بسم الله الرحمن الرحيم

Basic Principles and Perspectives in Medical Chemistry and Biochemistry

Nucleic Acids

Part 1

4th Medical and Biochemistry (BIQC-101) Lecture
Second Semester

by
Prof. Dr. Salih Mahdi Salman

Nucleic Acids

Learning Objectives

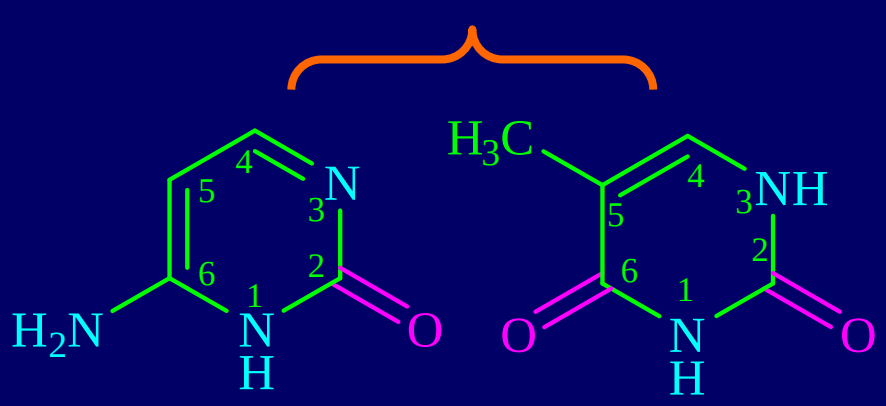
Students will be able to

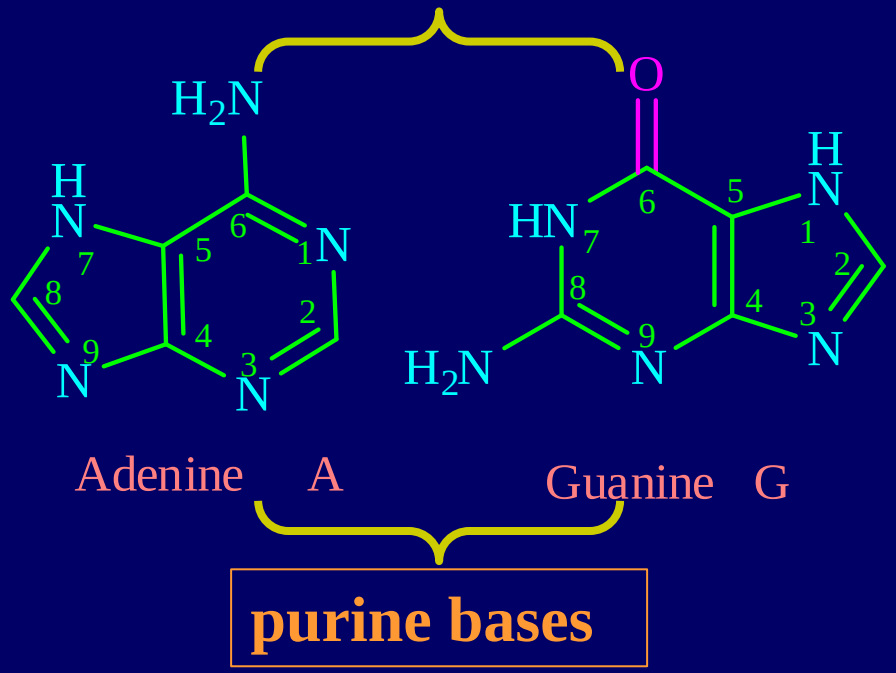
1. Describe the structure of a nucleotide as being a phosphate group, pentose sugar (either ribose or deoxyribose), and a nitrogen containing base,
2. Recall that the nitrogenous bases are adenine, cytosine, guanine, and thymine in DNA, or uracil in RNA, and the base pairings that occur,
3. State that a nucleic acid is formed from many nucleotides, joined by condensation reactions,
4. Compare and contrast the structures of DNA and RNA,
5. Explain the importance of DNA in storing genetic material and safely transferring genetic information between organisms.

Introduction

- Nucleic acids are naturally occurring chemical compounds that serve as the primary information-carrying molecules in cells and makeup the genetic material.
- The first isolation of DNA was accomplished by Johann Friedrich 1870. In the 1920's nucleic acids were found to be major components of chromosomes.
- Nucleic acids are the third class of biopolymers (polysaccharides and proteins being the others)
- Elemental analysis of nucleic acids showed the presence of phosphorus, in addition to the usual C, H, N & O.
- Unlike proteins, nucleic acids contained no sulfur.

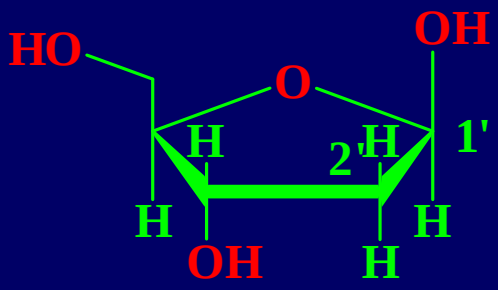
- Complete hydrolysis of chromosomal nucleic acids gave inorganic phosphate, 2-deoxyribose and four different heterocyclic bases (nitrogen bases).



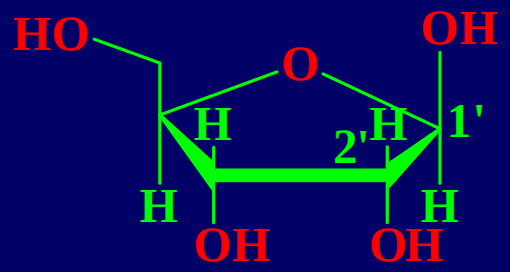


- The two monocyclic bases are classified as pyrimidines, and the two bicyclic bases are purines.
- Each has at least one N-H site at which an organic substituent may be attached. They are all polyfunctional bases, and may exist in tautomeric forms.

The corresponding N-glycosides of the common sugar ribose are the building blocks of RNA.

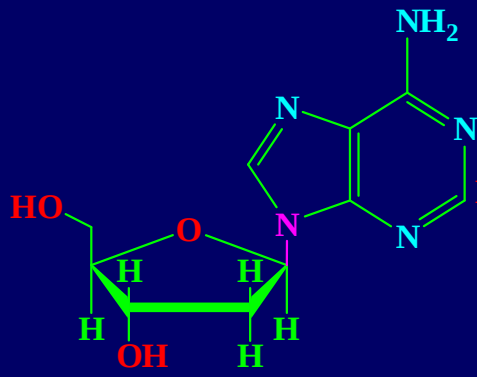


2'-deoxyribose

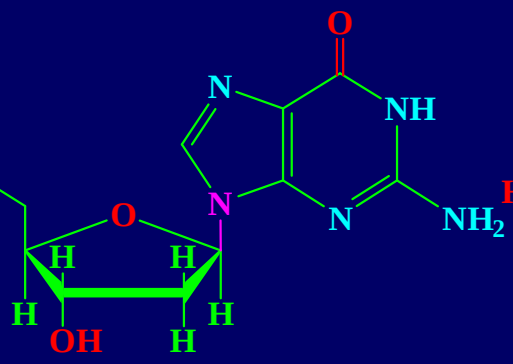


Ribose

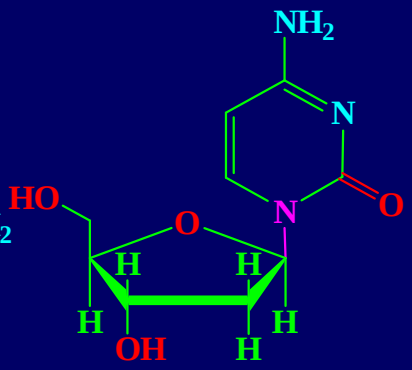
Base-catalyzed hydrolysis of DNA gave four nucleoside products, which proved to be N-glycosides of 2'-deoxyribose combined with the heterocyclic amines (nitrogen bases).



