Nucleic Acids & Replication

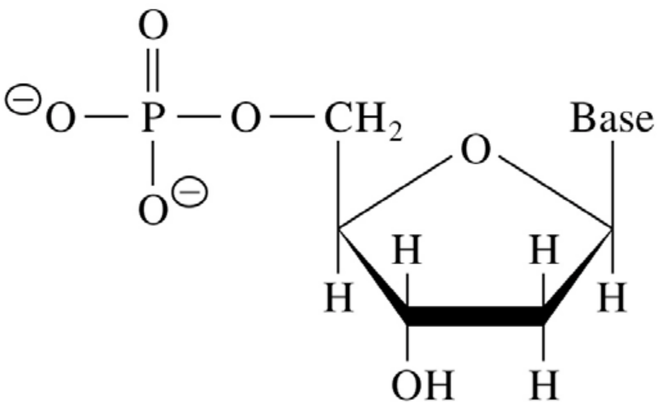
- **Nucleic acids** represent the fourth major class of biomolecules (other major classes of biomolecules are proteins, carbohydrates, fats)
- **Genome** - the genetic information of an organism

Information flow:

DNA ⟶ **RNA** ⟶ **PROTEIN**

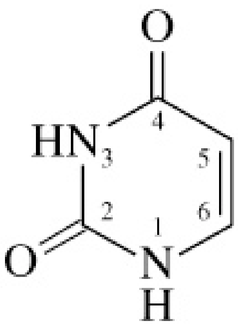
Nucleotides Are the Building Blocks of Nucleic Acids

- Nucleic acids are polynucleotides
- Nucleotides are phosphate esters of **nucleosides**

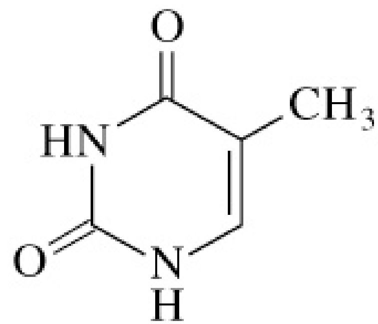


Major pyrimidines and purines

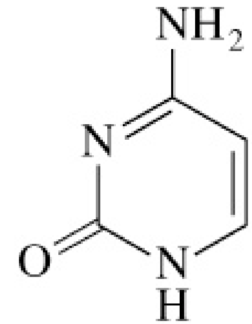
PYRIMIDINES



Uracil
(2,4-Dioxopyrimidine)

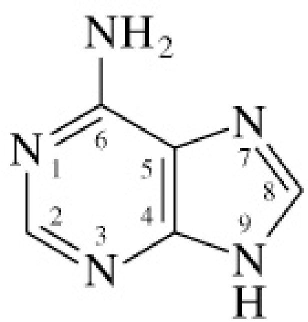


Thymine
(2,4-Dioxo-5-methylpyrimidine)

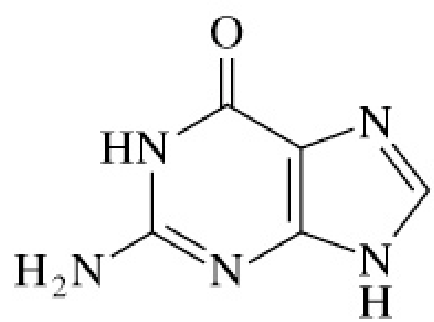


Cytosine
(2-Oxo-4-aminopyrimidine)

PURINES

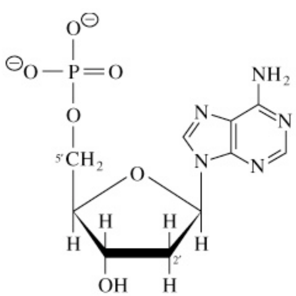


Adenine
(6-Aminopurine)

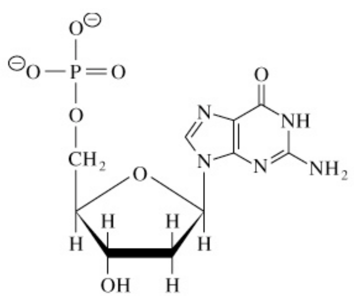


Guanine
(2-Amino-6-oxopurine)

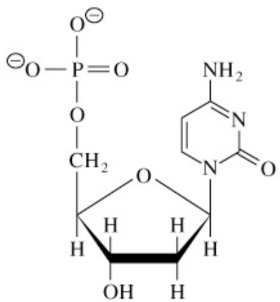
Structures of the deoxyribonucleoside-5’-monophosphates



