27.23
Pyrimidines and Purines

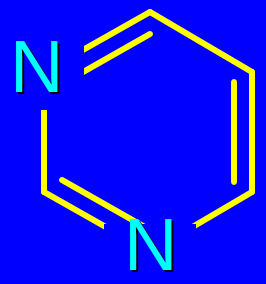
Pyrimidines and Purines

In order to understand the structure and properties of DNA and RNA, we need to look at their structural components.

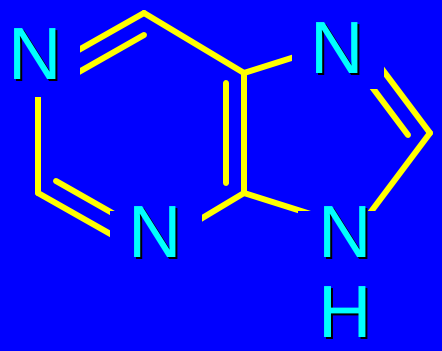
We begin with certain heterocyclic aromatic compounds called pyrimidines and purines.

Pyrimidines and Purines

Pyrimidine and purine are the names of the parent compounds of two types of nitrogen-containing heterocyclic aromatic compounds.



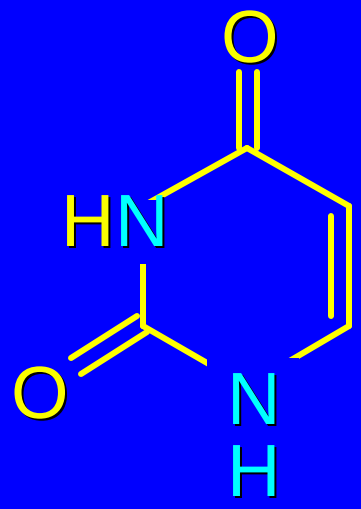
Pyrimidine



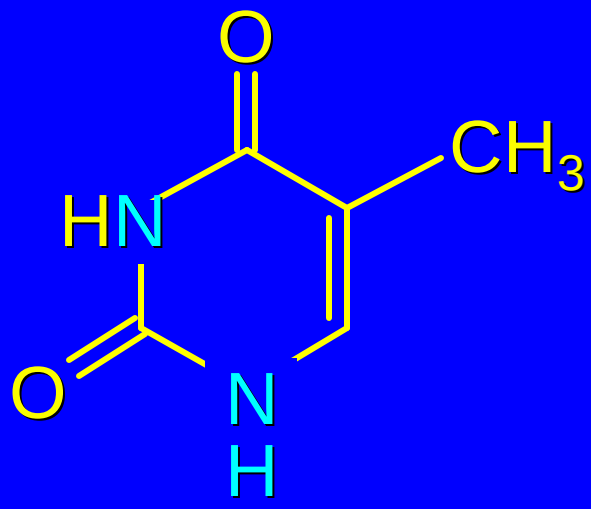
Purine

Important Pyrimidines

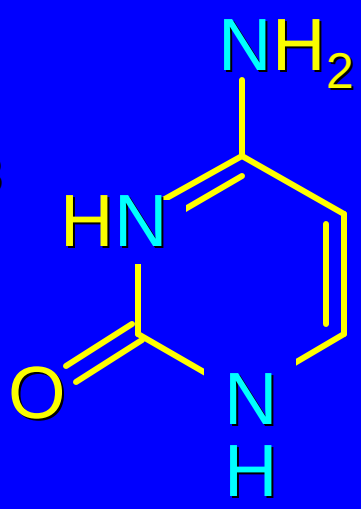
Pyrimidines that occur in DNA are cytosine and thymine. Cytosine and uracil are the pyrimidines in RNA.



Uracil



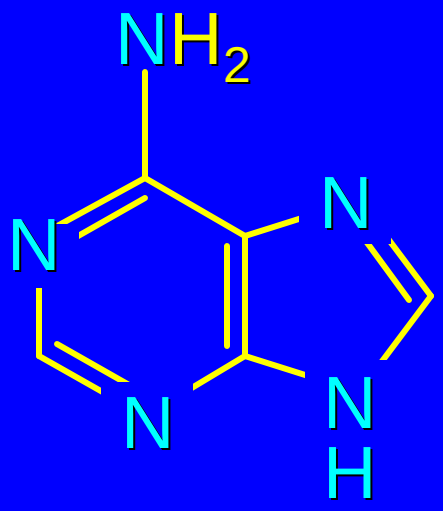
Thymine



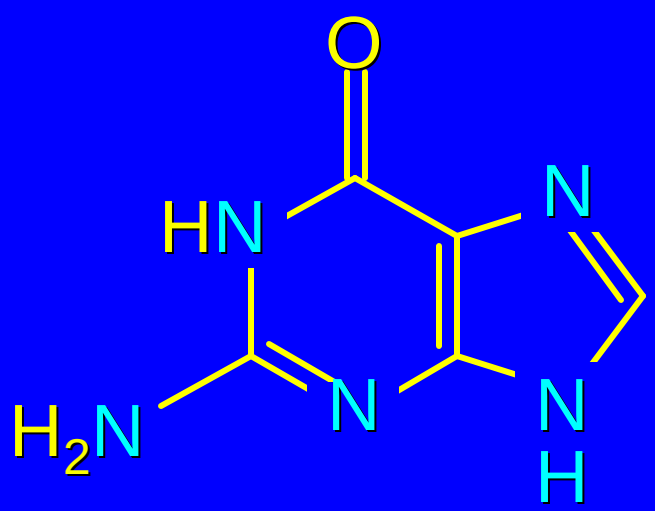
Cytosine

Important Purines

Adenine and guanine are the principal purines of both DNA and RNA.



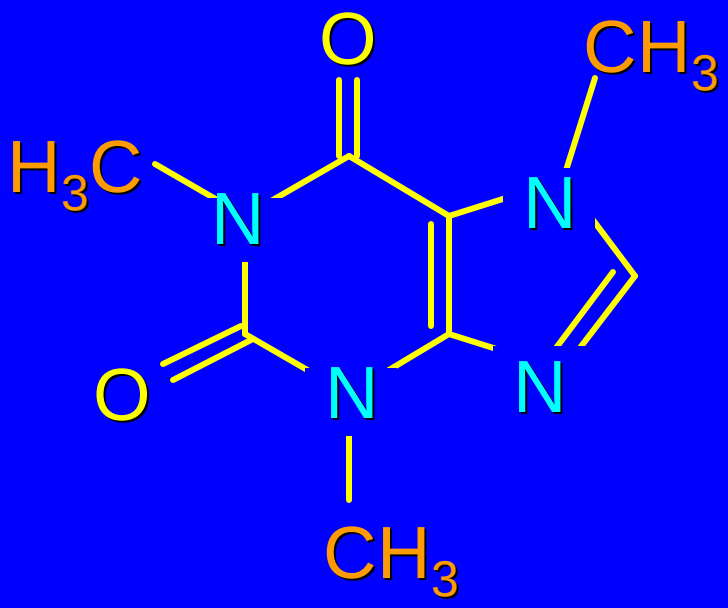
Adenine



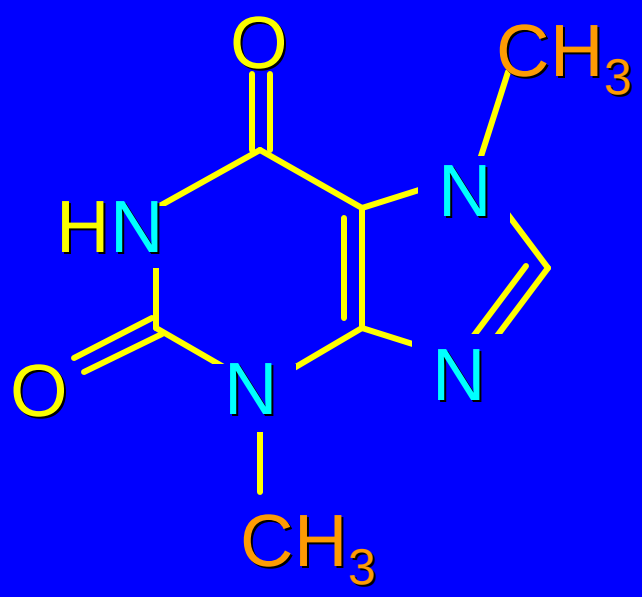
Guanine

Caffeine and Theobromine

Caffeine (coffee) and theobromine (coffee and tea) are naturally occurring purines.



Caffeine



Theobromine

27.24
Nucleosides

Nucleosides

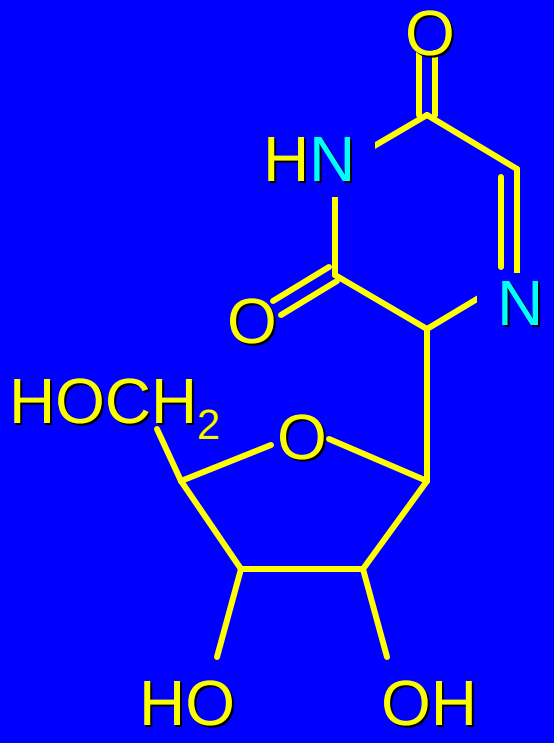
The classical structural definition is that a nucleoside is a pyrimidine or purine N-glycoside of D-ribofuranose or 2-deoxy-D-ribofuranose.