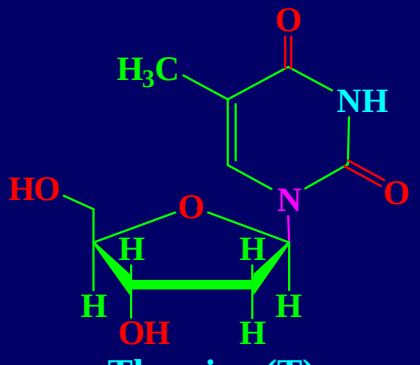
Adenine (A)
DNA & RNA



Guanine (G)
DNA & RNA

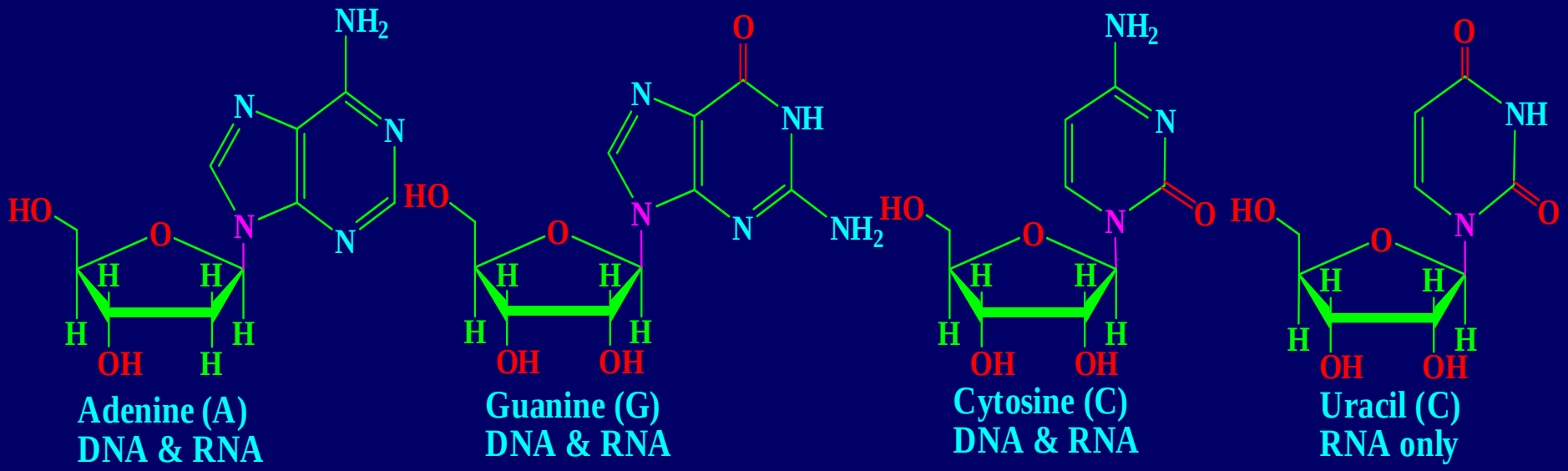


Cytosine (C)
DNA & RNA



Thymine (T)
DNA only

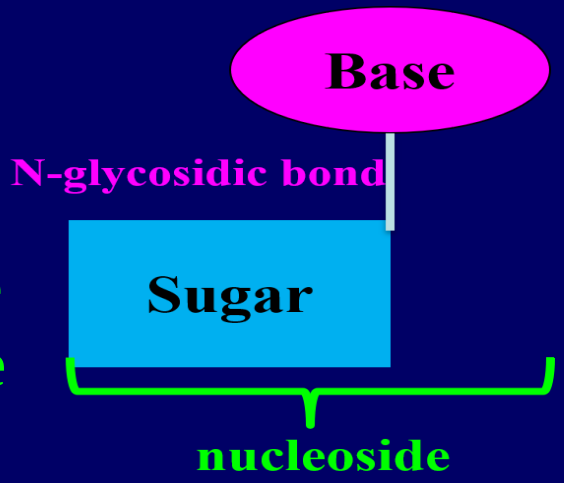
While base-catalyzed hydrolysis of RNA gave four nucleoside products, which proved to be N-glycosides of ribose combined with the heterocyclic amines (nitrogen bases).



Nucleosides

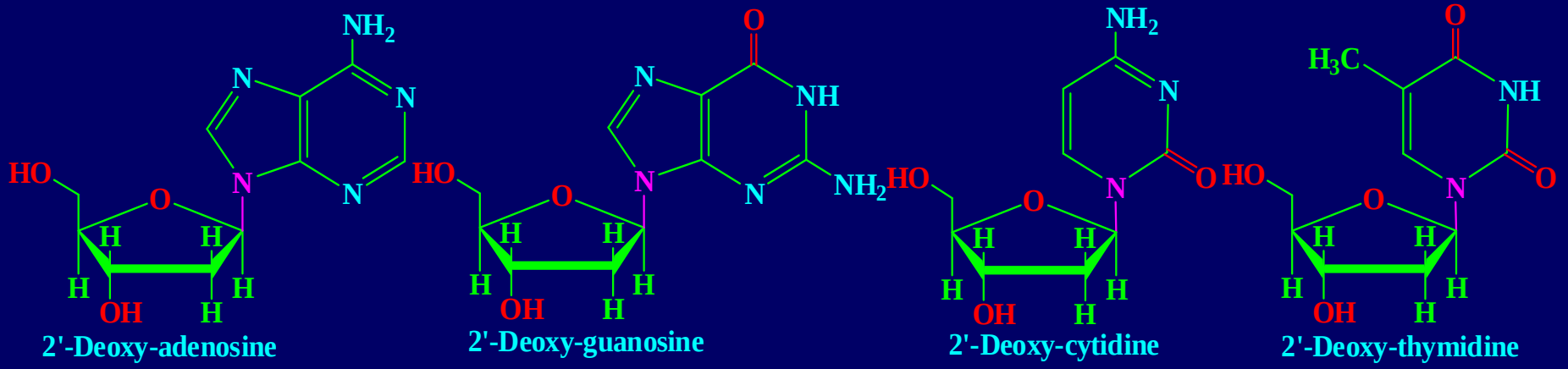
A nucleoside consists of a nitrogen base linked by a glycosidic bond to C1' of a ribose or deoxyribose.

Nucleosides are named by changing the nitrogen base ending to *-osine* for purines and *–idine* for pyrimidines



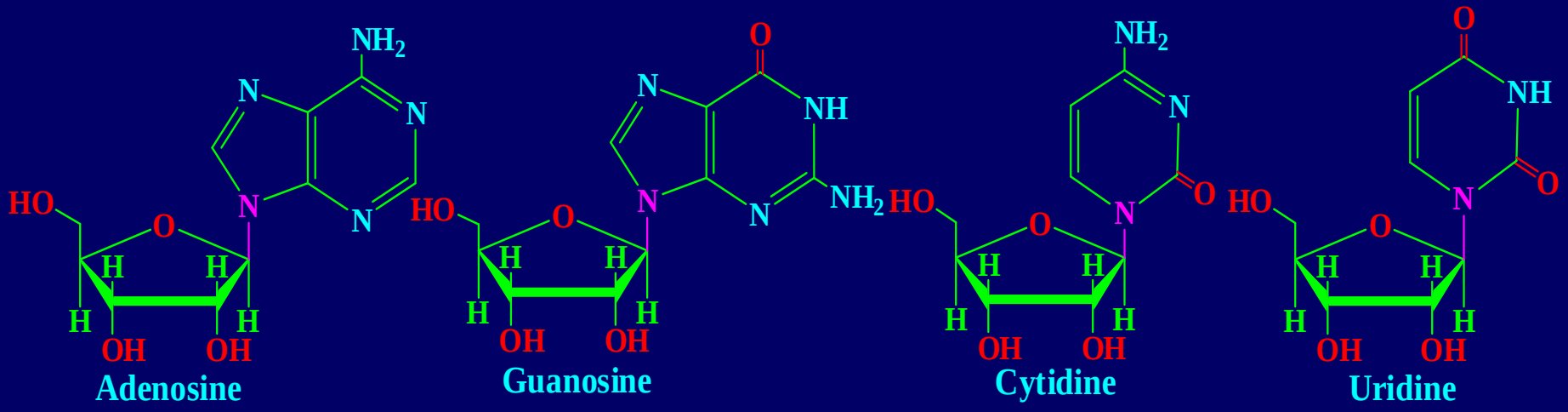
Name DNA Nucleosides

Base	Sugar	Nucleoside
Adenine (A)	Deoxyribose	2'-Deoxyadenosine
Guanine (G)	Deoxyribose	2'-Deoxyguanosine
Cytosine (C)	Deoxyribose	2'-Deoxycytidine
Thymine (T)	Deoxyribose	2'-Deoxythymidine



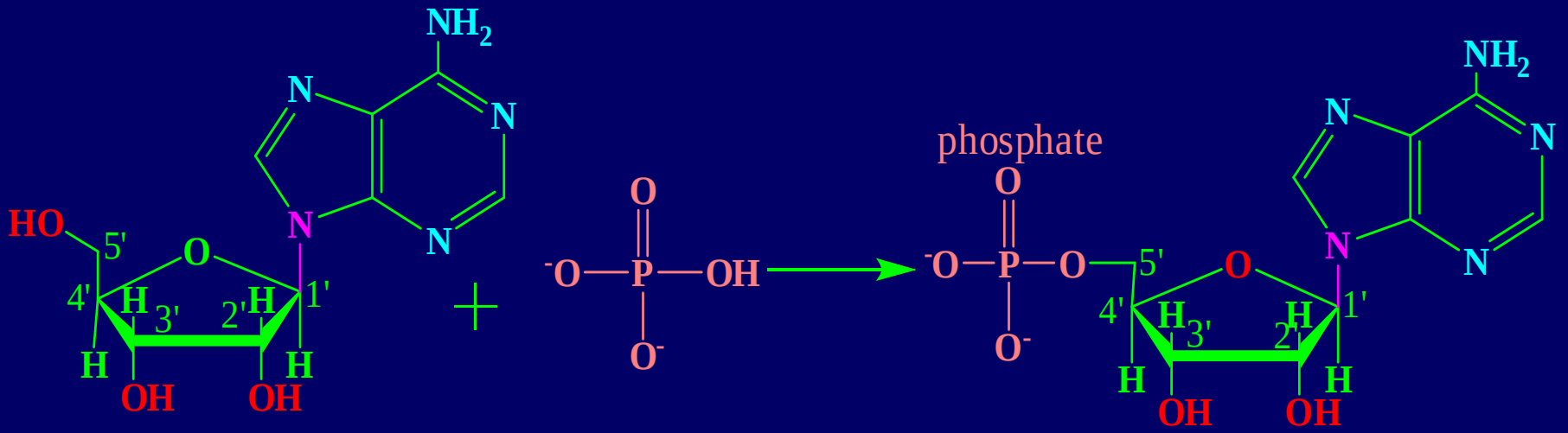
Name of RNA Nucleosides

Base	Sugar	Nucleoside
Adenine (A)	ribose	Adenosine
Guanine (G)	ribose	Guanosine
Cytosine (C)	ribose	Cytidine
Uracil (U)	ribose	Uridine