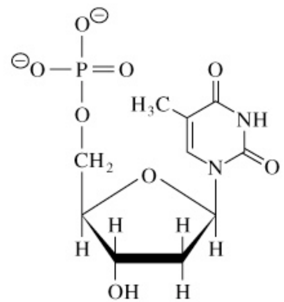
2′-Deoxyadenosine 5′-monophosphate
(Deoxyadenylate, dAMP)



2′-Deoxyguanosine 5′-monophosphate
(Deoxyguanylate, dGMP)

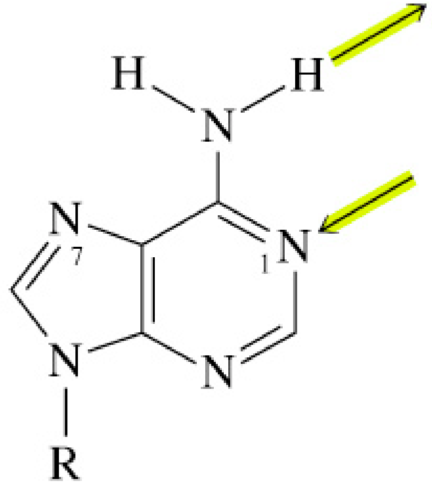


2′-Deoxycytidine 5′-monophosphate
(Deoxycytidylate, dCMP)

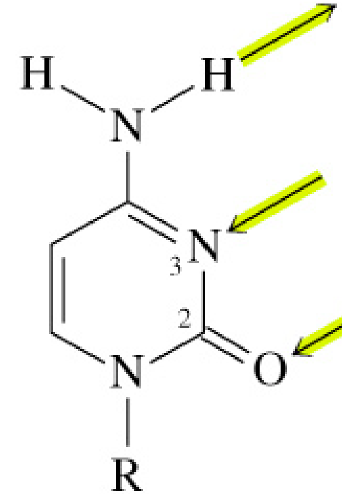


2′-Deoxythymidine 5′-monophosphate
(Thymidylate, dTMP)