Informal use has extended this definition to apply to purine or pyrimidine N-glycosides of almost any carbohydrate.

The purine or pyrimidine part of a nucleoside is referred to as a *purine or pyrimidine base*.

Uridine and Adenosine

Uridine and adenosine are pyrimidine and purine nucleosides respectively of D-ribofuranose.



Uridine
(a pyrimidine nucleoside)

Adenosine
(a purine nucleoside)

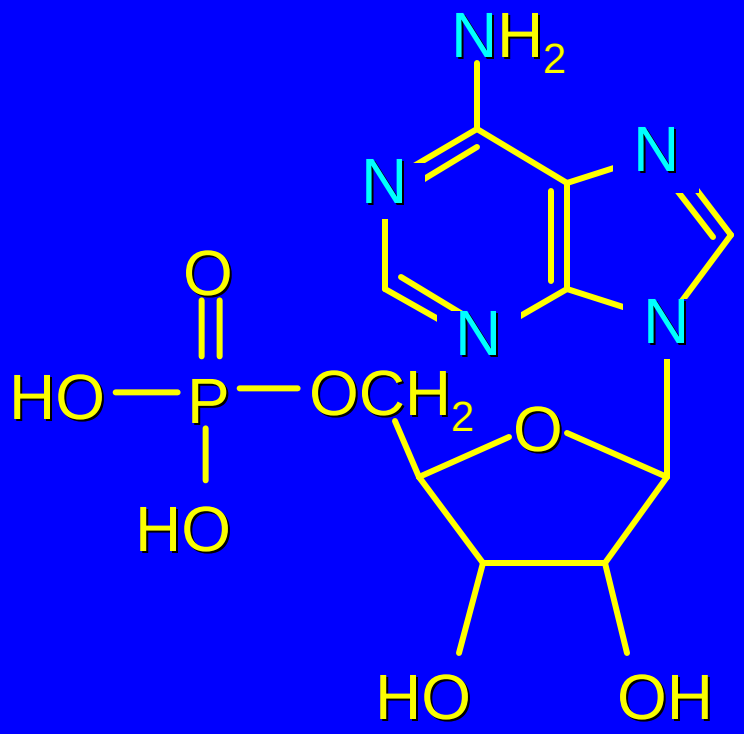
27.25
Nucleotides

Nucleotides

Nucleotides are phosphoric acid esters of nucleosides.

Adenosine 5'-Monophosphate (AMP)

Adenosine 5'-monophosphate (AMP) is also called 5'-adenylic acid.



Adenosine 5'-Monophosphate (AMP)

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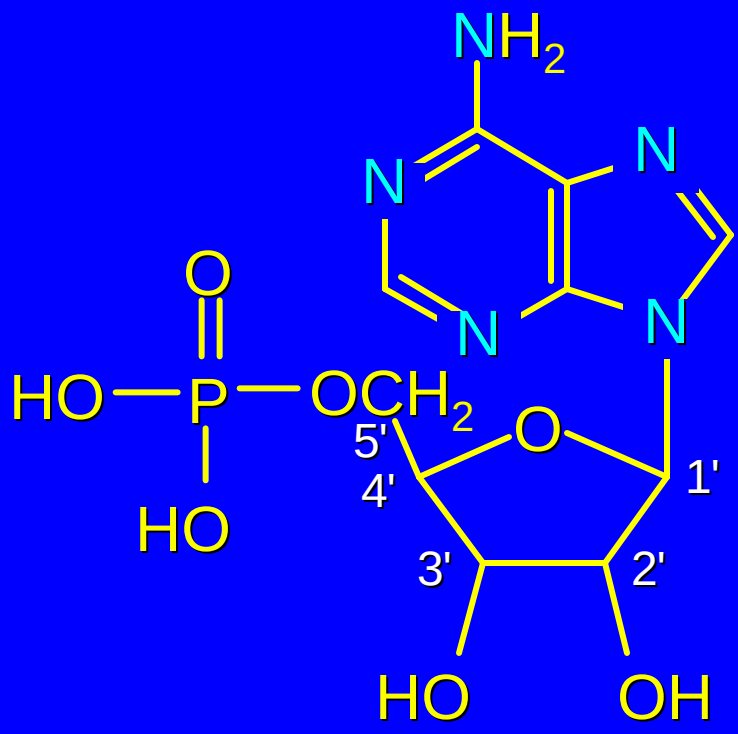
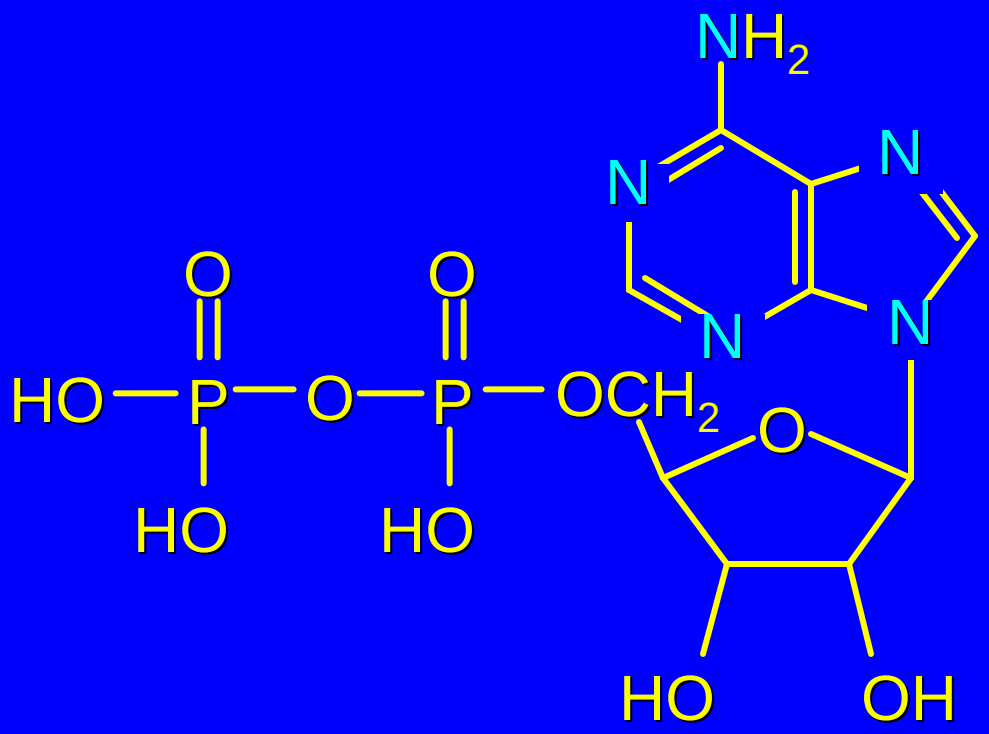
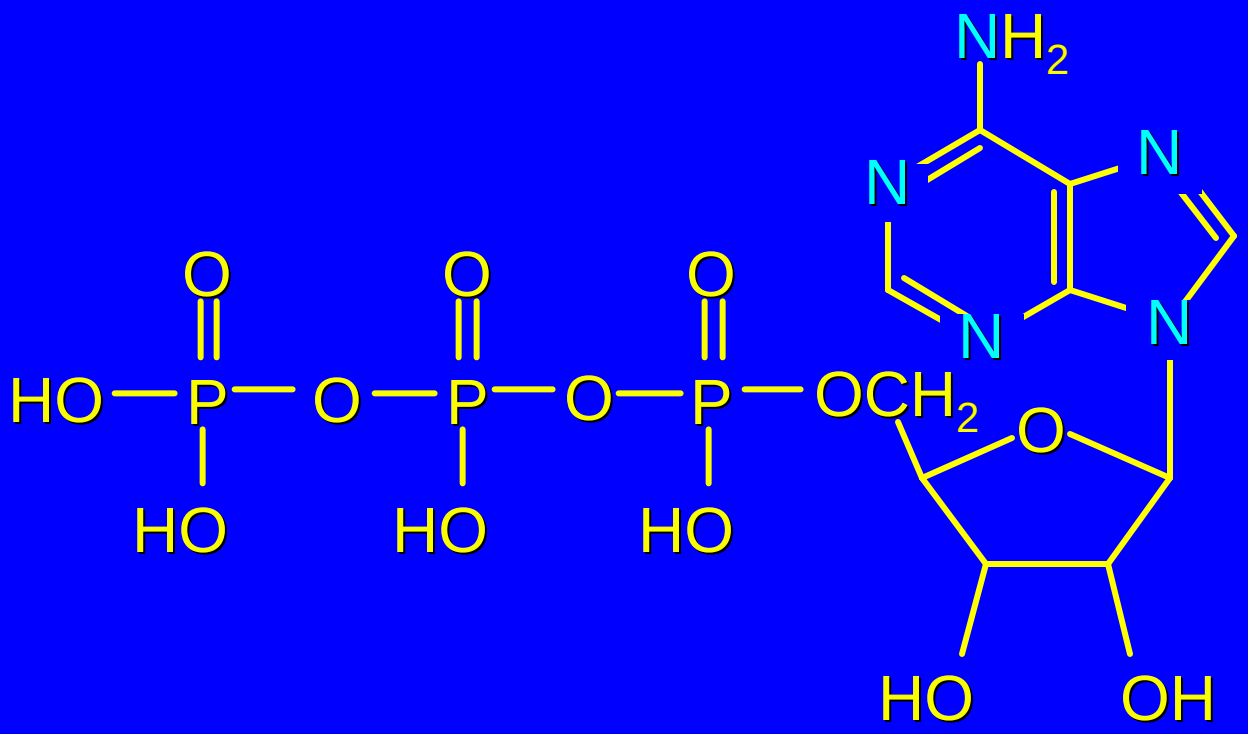


Adenosine Diphosphate (ADP)



Adenosine Triphosphate (ATP)



ATP Stores Energy

Each step is endothermic.