Nucleotides

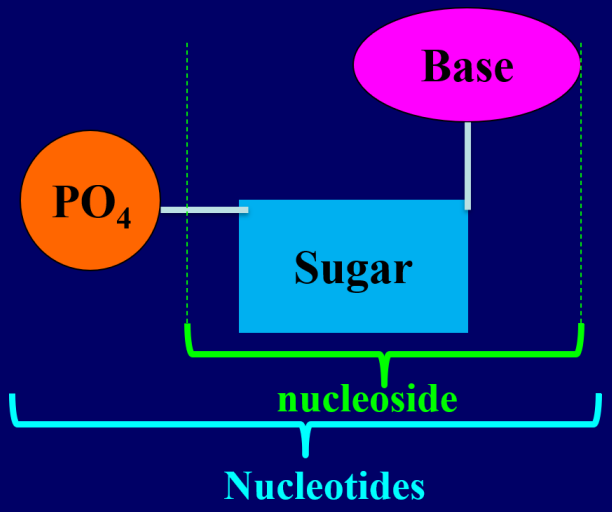
- A nucleotide is a nucleoside that forms a phosphate ester with the C5’ OH group of ribose or deoxyribose.
- Nucleotides are named using the name of the nucleoside followed by 5’-monophosphate.
- Anhydride-like di- and tri-phosphate nucleotides have been identified as important energy carriers in biochemical reactions, the most common being ATP (adenosine 5'-triphosphate).
- They may be obtained by selective hydrolysis of DNA through the action of nuclease enzymes



Adenosine

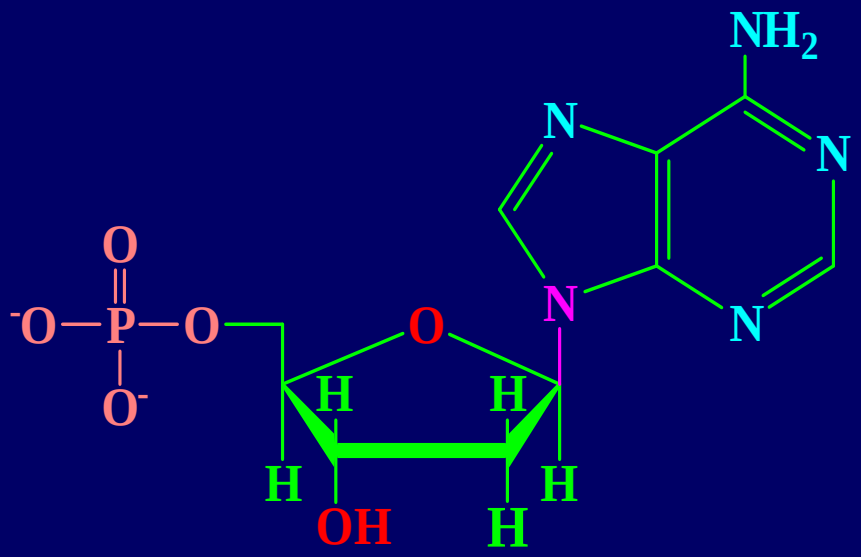
Adenosine 5’-monophosphate AMP

Nucleotides Composition

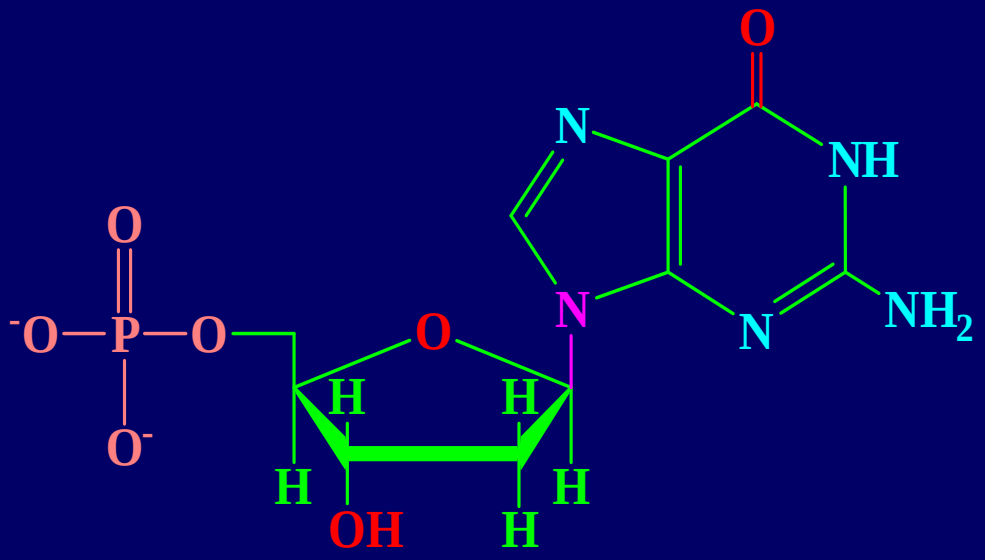


Names of DNA Base Derivatives

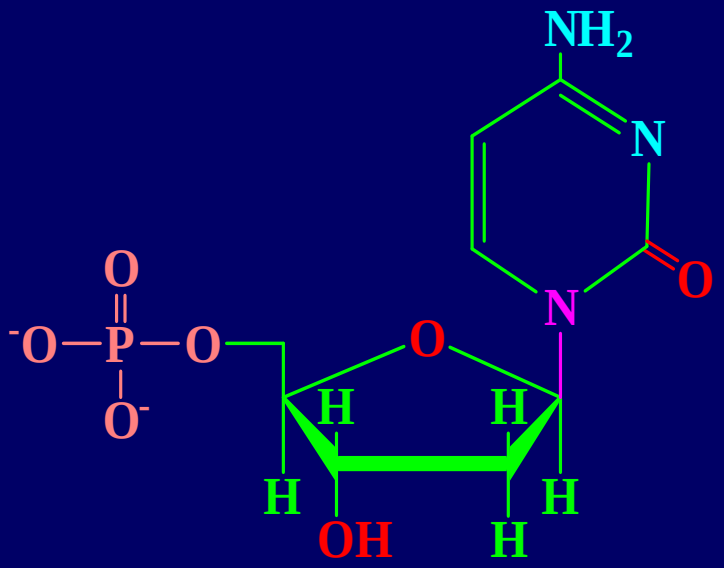
Base	Nucleoside	5'-Nucleotide
Adenine	2'-Deoxyadenosine	2'-Deoxyadenosine-5'-monophosphate
Cytosine	2'-Deoxycytidine	2'-Deoxycytidine-5'-monophosphate
Guanine	2'-Deoxyguanosine	2'-Deoxyguanosine-5'-monophosphate
Thymine	2'-Deoxythymidine	2'-Deoxythymidine-5'-monophosphate



