one?

Nucleotide linking

What is the effect of the presence or absence of hydroxyl (OH) group on carbon 2 of the sugar on the stability of DNA and RNA?

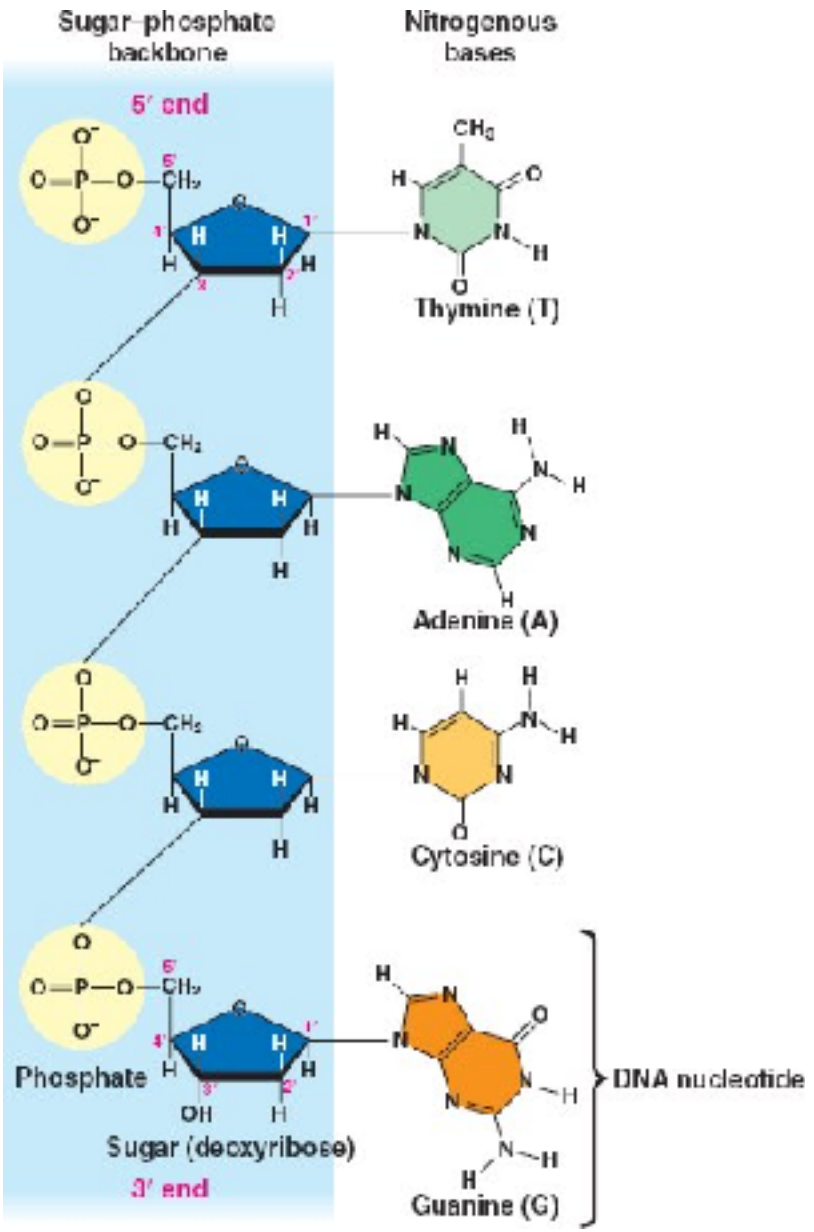
Nucleotide linking

- The hydroxyl group (OH) on carbon 2 of RNA's ribose sugar makes it more susceptible to backbone hydrolysis and thus degradation of the molecule.
- The deoxy nature of DNA's sugar prevents backbone hydrolysis and contribute to its overall stability.