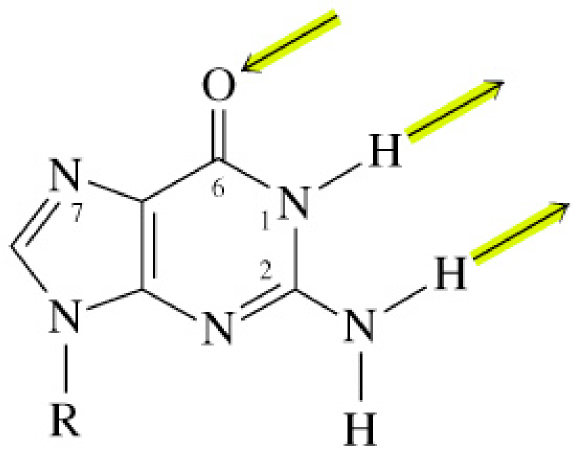
- Hydrogen bond sites in nucleic acids



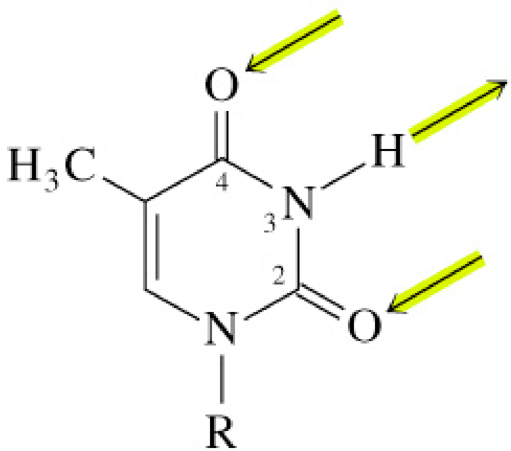
(Deoxy)Adenosine



(Deoxy)Cytidine



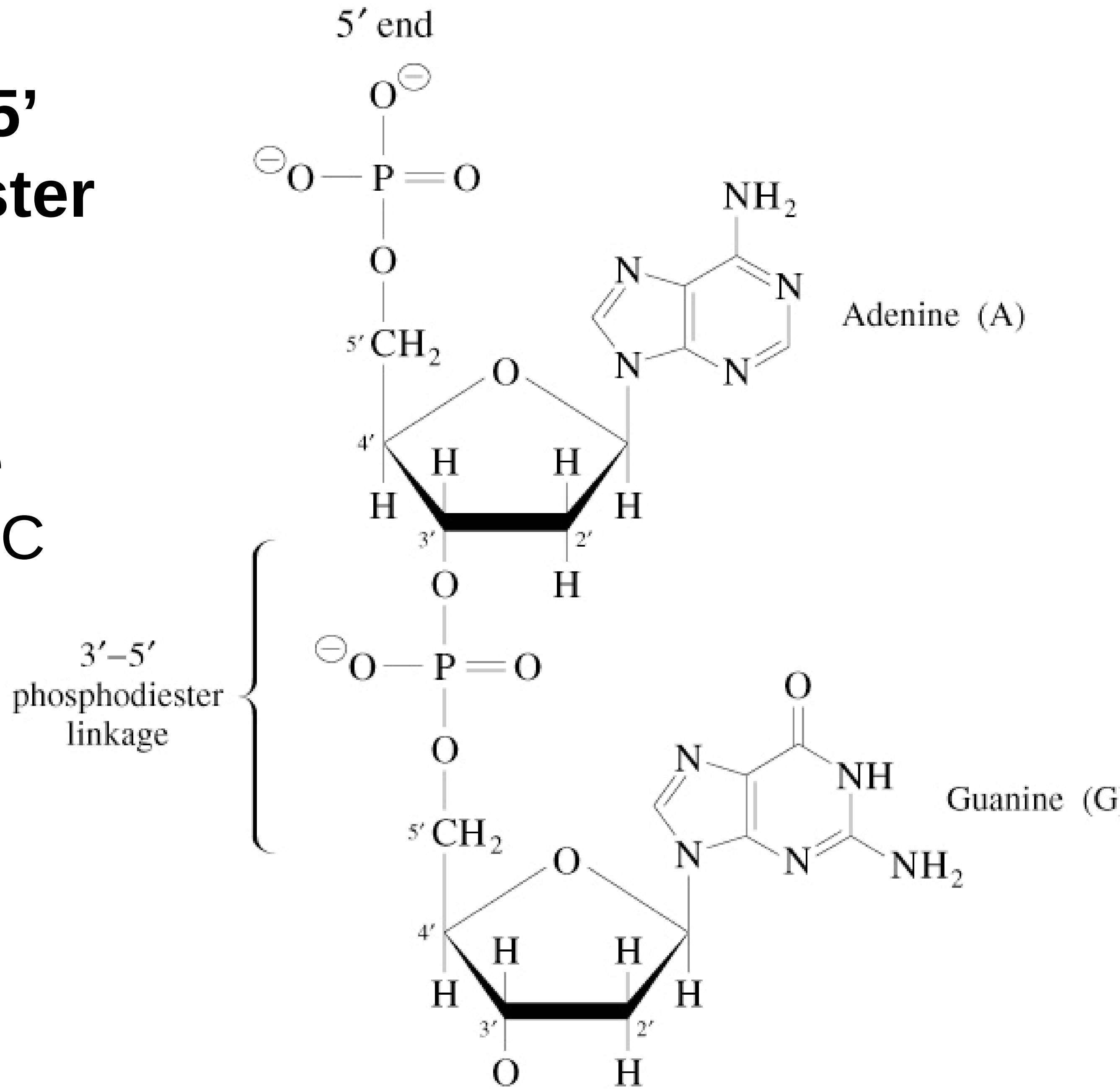
(Deoxy)Guanosine



(Deoxy)Thymidine

Nucleotides joined by 3’-5’ phosphodiester linkages

Structure of the tetranucleotide pdApdGpdTpdC



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19.2 DNA Is Double-Stranded

Table 19.2

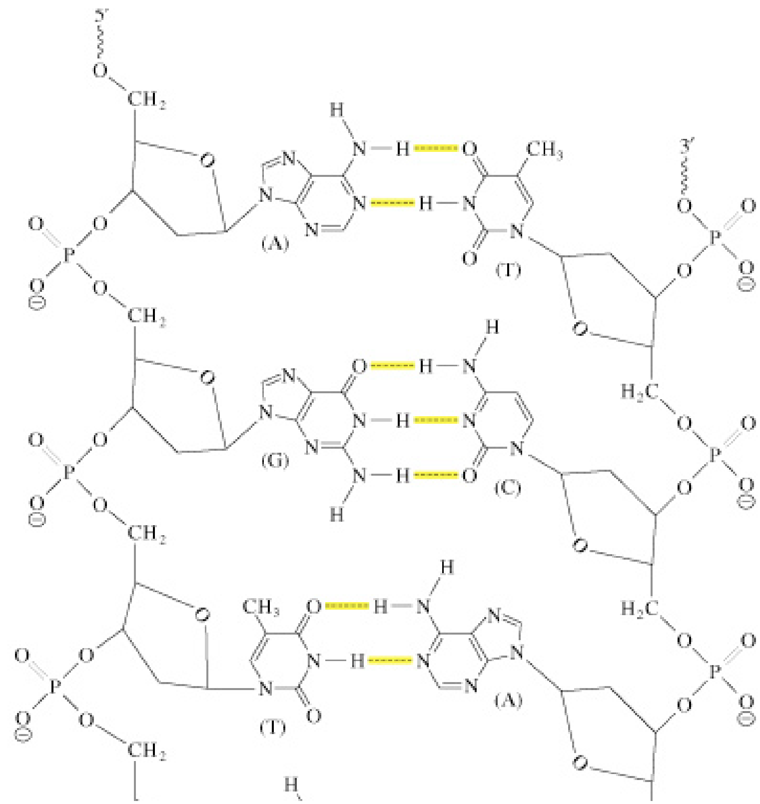