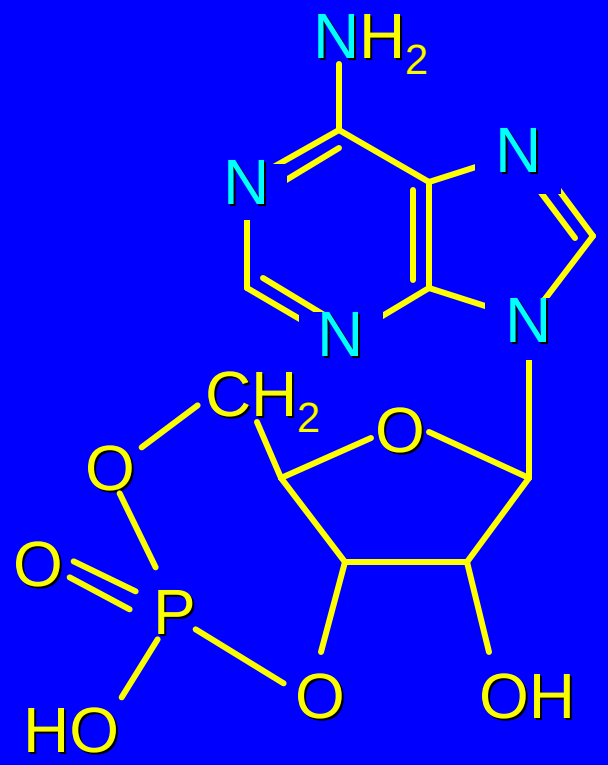
Energy for each step comes from carbohydrate metabolism (glycolysis).

Reverse process is exothermic and is the source of biological energy.

ΔG° for hydrolysis of ATP to ADP is –35 kJ/mol

Adenosine 3'-5'-Cyclic Monophosphate (cAMP)

Cyclic AMP is an important regulator of many biological processes.



27.26
Nucleic Acids

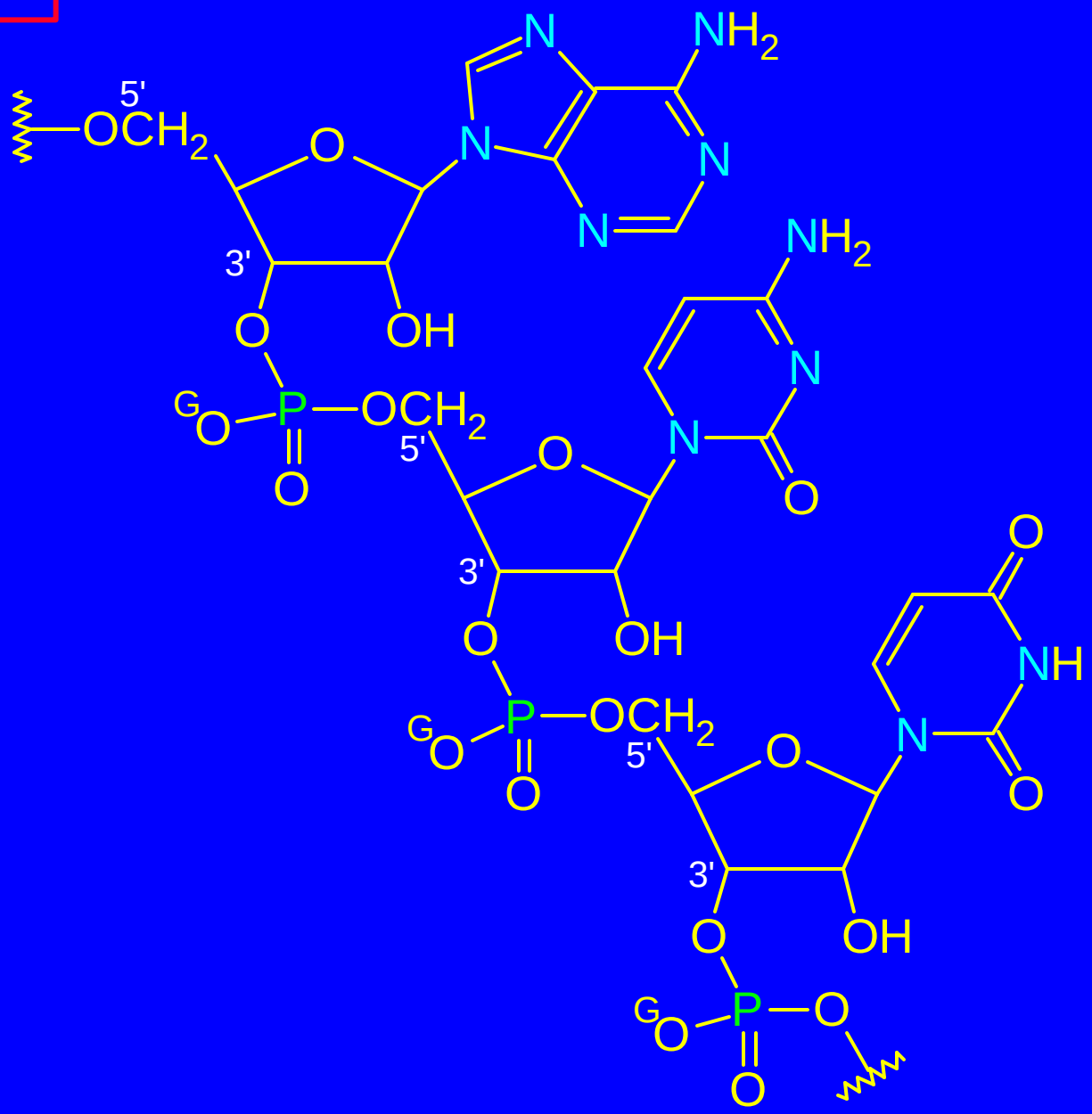
Nucleic Acids

Nucleic acids are polymeric nucleotides (*polynucleotides).*

5' Oxygen of one nucleotide is linked to the 3' oxygen of another.

Fig. 27.22

A section of a polynucleotide chain.



27.27
Structure and Replication of DNA: The Double Helix

Composition of DNA

Erwin Chargaff (Columbia Univ.) studied DNAs from various sources and analyzed the distribution of purines and pyrimidines in them.

The distribution of the bases adenine (A), guanine (G), thymine (T), and cytosine (C) varied among species.

But the total purines (A and G) and the total pyrimidines (T and C) were always equal.

Moreover: %A = %T, and %G = %C

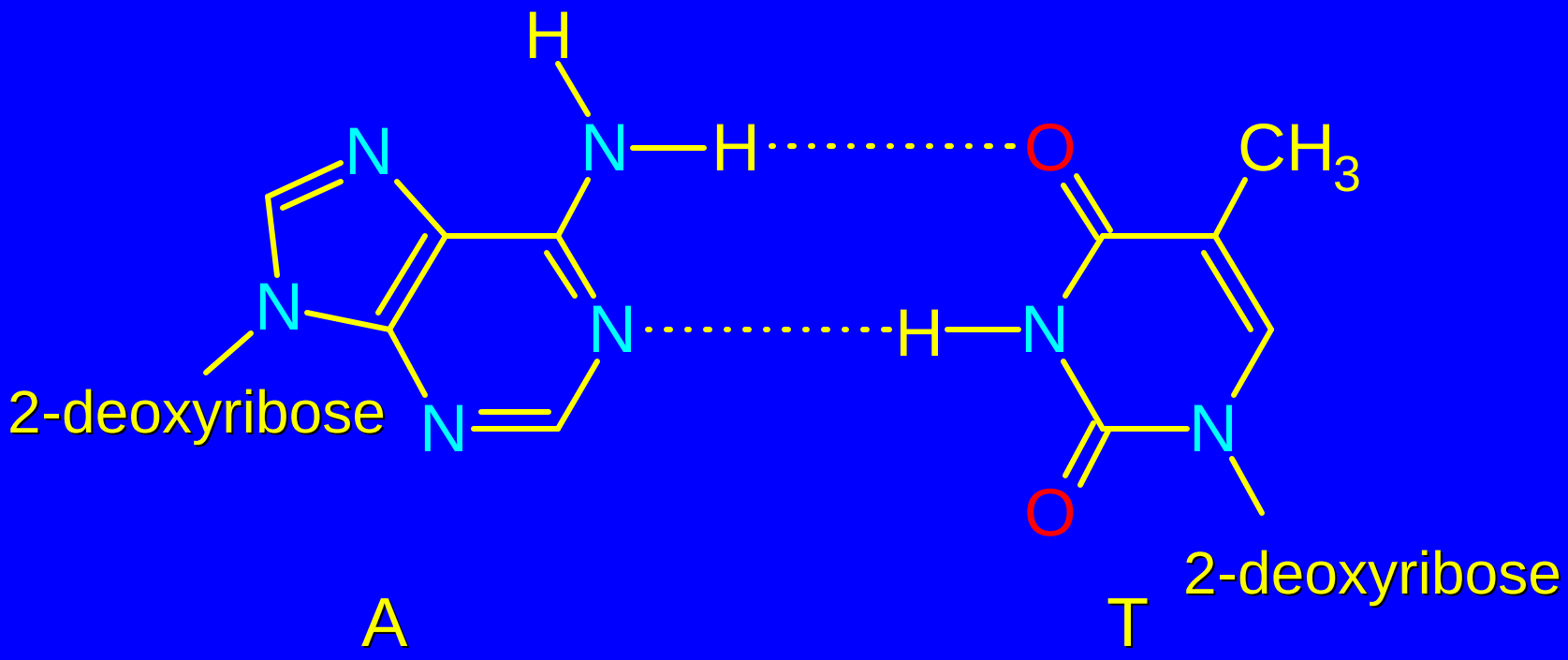
Composition of Human DNA

For example:

Purine	Pyrimidine
Adenine (A) 30.3%	Thymine (T) 30.3%
Guanine (G) 19.5%	Cytosine (C) 19.9%
Total purines: 49.8%	Total pyrimidines: 50.1%

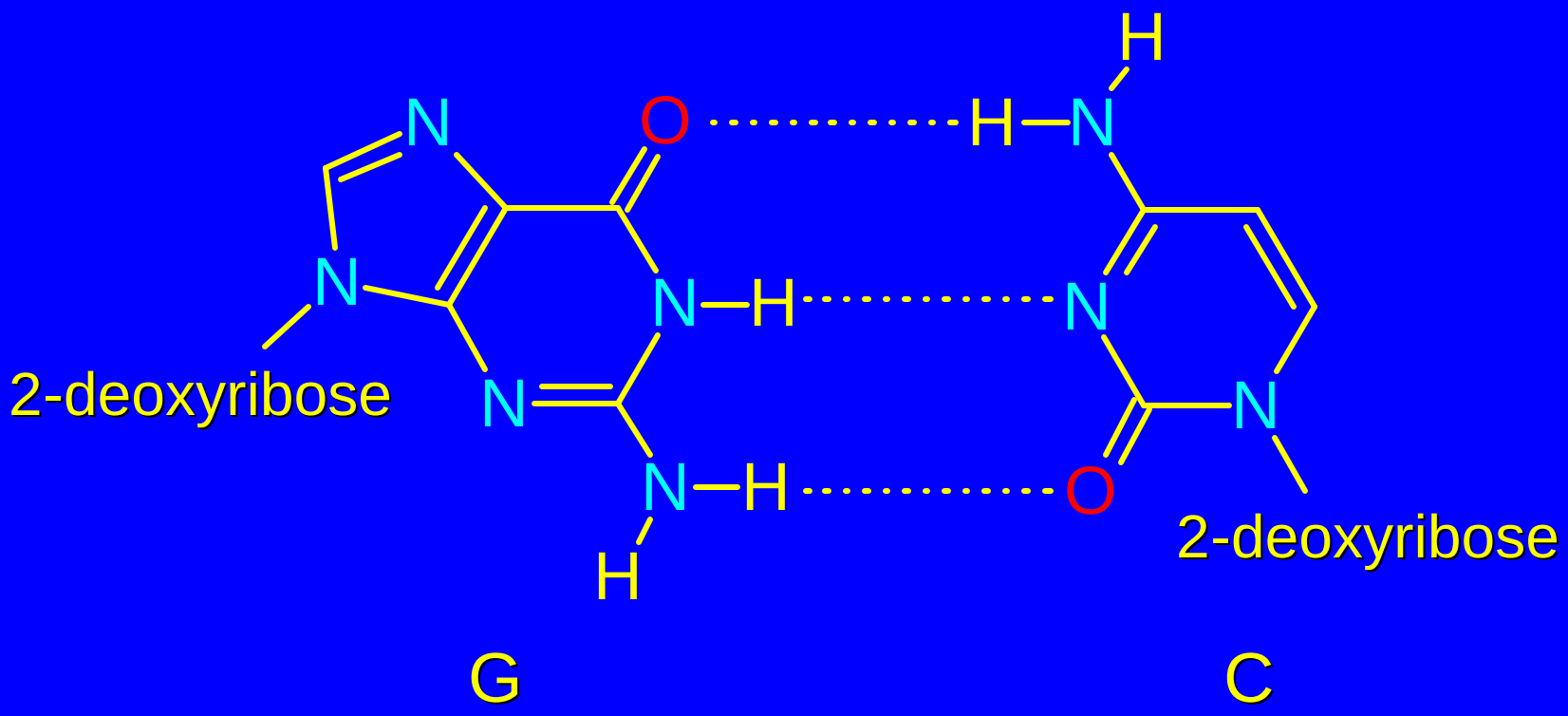
Base Pairing

Watson and Crick proposed that A and T were equal because of complementary hydrogen bonding.



Base Pairing

Likewise, the amounts of G and C were equal because of complementary hydrogen bonding.



The DNA Duplex

Watson and Crick proposed a double-stranded structure for DNA in which a purine or pyrimidine base in one chain is hydrogen bonded to its complement in the other.

Fig. 27.24

Two antiparallel strands of DNA are paired by hydrogen bonds between purine and pyrimidine bases.

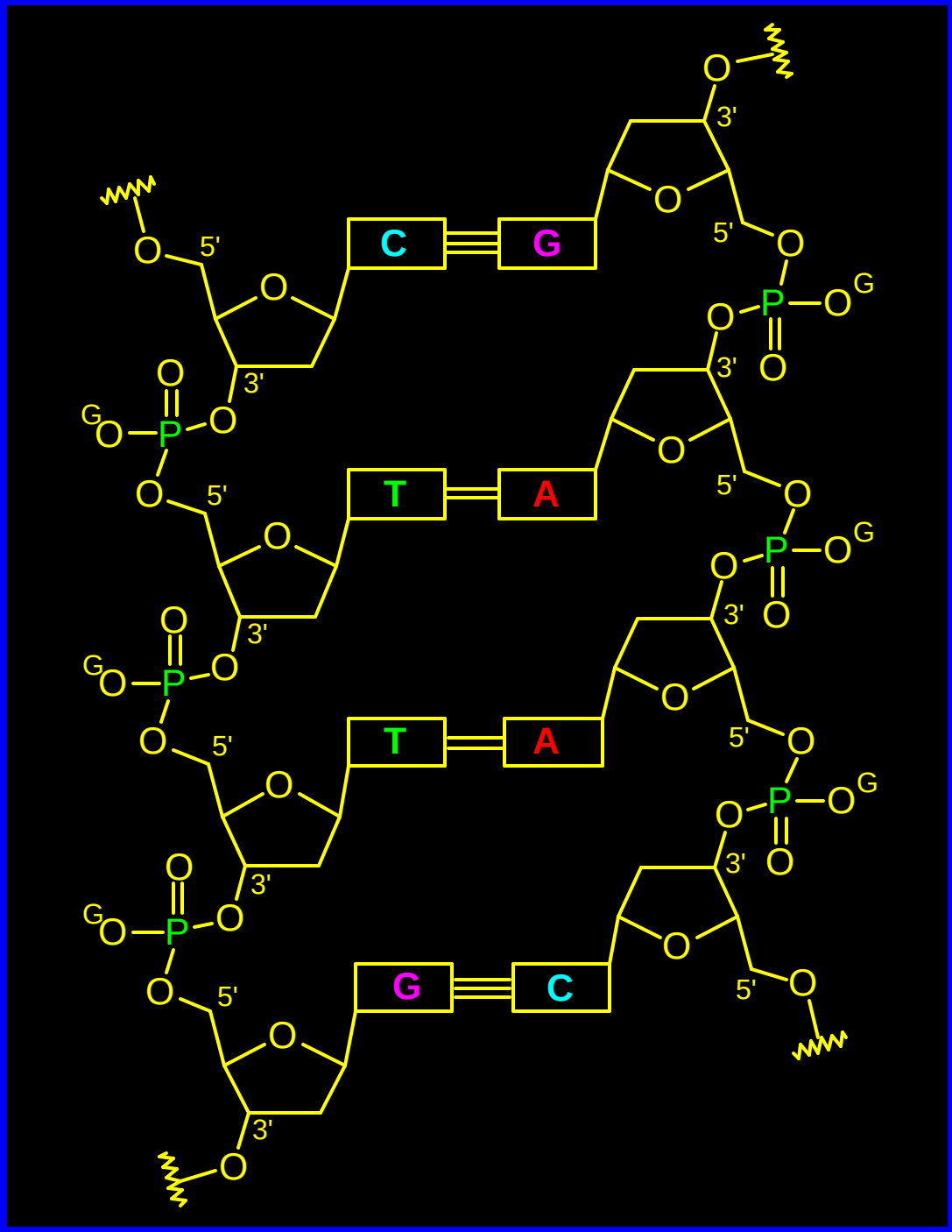
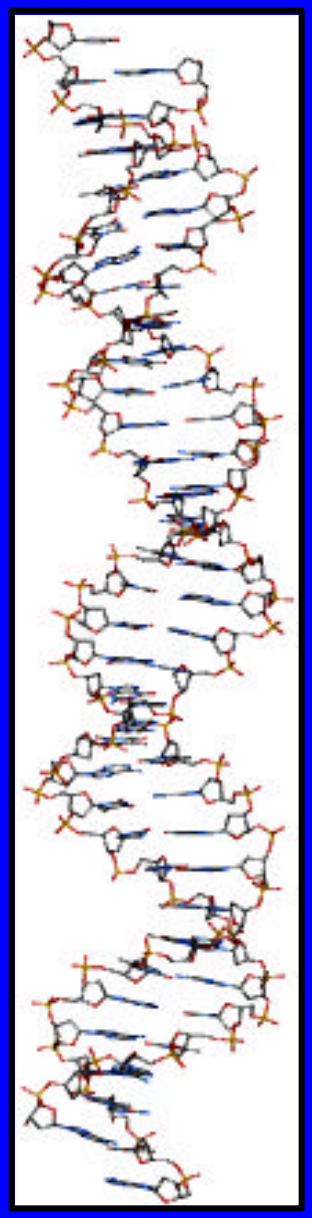


Fig. 27.25

Helical structure of DNA. The purine and pyrimidine bases are on the inside, sugars and phosphates on the outside.