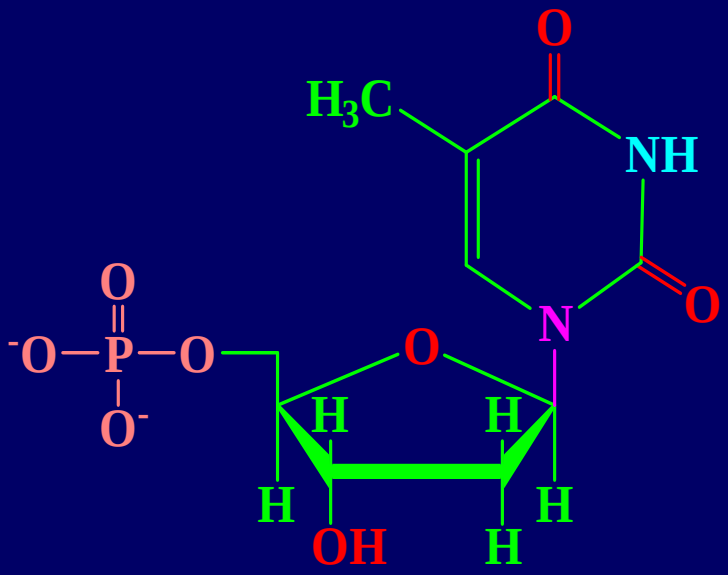
2'-Deoxyadenosine-5'-monophosphate



2'-Deoxyguanosine-5'-monophosphate

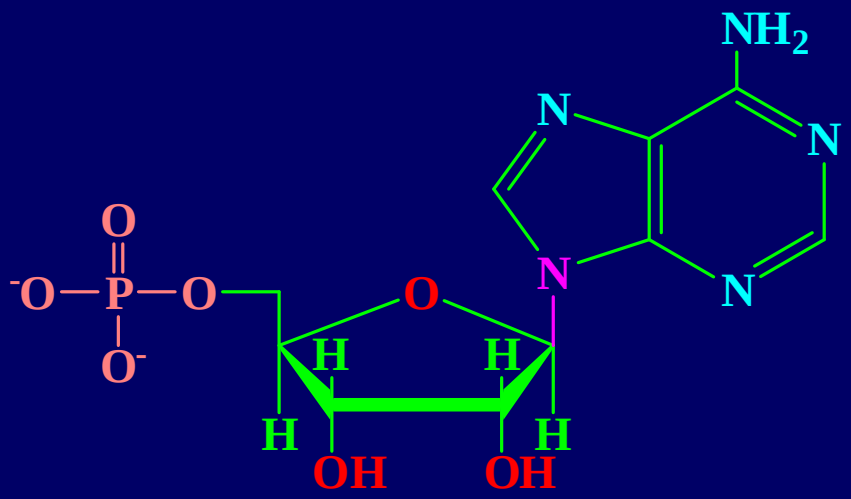


2'-Deoxycytidine-5'-monophosphate

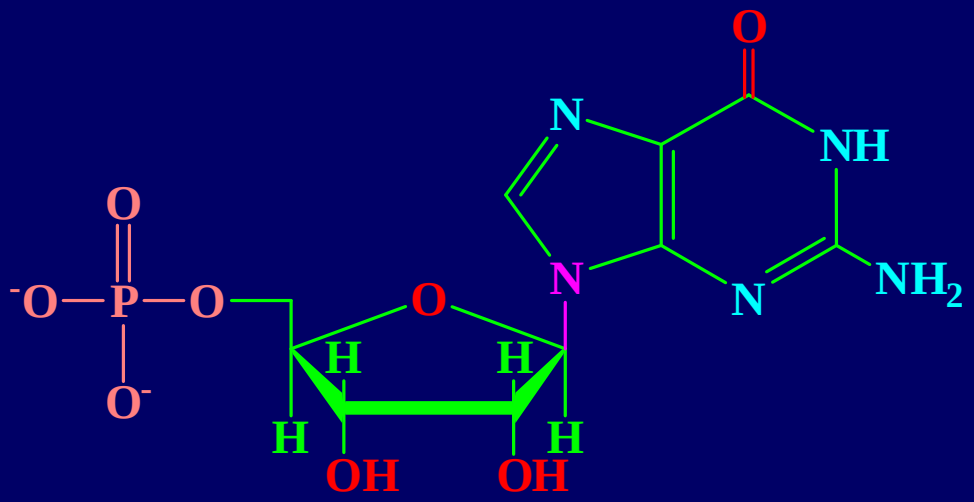


2'-Deoxythymidine-5'-monophosphate

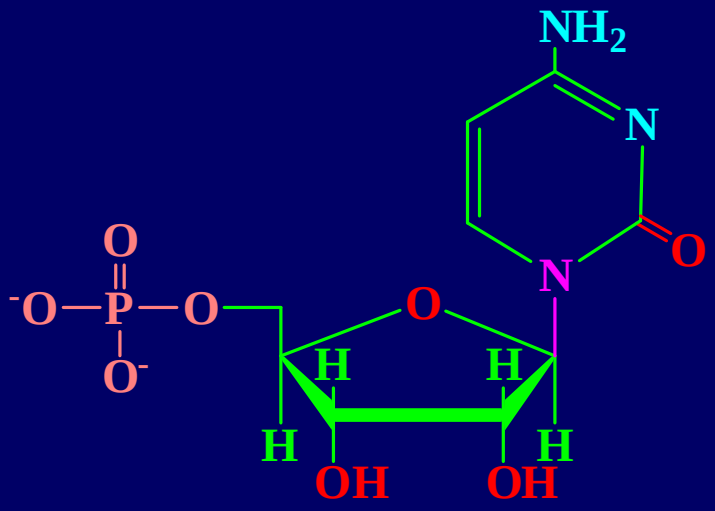
Names of RNA Base Derivatives



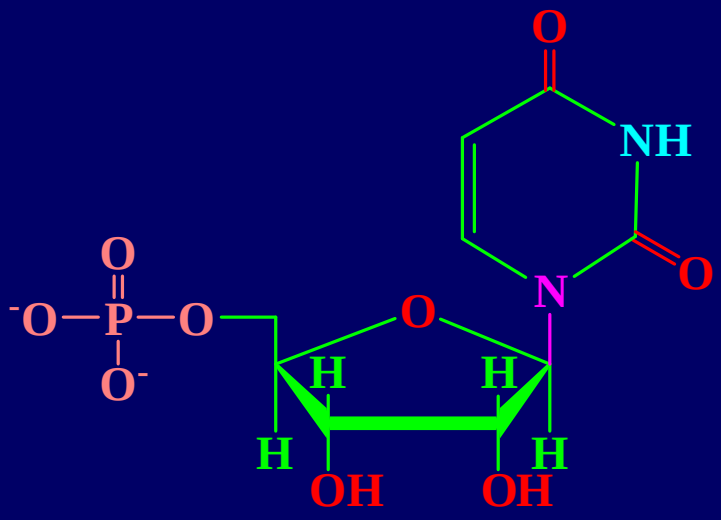
Adenosine-5'-monophosphate



Guanosine-5'-monophosphate

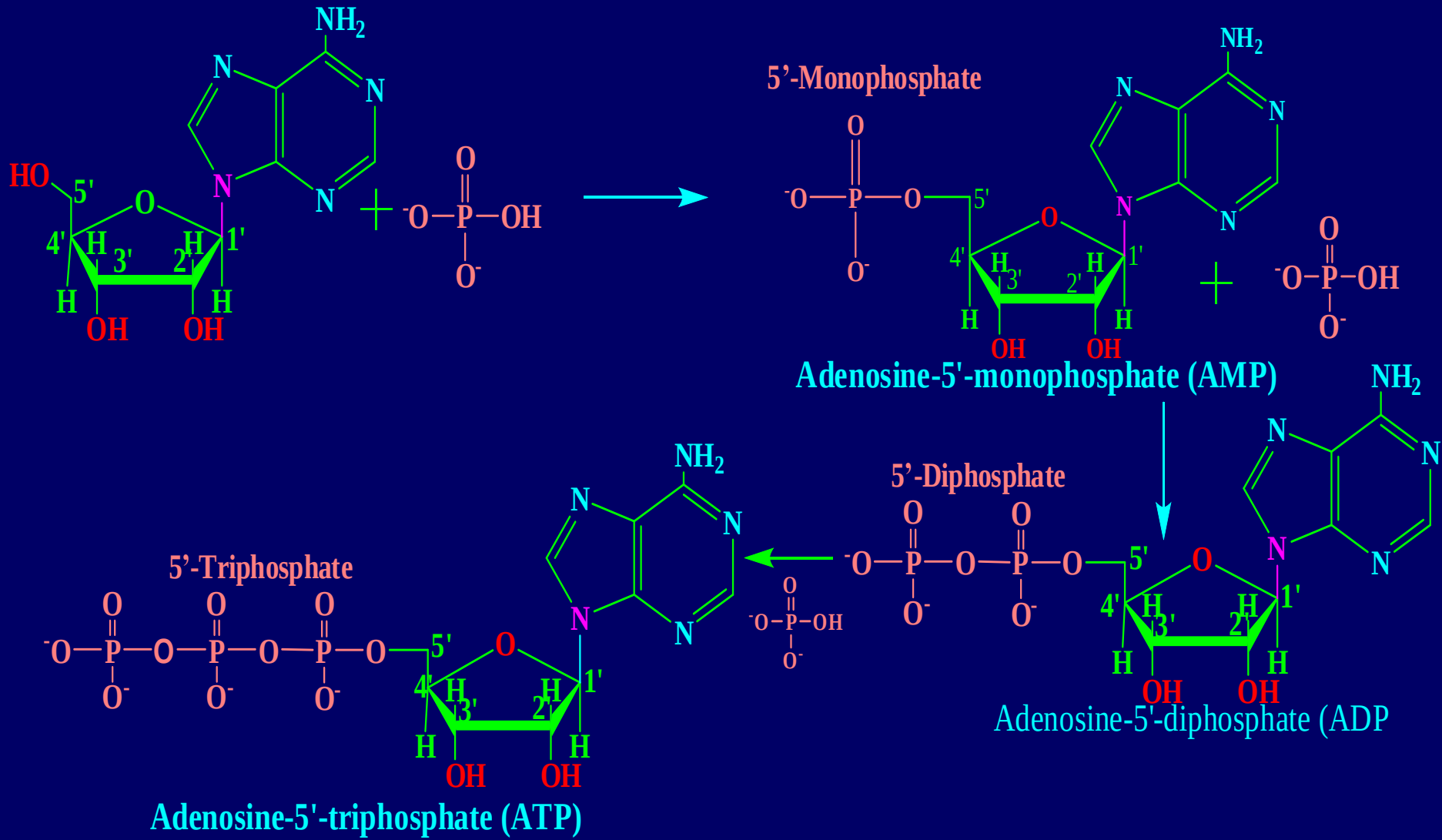


Cytidine-5'-monophosphate



Uridine-5'-monophosphate

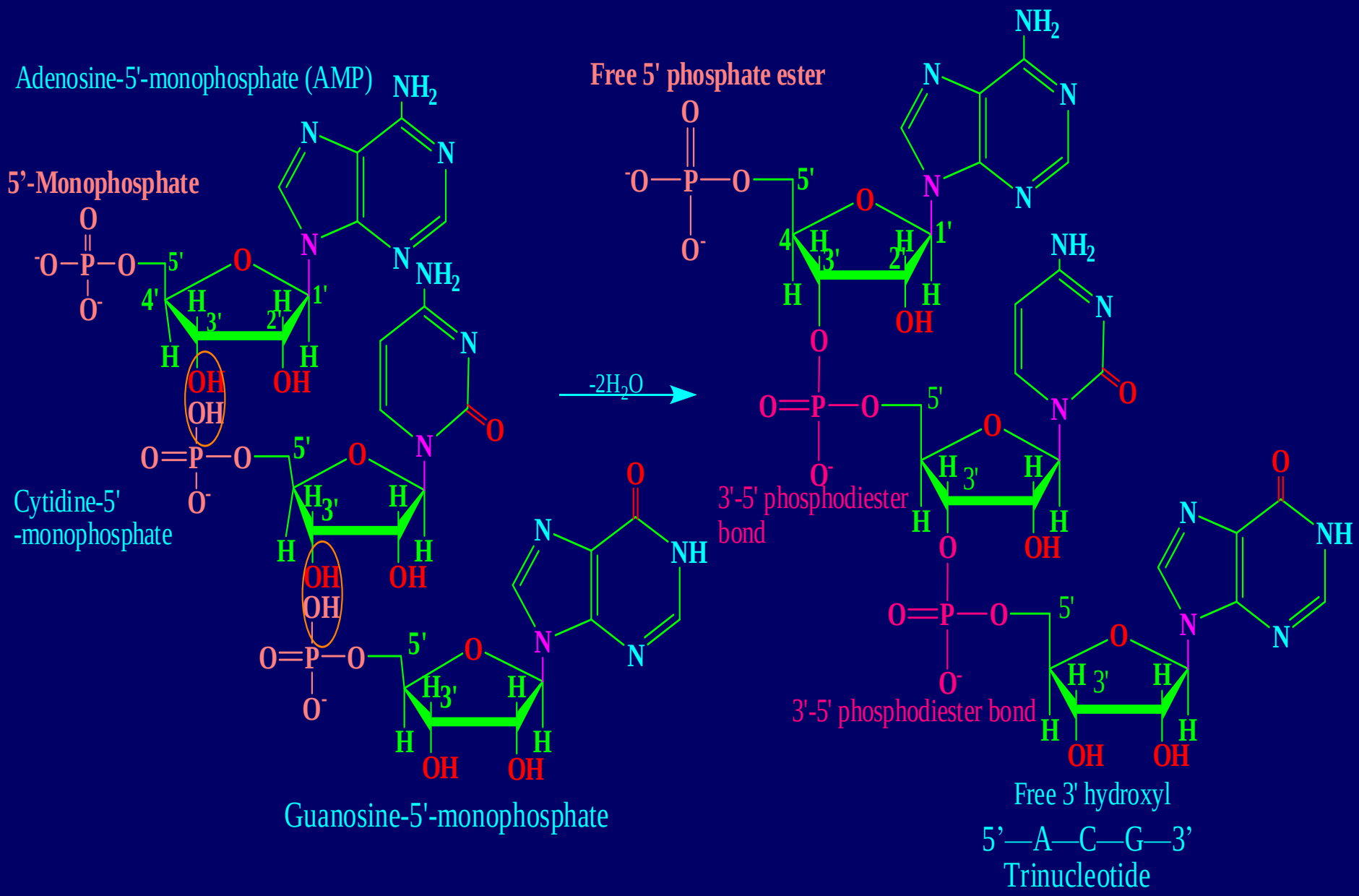
Additional phosphate groups can be added to the nucleoside 5'-monophosphates to form diphosphates and triphosphates.



ATP is the major energy source for cellular activity

The Chemical Nature of DNA & RNA