TABLE 19.2 Base composition of DNA (mole%) and ratios of bases

Source	A	G	C	T	A/T[a]	G/C[a]	(G + C)	Purine/ pyrimidine[a]
Escherichia coli	26.0	24.9	25.2	23.9	1.09	0.99	50.1	1.04
Mycobacterium tuberculosis	15.1	34.9	35.4	14.6	1.03	0.99	70.3	1.00
Yeast	31.7	18.3	17.4	32.6	0.97	1.05	35.7	1.00
Cow	29.0	21.2	21.2	28.7	1.01	1.00	42.4	1.01
Pig	29.8	20.7	20.7	29.1	1.02	1.00	41.4	1.01
Human	30.4	19.9	19.9	30.1	1.01	1.00	39.8	1.01

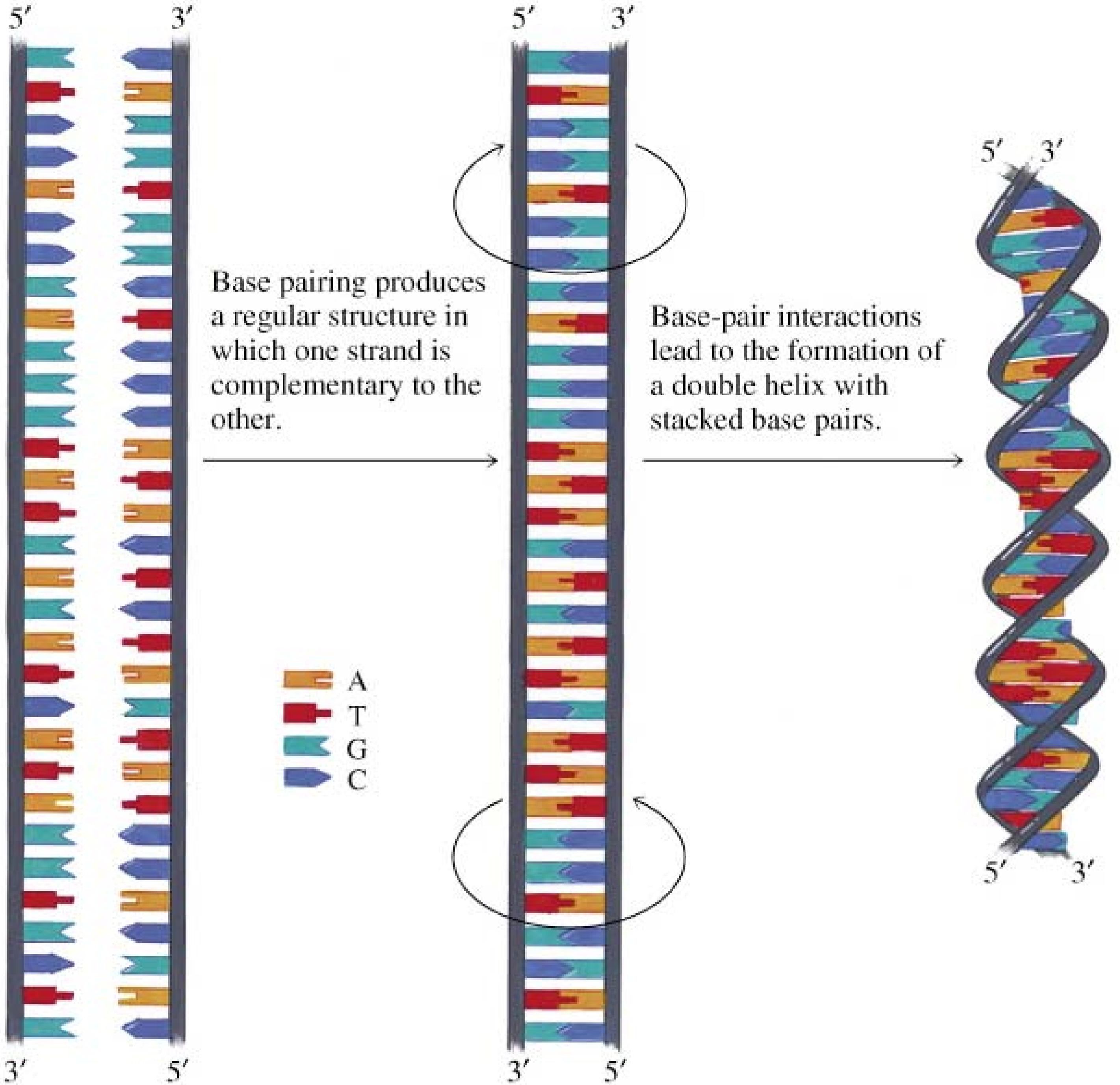
[a] Deviations from a 1:1 ratio are due to experimental variations.