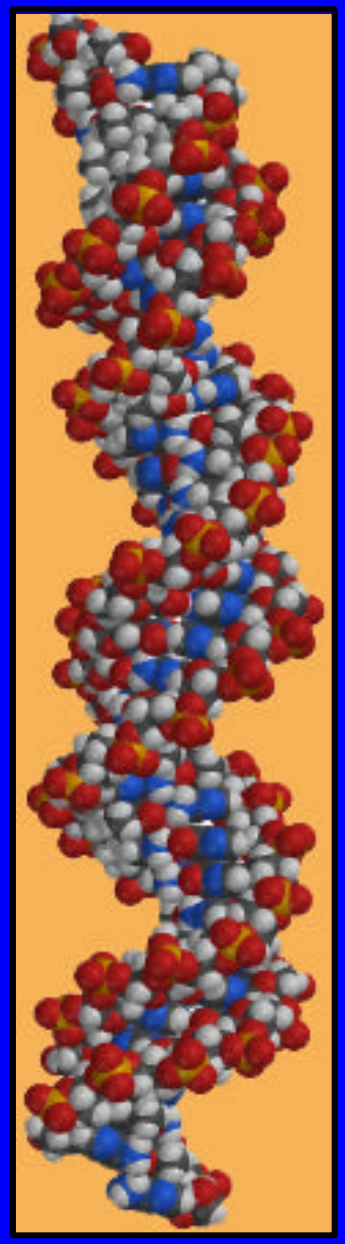
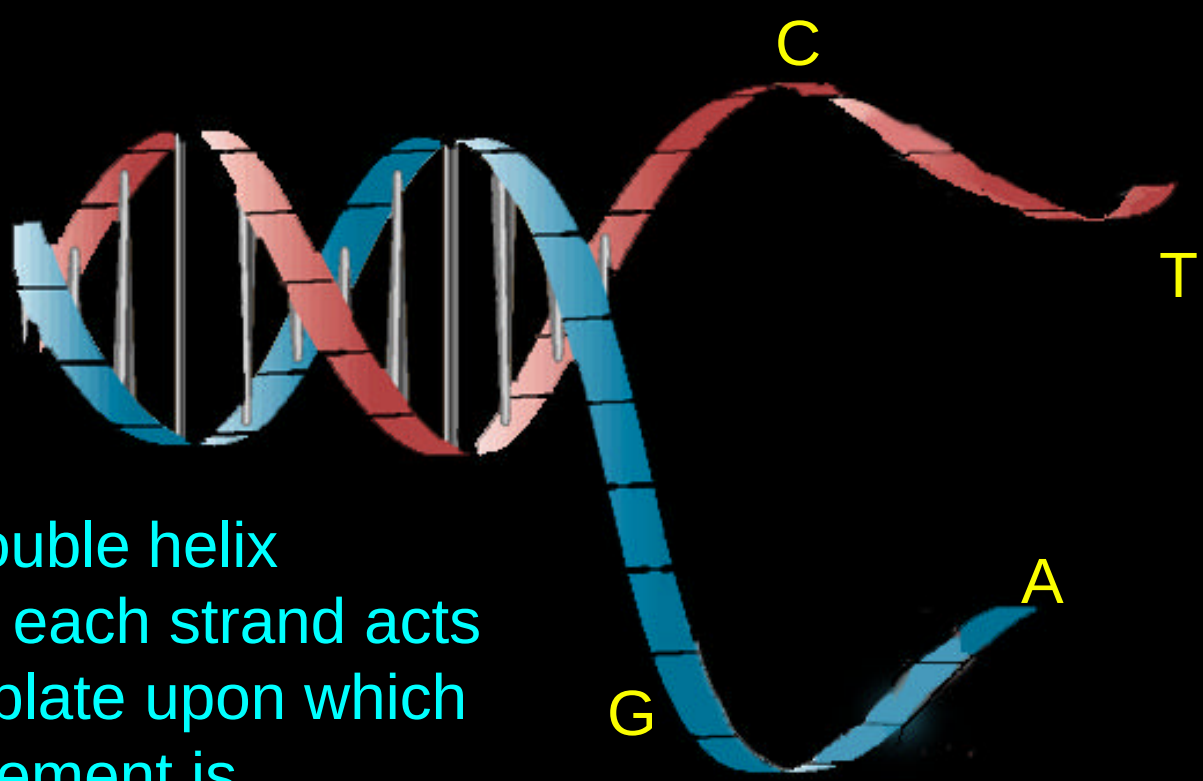
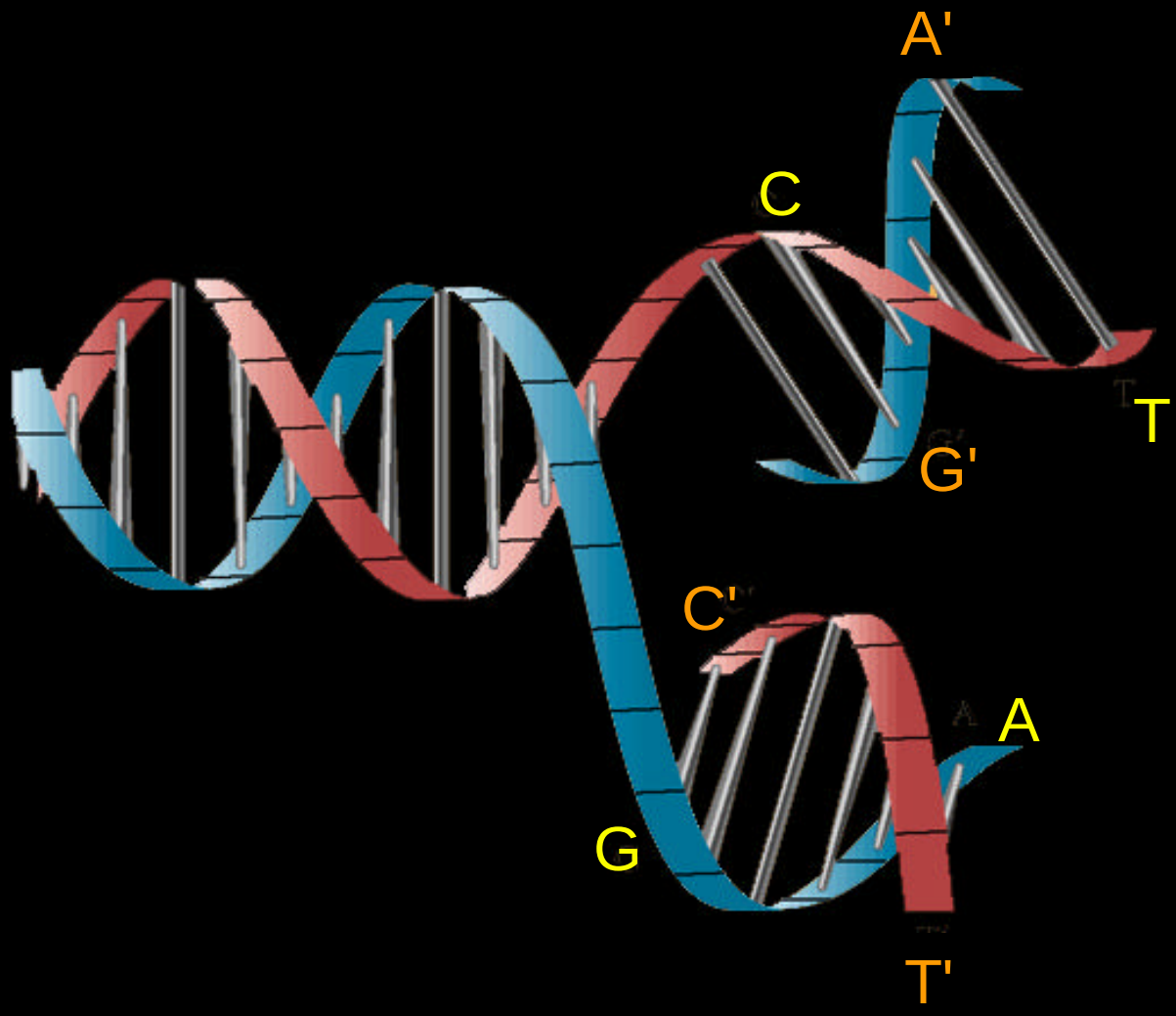


Fig. 27.26 DNA Replication



As the double helix unwinds, each strand acts as a template upon which its complement is constructed.

Fig. 27.26 DNA Replication



27.28
DNA-Directed Protein Biosynthesis

DNA and Protein Biosynthesis

According to Crick, the "central dogma" of molecular biology is:

"DNA makes RNA makes protein."

Three kinds of RNA are involved.

- messenger RNA (mRNA)
- transfer RNA (tRNA)
- ribosomal RNA (rRNA)

There are two main stages.