- The chemical linkage between nucleotide units in nucleic acids is a phosphodiester, which connects the 5'-hydroxyl group of one nucleotide to the 3'-hydroxyl group of the next nucleotide.
- The nucleotides in nucleic acids are joined by phosphodiester bonds.
- phosphodiester formed by Polymerase and Ligase activities
- Two nucleotides joined by a phosphodiester linkage gives a dinucleotide.
- Three nucleotides joined by two phosphodiester linkages gives a trinucleotide, etc.
- A polynucleotide of about 50 or fewer nucleotides is called an oligonucleotide.
- Nucleic acid sequences are written from left to right, from the 5'-end to the 3'-end.
- Nucleic acids are negatively charged.

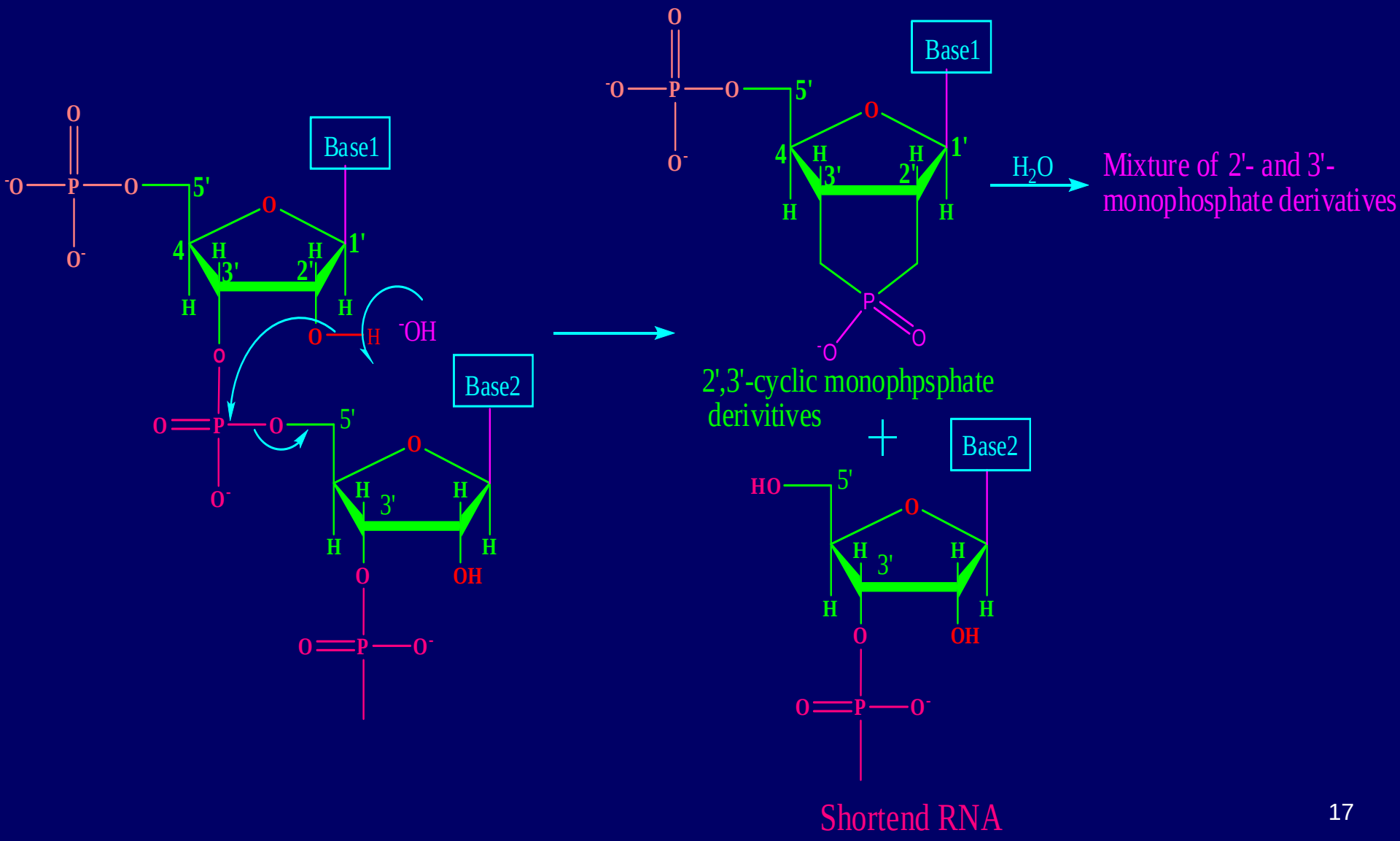

Adenosine-5'-monophosphate (AMP)
5'-Monophosphate
Cytidine-5'
-monophosphate
Guanosine-5'-monophosphate
-2H2O
Free 5' phosphate ester
3'-5' phosphodiester bond
3'-5' phosphodiester bond
Free 3' hydroxyl
5'—A—C—G—3'
Trinucleotide