Polynucleotides

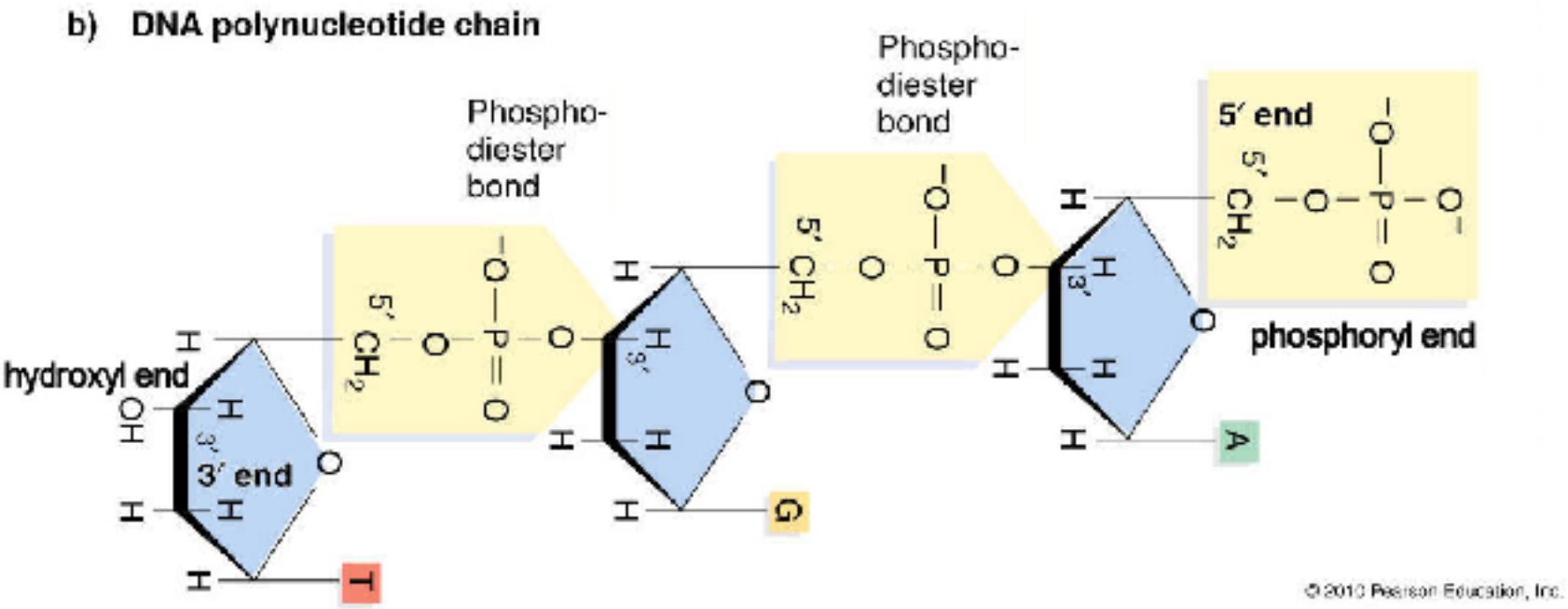
- What is DNA polarity?
- A number of polynucleotides have two **different** ends.



Polynucleotides

- **5’ end:** where the 5’ carbon at one end of the molecule has a phosphate group.

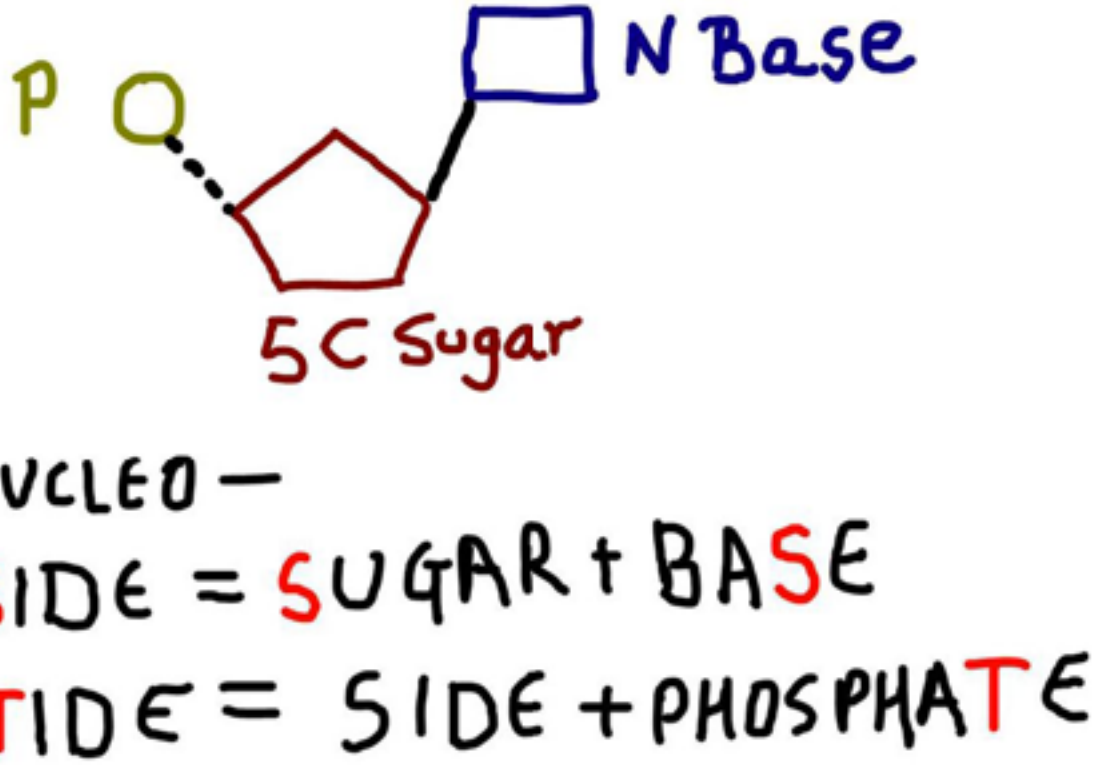
- **3’ end:** where the 3’ carbon at the other end of the molecule has a hydroxyl group.



Expectations

- You know the chemical composition of DNA and RNA.
- You know the two chemical differences between DNA and RNA.
- You know the names and terminology of the chemical units of DNA and RNA.

For a smile



There are mistakes here. Can you find them?