- transcription
- translation

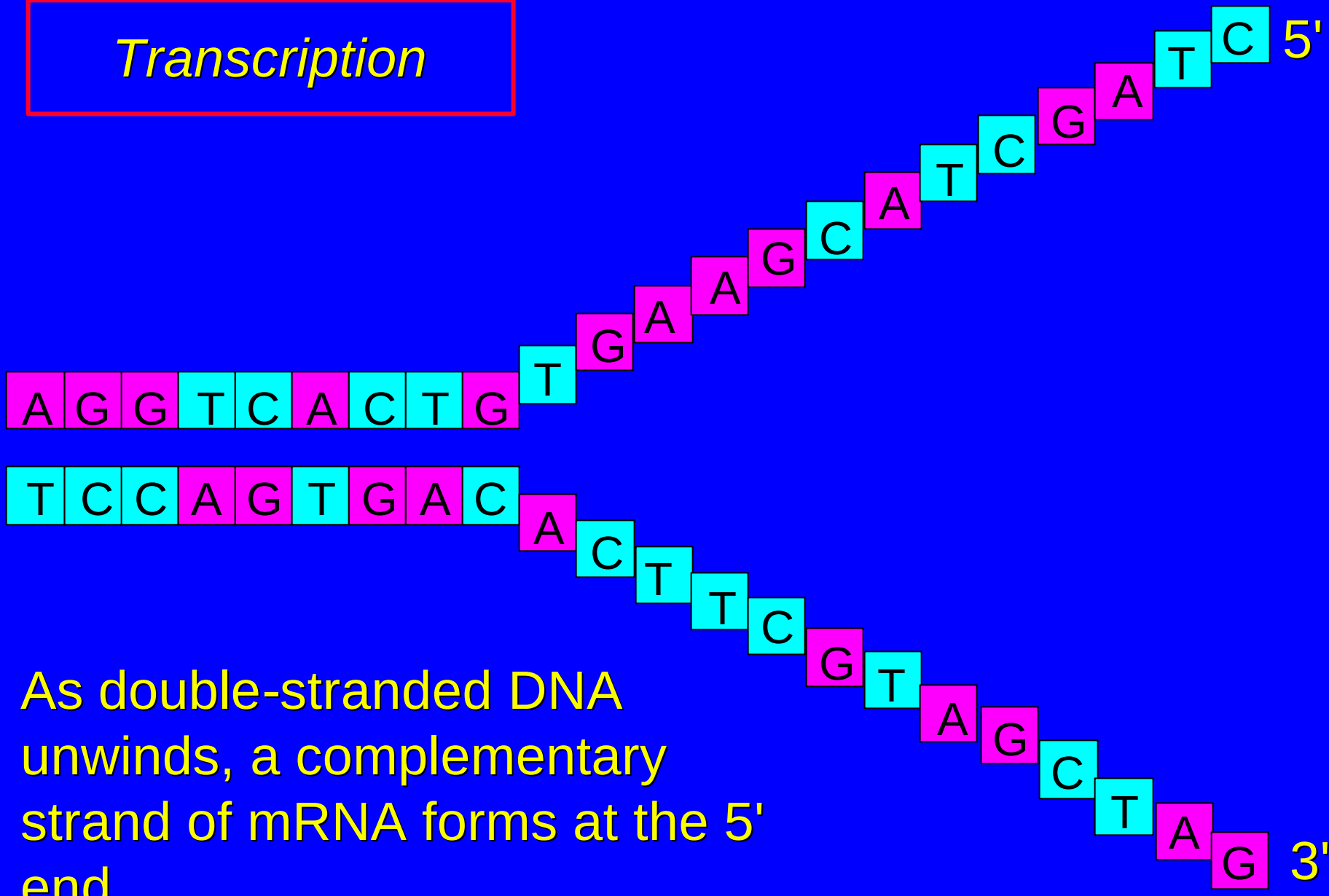
Transcription

Transcription is the formation of a strand of mRNA using one of the DNA strands as a template.

The nucleotide sequence of the mRNA is complementary to the nucleotide sequence of the DNA template.

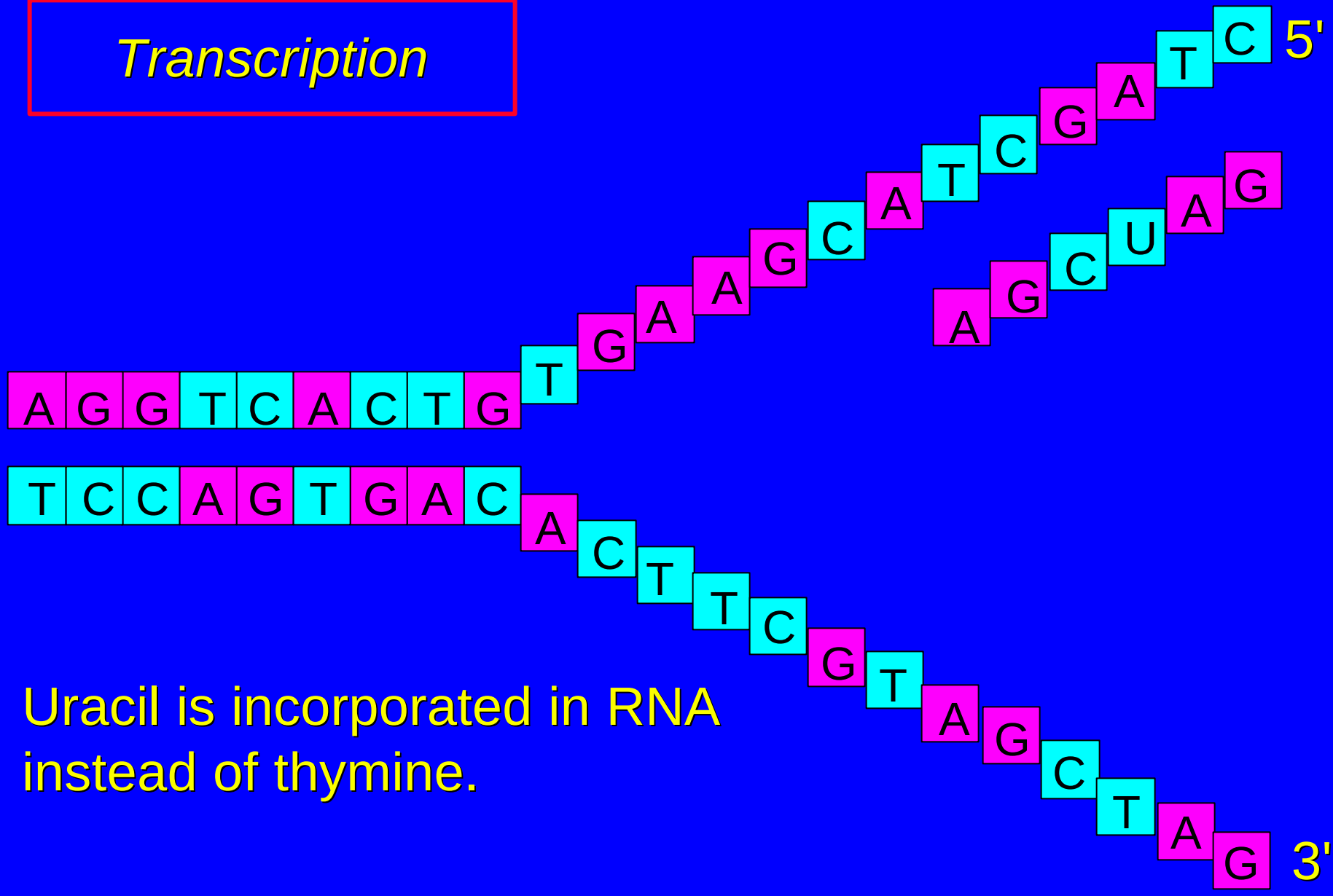
Transcription begins at the 5' end of DNA and is catalyzed by the enzyme *RNA polymerase*.

Transcription



As double-stranded DNA unwinds, a complementary strand of mRNA forms at the 5' end.

Transcription



Uracil is incorporated in RNA instead of thymine.

Translation

The nucleotide sequence of mRNA codes for the different amino acids found in proteins.

There are three nucleotides per codon.

There are 64 possible combinations of A, U, G, and C.

The genetic code is redundant. Some proteins are coded for by more than one codon.

Table 27.4: mRNA Codons

Alanine	Arginine	Asparagine	Aspartic Acid	Cysteine
GCU GCA GCC GCG	CGU CGA AGA CGC CGG AGG	AAU AAC	GAU GAC	UGU UGC
Glutamic acid	**Glutamine**	**Glycine**	**Histidine**	**Isoleucine**
GAA GAG	CAA CAG	GGU GGA GGC GGG	CAU CAC	AUU AUA AUC
Leucine	**Lysine**	**Methionine**	**Phenylalanine**	**Proline**
UUA CUU CUA UUG CUC CUG	AAA AAG	AUG	UUU UUC	CCU CCA CCC CG
Serine	**Threonine**	**Tryptophan**	**Tyrosine**	**Valine**
UCU UCA AGU UCC UCG AGC	ACU ACA ACC ACG	UGG	UAU UAC	GUU GUA GUC GUG