Two Antiparallel Strands Form a Double Helix

- Two strands run in opposite directions
- Bases in opposite strands pair by <u>complementary</u> <u>hydrogen</u> <u>bonding</u>
- Adenine (A) - Thymine (T)
- Guanine (G) - Cytosine (C)



- Complementary base pairing and stacking in DNA



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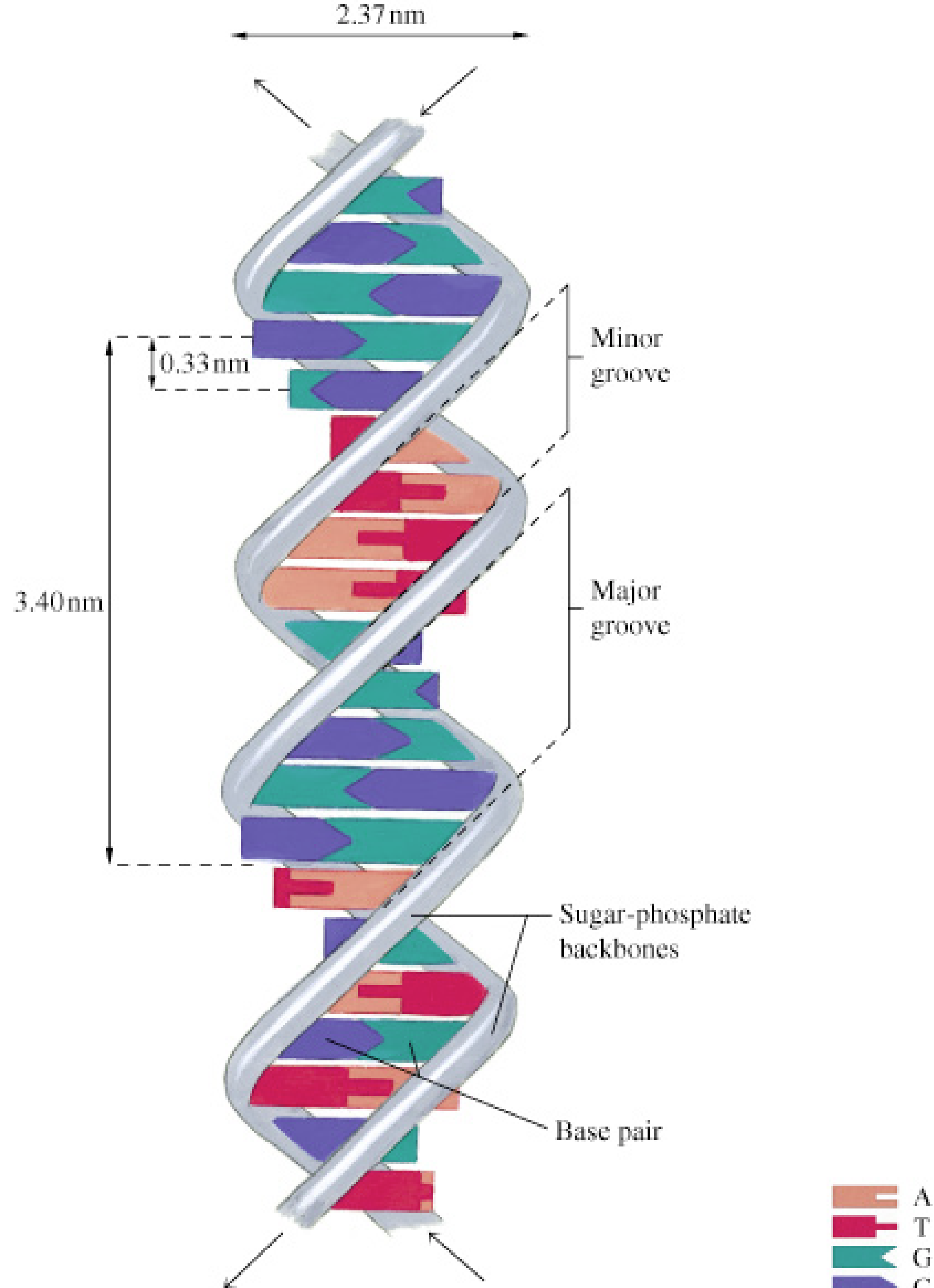
Three dimensional structure of DNA