Functions of Nucleotides

1. Nucleoside 5'-triphosphates are carriers of energy
2. Bases serve as recognition units
3. Cyclic nucleotides are signal molecules and regulators of cellular metabolism and reproduction
4. ATP is central to energy metabolism
5. GTP drives protein synthesis
6. CTP drives lipid synthesis
7. UTP drives carbohydrate metabolism

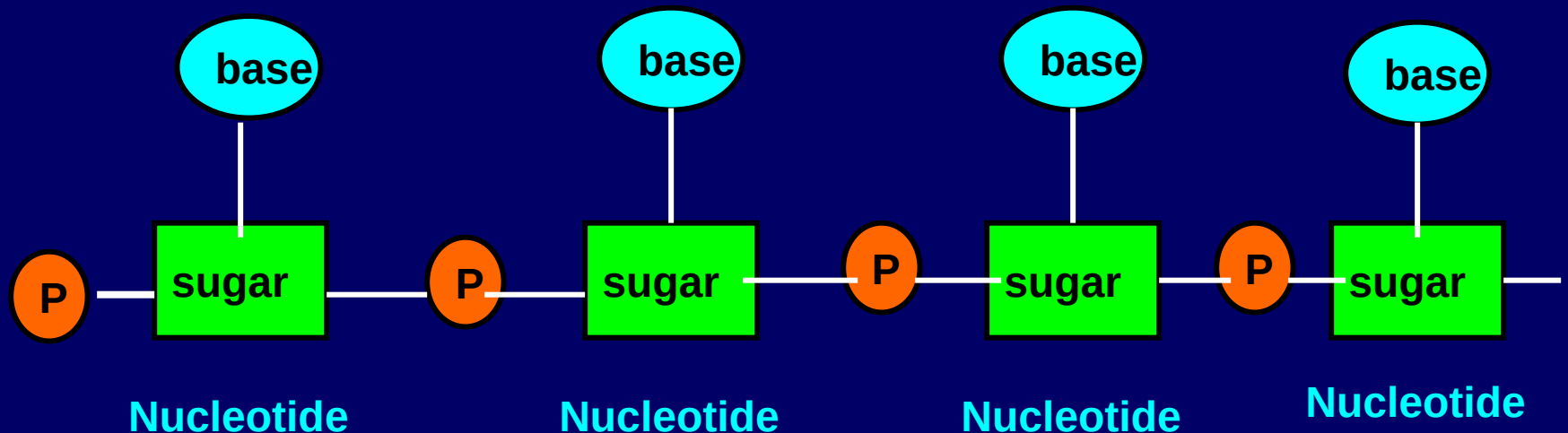
Cyclic nucleotides

Hydrolysis of RNA under alkaline conditions



Nucleic Acids

- Nucleic acids were first isolated by Friedrich Miescher in 1869.
- Nucleic acids are the third class of biopolymers (polysaccharides and proteins being the others)
- Large molecules consisting of long chains of monomers called nucleotides.
- Polymers of at least four nucleotides.
- The nucleotides are all orientated in the same direction. Linked 3' to 5' by phosphodiester bridges



Structure of Nucleic

primary structure

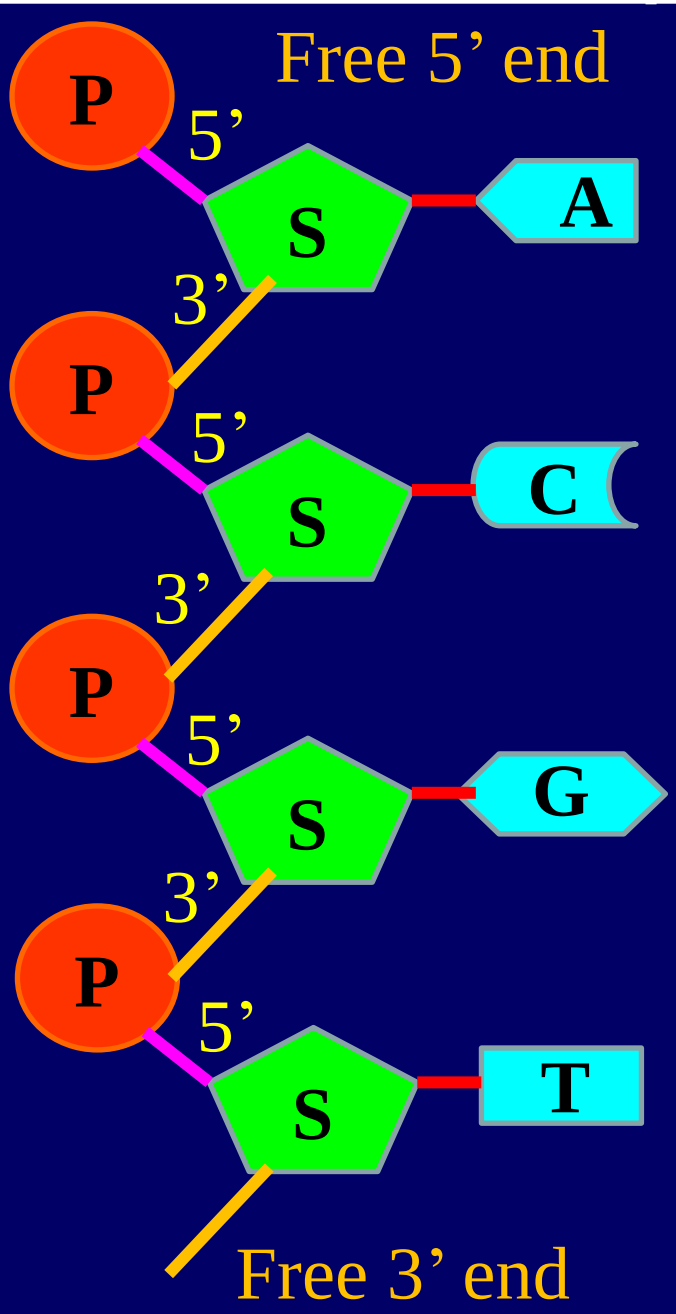
The **primary structure** of a nucleic acid is the nucleotide sequence.

The nucleotides in nucleic acids are joined by 3’- 5’ phosphodiester bonds.

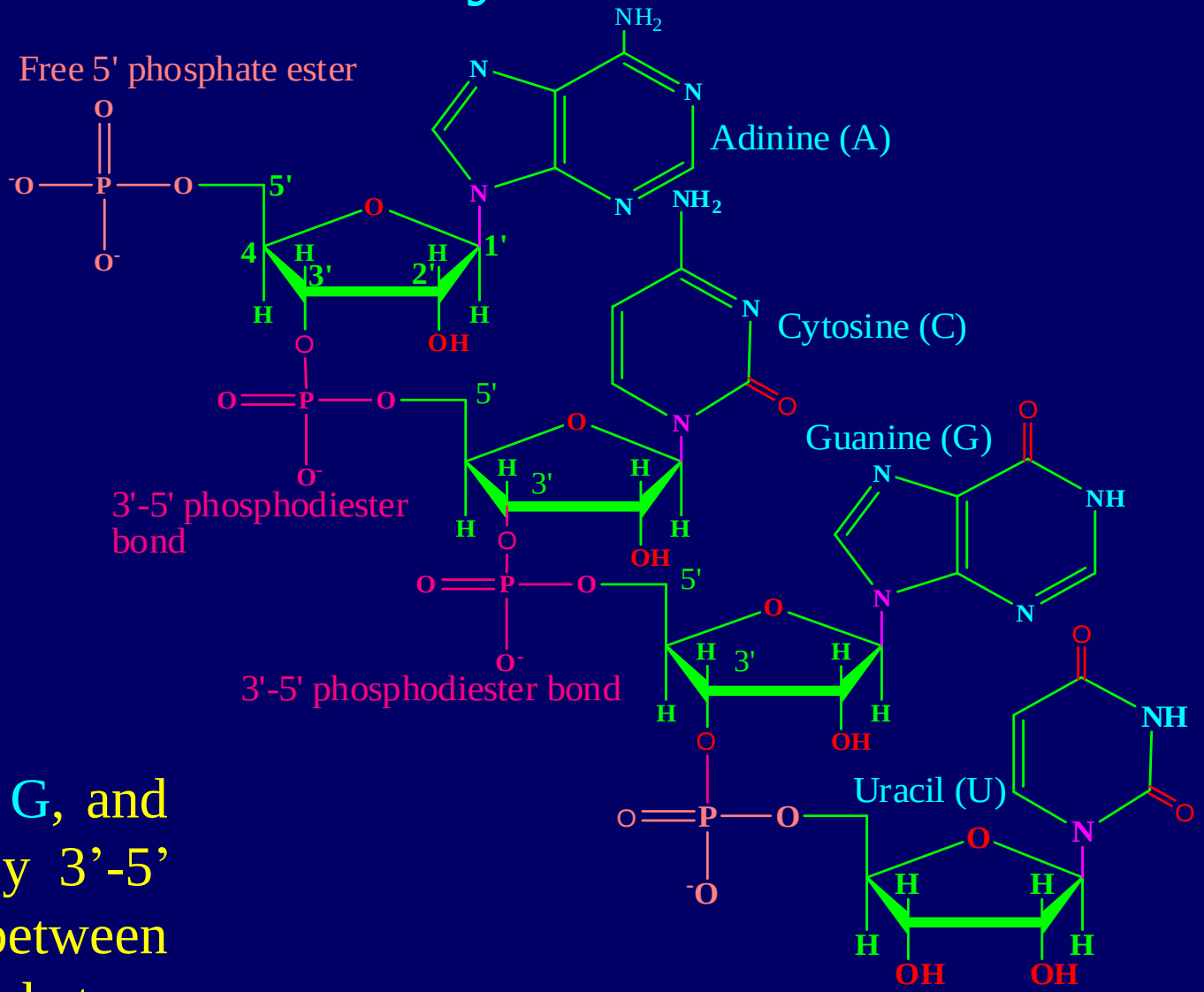
The sequence is read from the free 5’-end using the letters of the bases