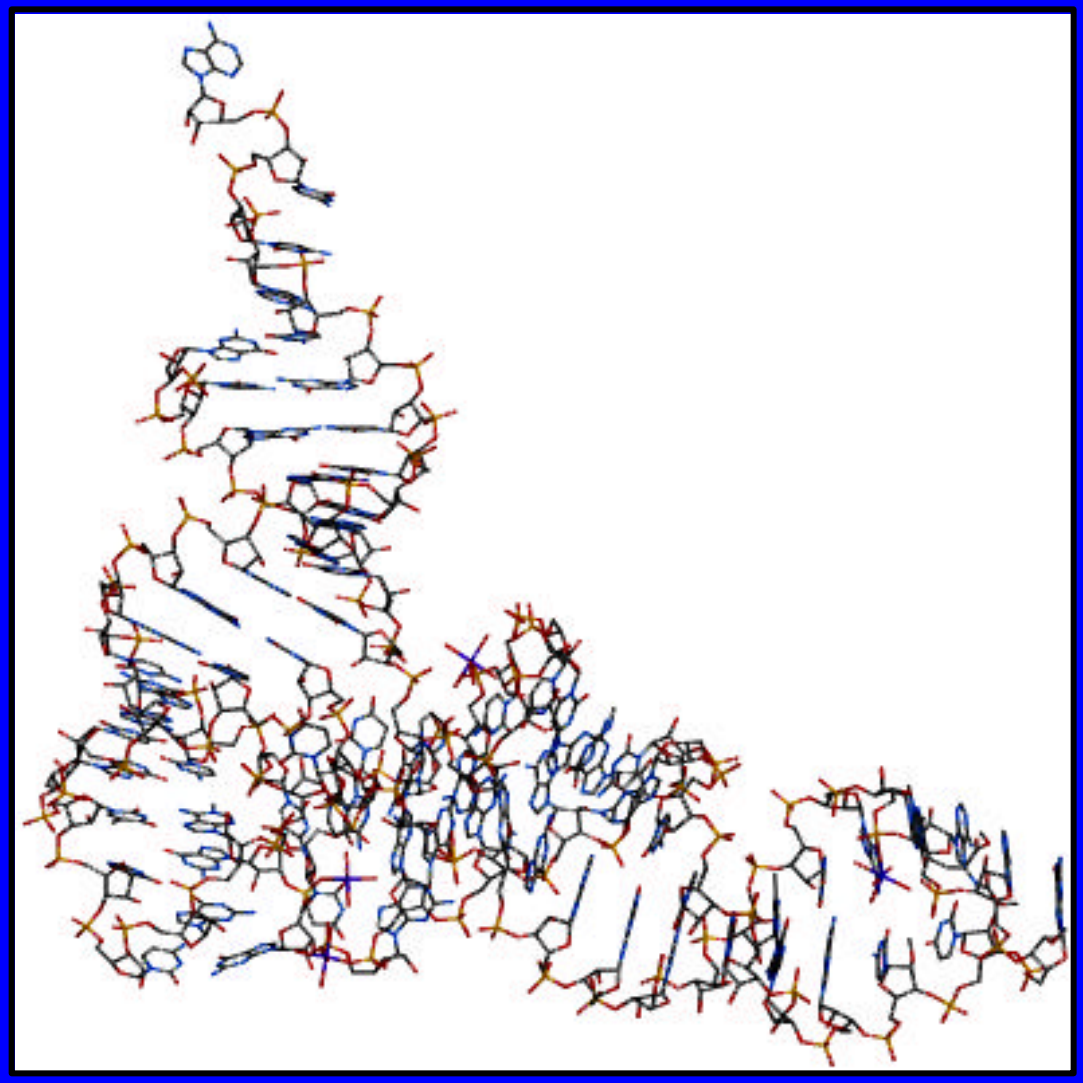
Transfer tRNA

There are 20 different tRNAs, one for each amino acid.

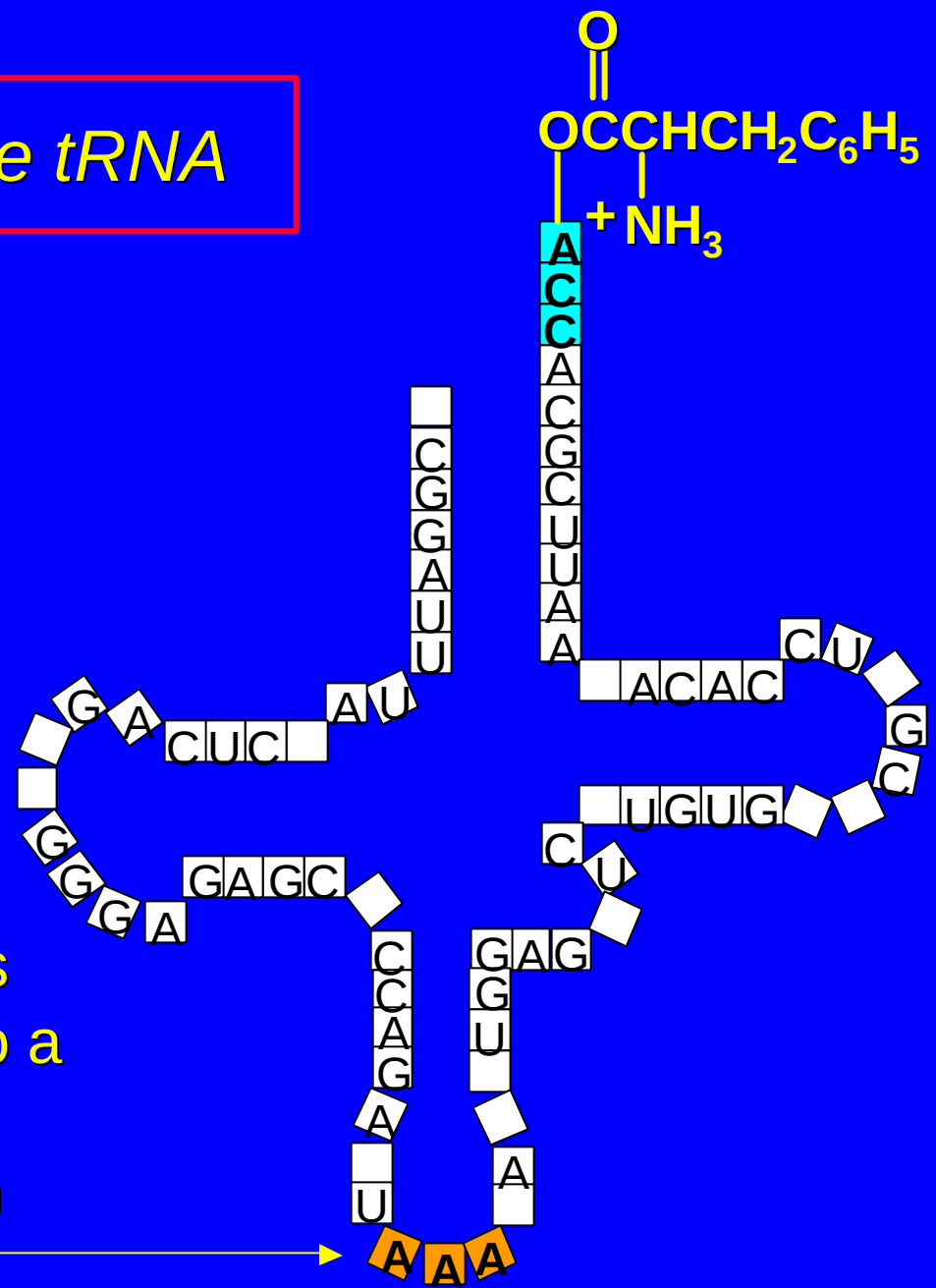
Each tRNA is single stranded with a CCA triplet at its 3' end.

A particular amino acid is attached to the tRNA by an ester linkage involving the carboxyl group of the amino acid and the 3' oxygen of the tRNA.

Phenylalanine tRNA



Phenylalanine tRNA



This AAA triplet is complementary to a UUU triplet of mRNA; it is an *anticodon*.

27.29
DNA Sequencing

DNA Sequencing

Restriction enzymes cleave the polynucleotide to smaller fragments.

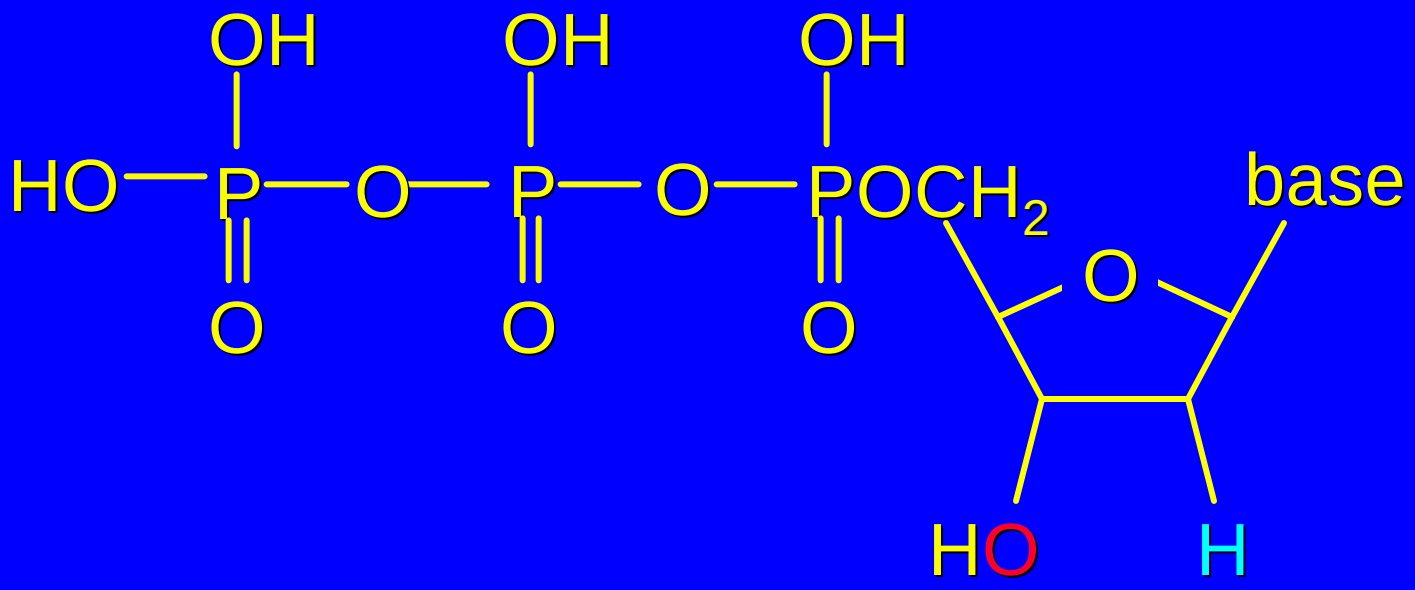
These smaller fragments (100-200 base pairs) are sequenced.

The two strands are separated.