- A double helix has two grooves of unequal width: **major groove** and **minor groove**
- Within each groove base pairs are exposed and are accessible to interactions with other molecules
- DNA-binding proteins can use these interactions to “read” a specific sequence

Fig 19.14

- Structure of B-DNA
- Sugar phosphate backbone outside
- Stacking creates two unequal grooves (major and minor)



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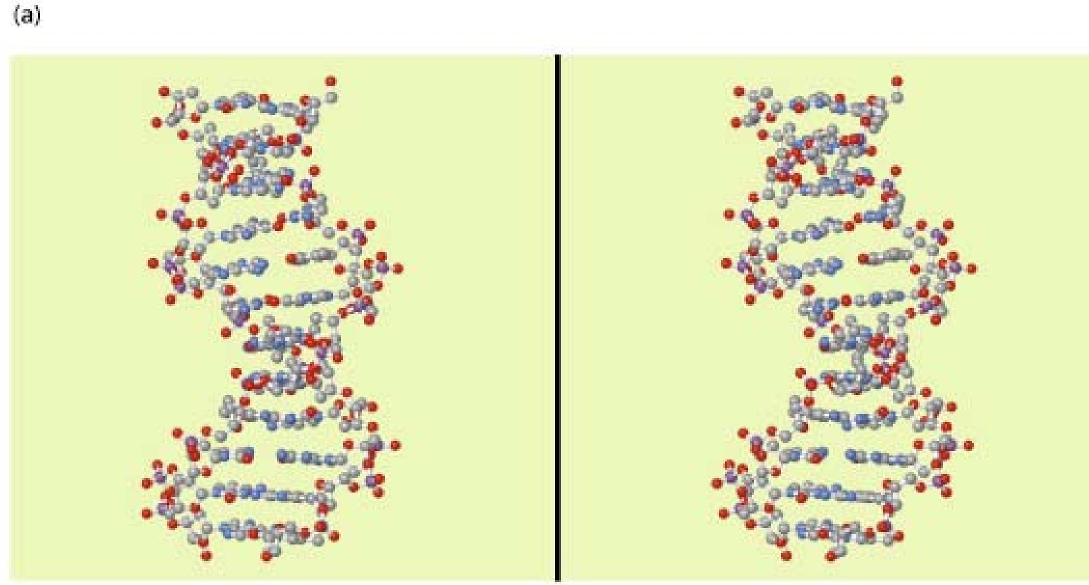
Stereo view of B-DNA