This example reads:

5’—A—C—G—T—3’

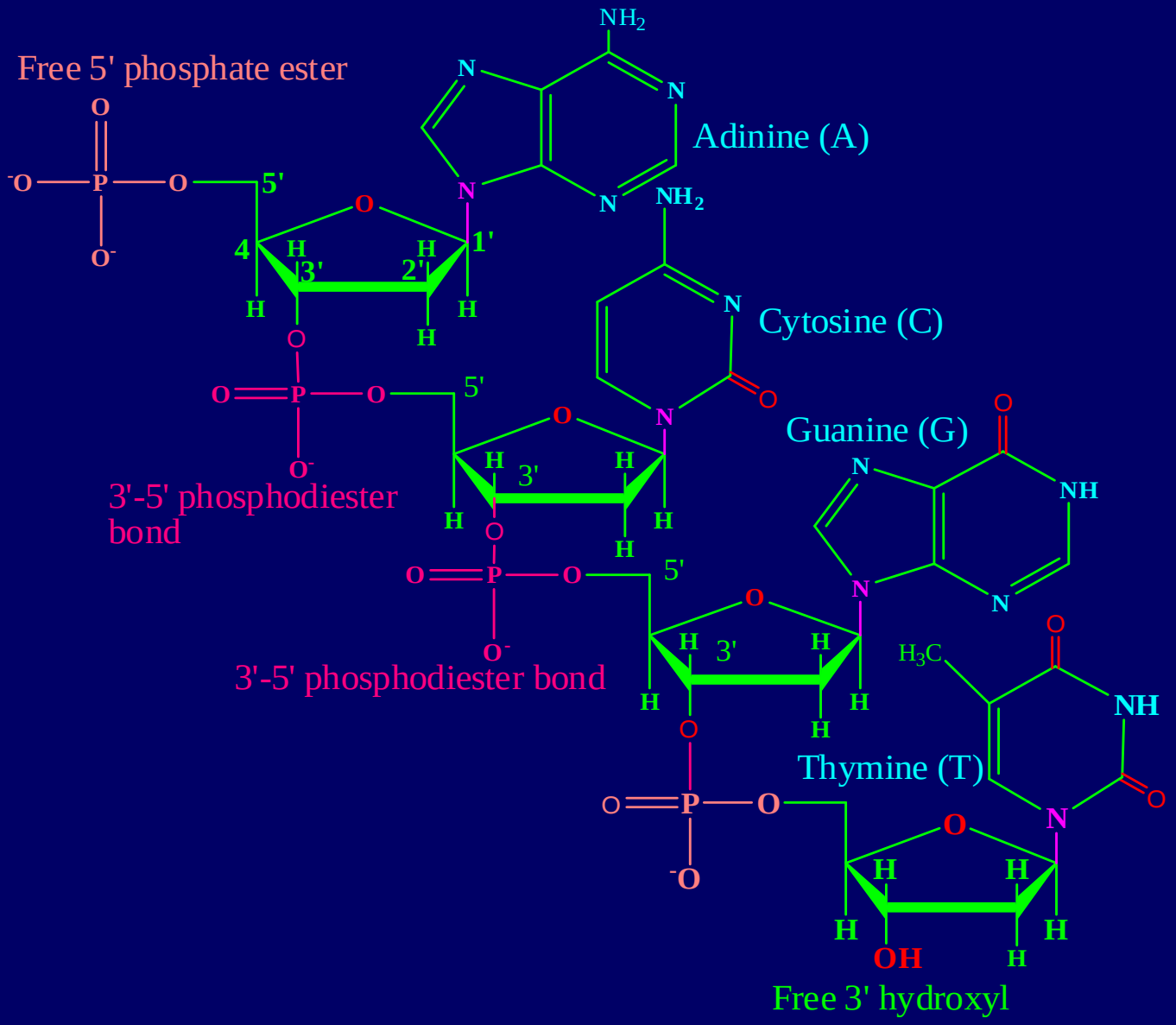


Example of RNA Primary Structure



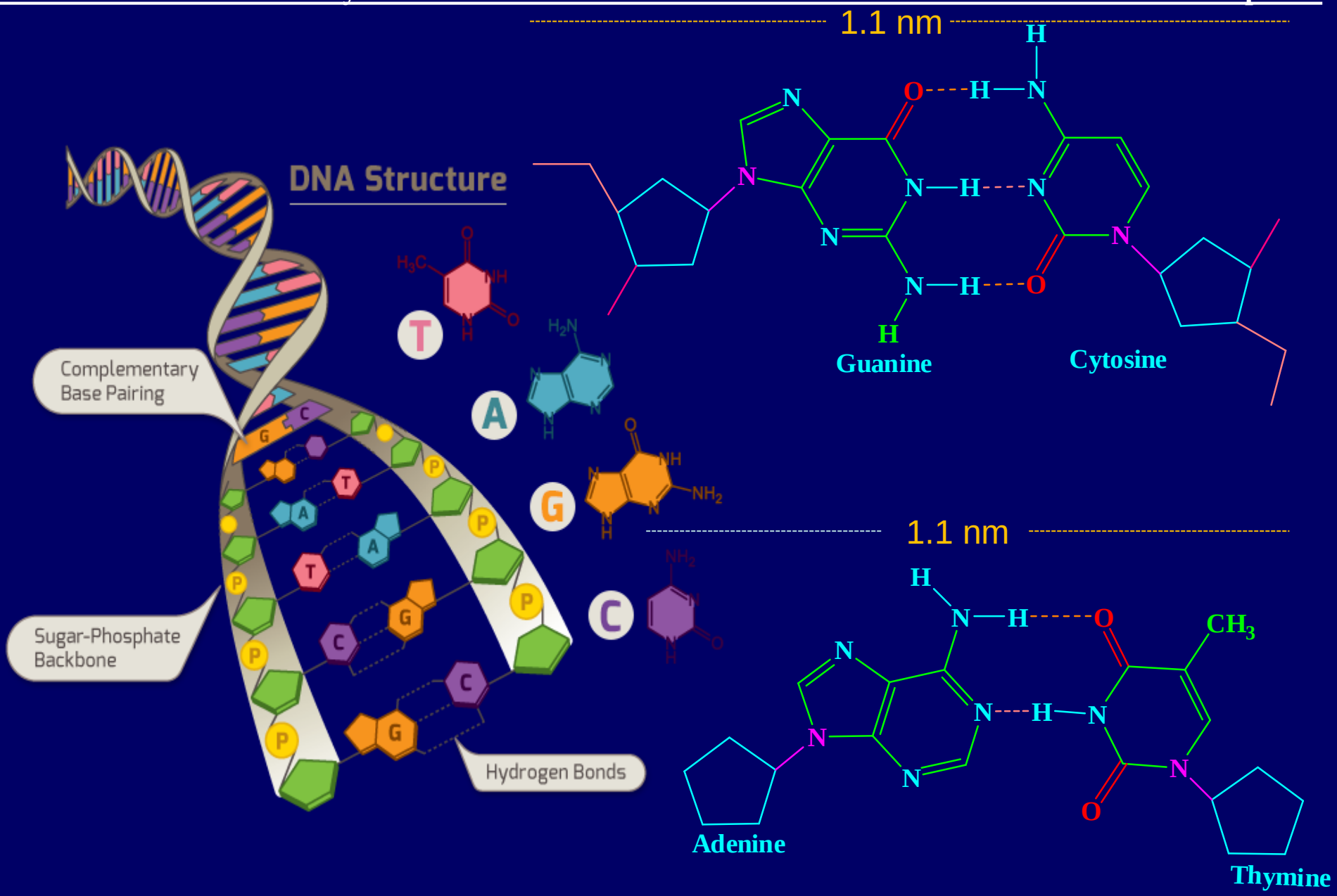
In RNA, A, C, G, and U are linked by 3'-5' ester bonds between ribose and phosphate