DNA Sequencing

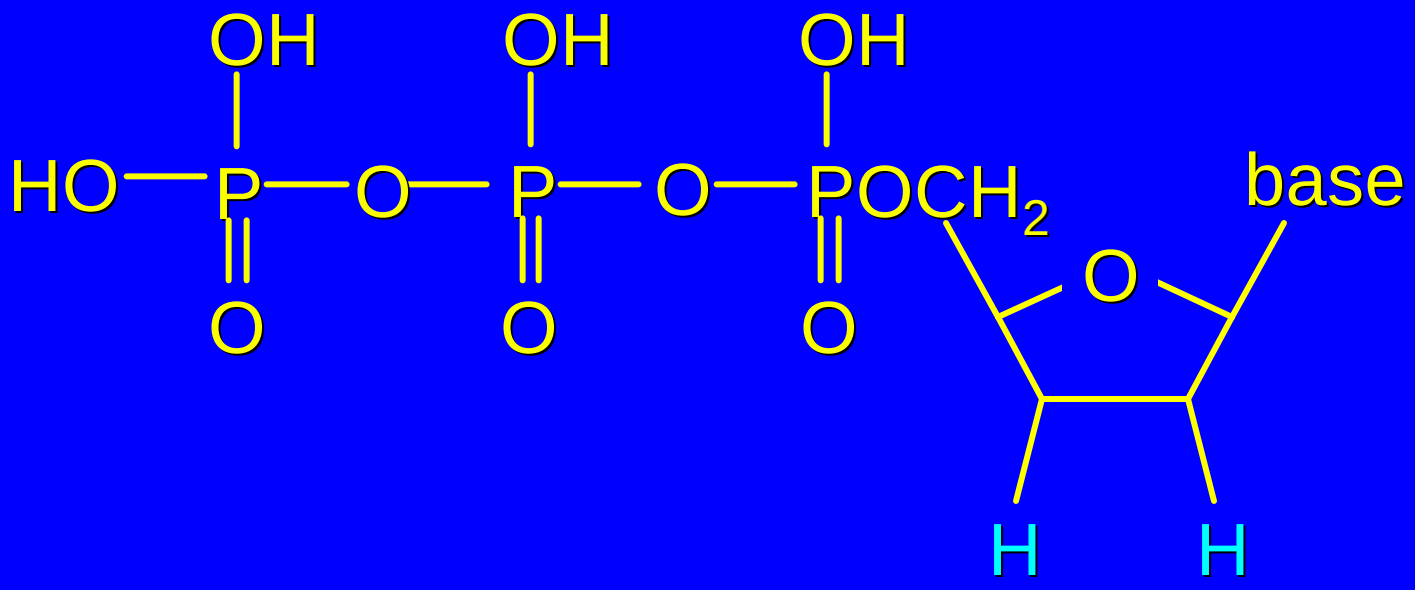
Single stranded DNA divided in four portions.

Each tube contains adenosine, thymidine, guanosine, and cytidine plus the triphosphates of their 2'-deoxy analogs.



DNA Sequencing

The first tube also contains the 2,'3'-dideoxy analog of adenosine triphosphate (ddATP); the second tube the 2,'3'-dideoxy analog of thymidine triphosphate (ddTTP), the third contains ddGTP, and the fourth ddCTP.



DNA Sequencing

Each tube also contains a "primer," a short section of the complementary DNA strand, labeled with radioactive phosphorus (^{32}P).

DNA synthesis takes place, producing a complementary strand of the DNA strand used as a template.

DNA synthesis stops when a dideoxynucleotide is incorporated into the growing chain.

DNA Sequencing

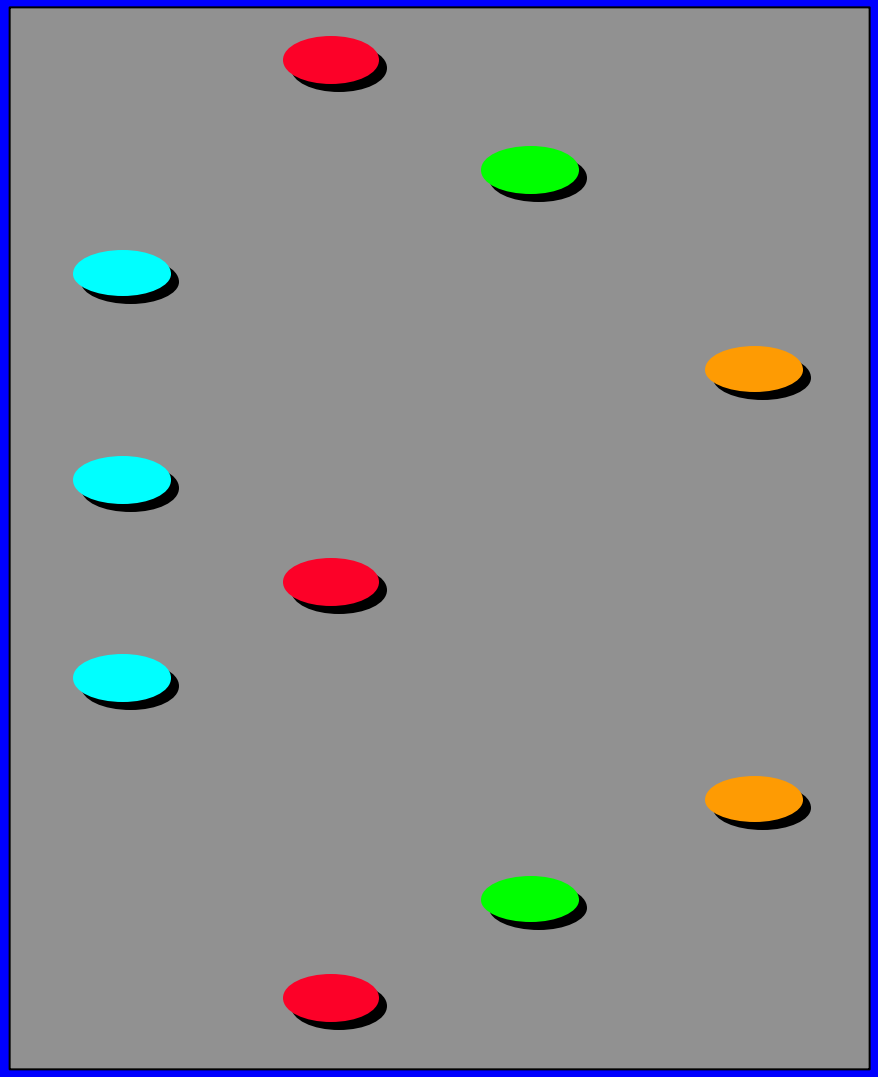
The contents of each tube are separated by electrophoresis and analyzed by autoradiography.

There are four lanes on the electrophoresis gel.

Each DNA fragment will be one nucleotide longer than the previous one.

Figure 27.29

ddA ddT ddG ddC



Sequence of fragment

T

TG

TGA

TGAC

TGACA

TGACAT

TGACATA

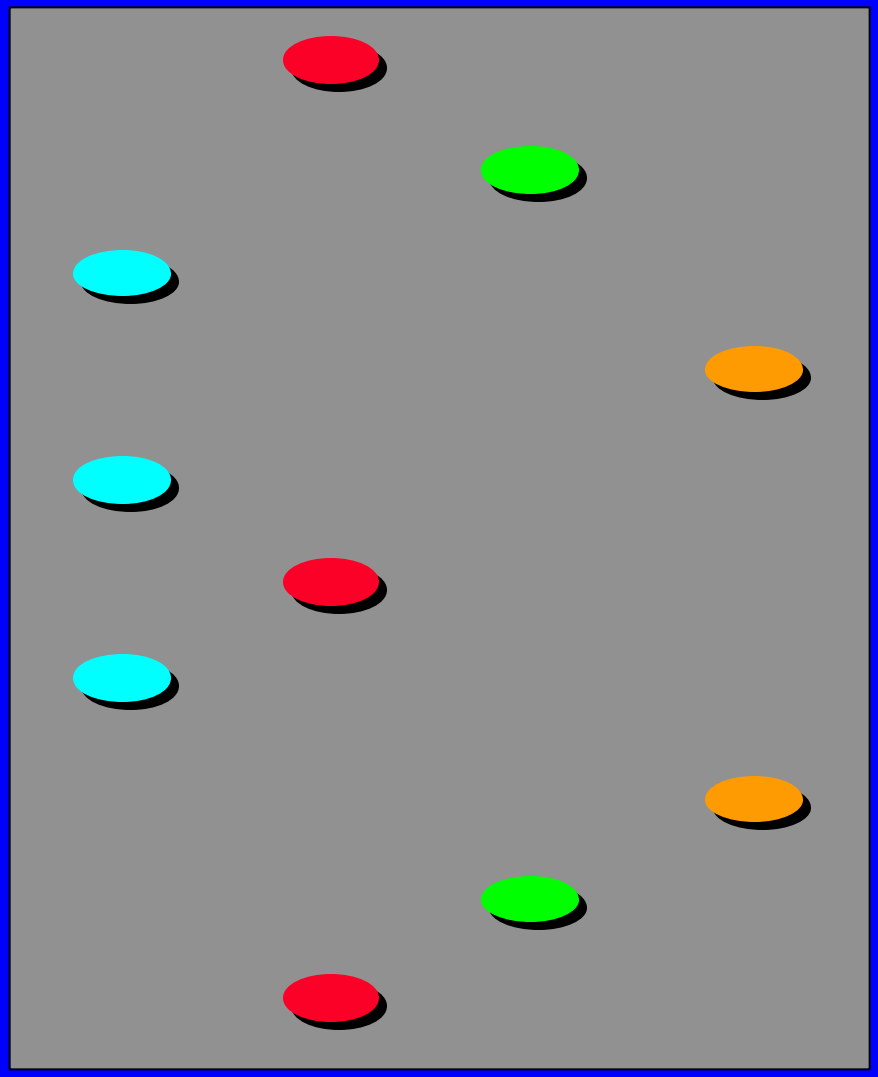
TGACATAC

TGACATACG

TGACATACGT

Figure 27.29

ddA ddT ddG ddC



Sequence of fragment	Sequence of original DNA
T	A
TG	AC
TGA	ACT
TGAC	ACTG
TGACA	ACTGT
TGACAT	ACTGTA
TGACATA	ACTGTAT
TGACATAC	ACTGTATG
TGACATACG	ACTGTATGC
TGACATACGT	ACTGTATGCA