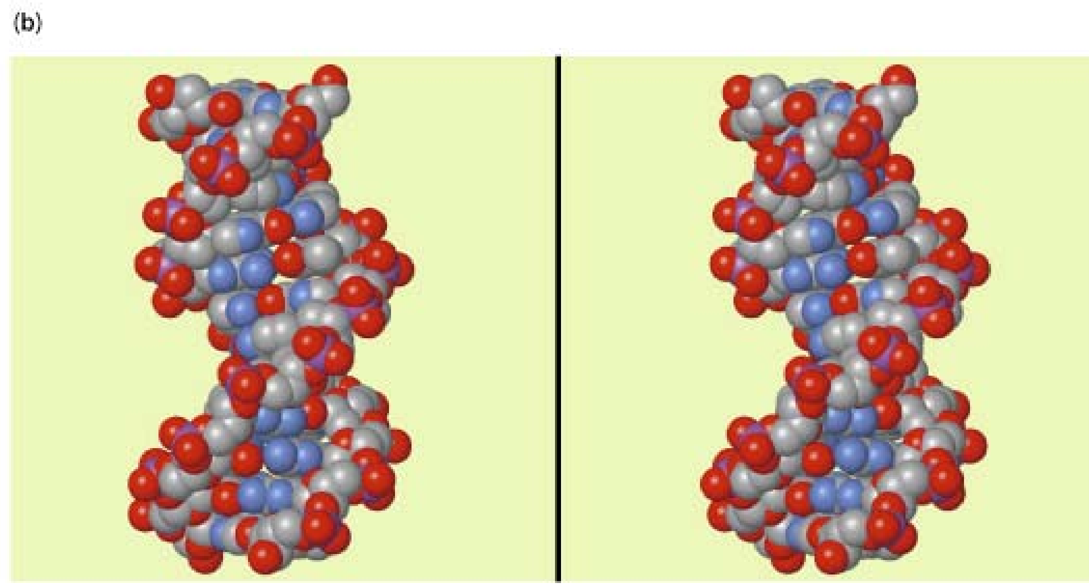
B-DNA is a right-handed helix, diam. = 2.37nm

- **Rise** (distance between stacked bases) =0.33nm
- **Pitch** (distance to complete one turn) = 3.40 nm
- Base pairs nearly perpendicular to sugar-phosphate backbones
- **Figure 19.15** Stereo views of B-DNA (next slide)

(a) Ball-and-stick model



(b) Space-filling model



Weak Forces Stabilize the Double Helix

(1) *Hydrophobic effects*. Burying purine and pyrimidine rings in the double helix interior

(2) *Stacking interactions*. Stacked base pairs form van der Waals contacts

(continued next slide)

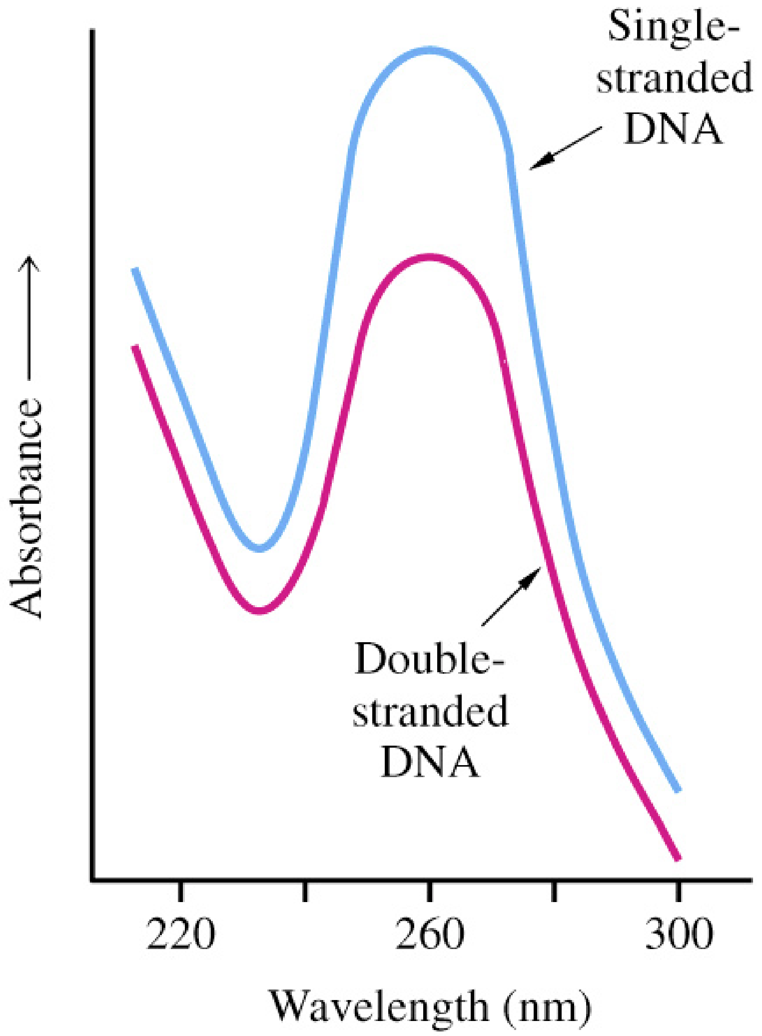
Weak forces (continued)

(3) *Hydrogen bonds*. Hydrogen bonding between base pairs.