Example of DNA Primary Structure



Secondary Structure

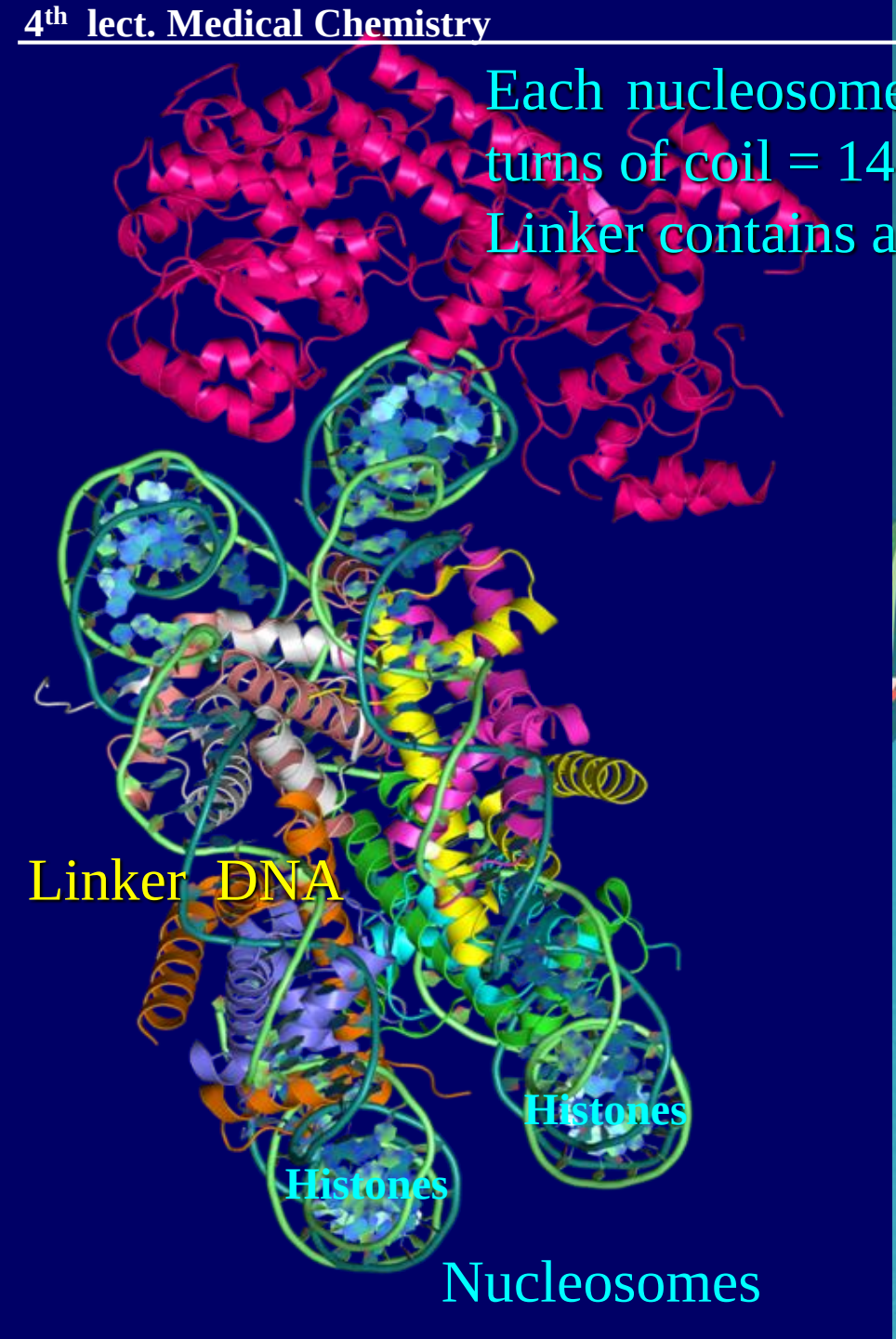
- In DNA there are two strands of nucleotides that wind together in a **double helix.**
- The strands run in opposite directions
- The bases are arranged in step-like pairs
- The **base pairs** are held together by hydrogen bonding
- The pairing of the bases from the two strands is very specific.
- The **complimentary base pairs** are **A-T(Two hydrogen bonds)** and **G-C (Three hydrogen bonds)**
- Each pair consists of a purine and a pyrimidine, so they are the same width, keeping the two strands at equal distances from each other

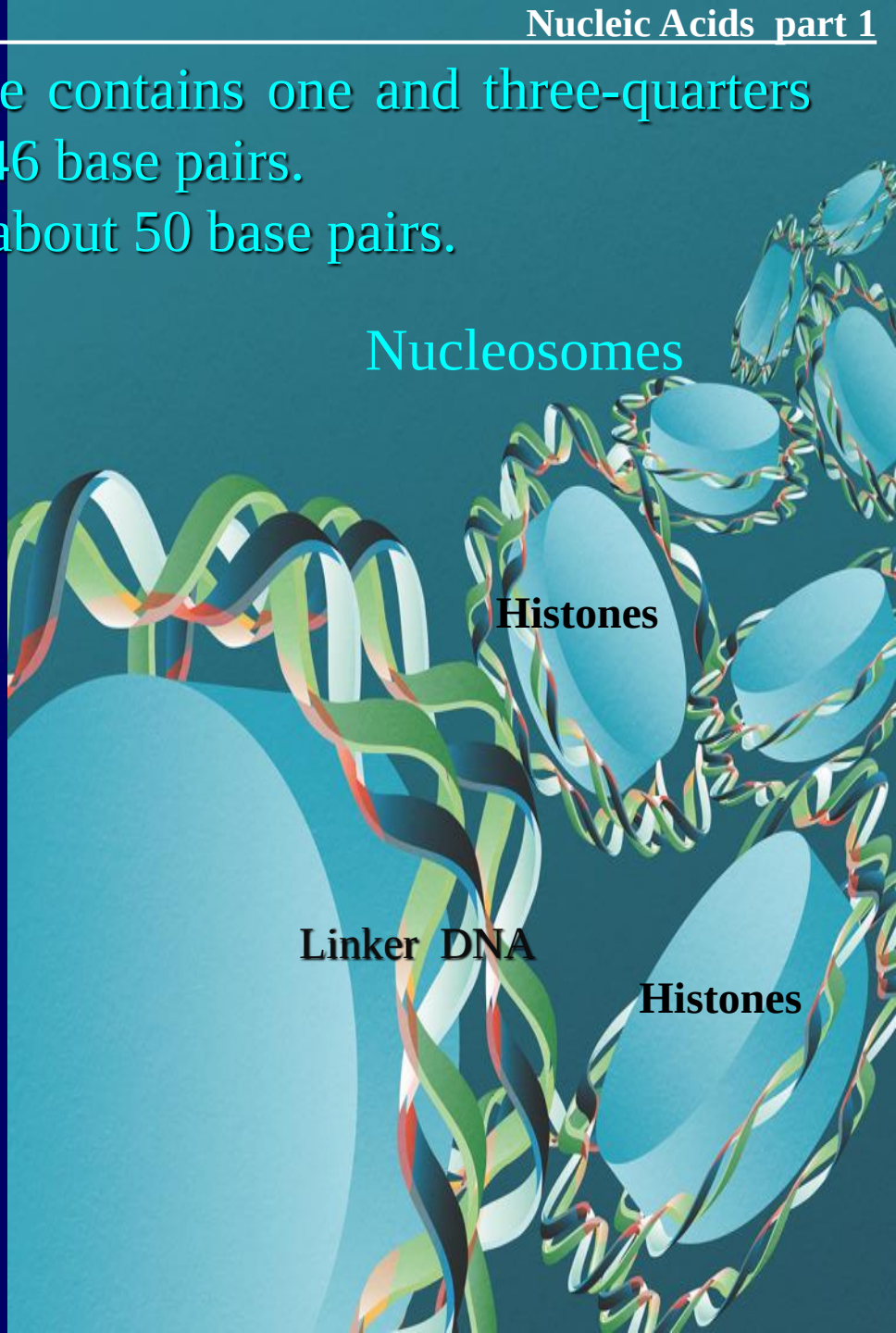

1.1 nm
DNA Structure
Complementary Base Pairing
Sugar-Phosphate Backbone
Hydrogen Bonds
T
A
G
C
Guanine
Cytosine
1.1 nm
Adenine
Thymine

Tertiary Structure of DNA: Supercoils

- A strand of DNA is too long (about 3 cm in length) to fit inside a cell unless it is coiled.
- Random coiling would reduce accessibility to critical regions.
- Efficient coiling of DNA is accomplished with the aid of proteins called **histones.**
- Histones are proteins rich in basic amino acids such as lysine and arginine.
- Histones are positively charged at biological pH. DNA is negatively charged.
- DNA winds around histone proteins to form nucleosomes.

Each nucleosome contains one and three-quarters turns of coil = 146 base pairs.
Linker contains about 50 base pairs.





thank you!