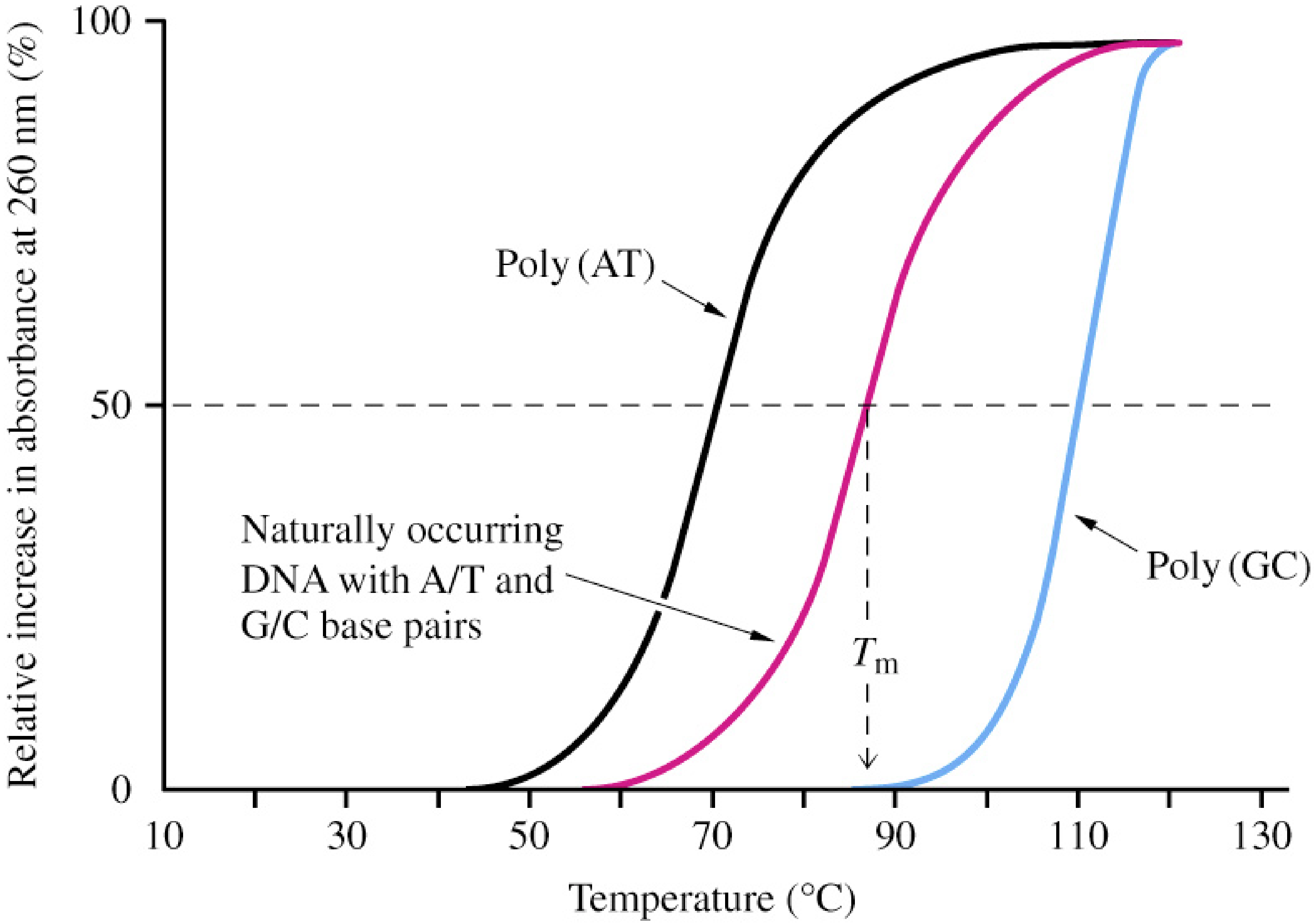
(4) *Charge-charge interactions*. Electrostatic repulsion of negatively charged phosphate groups is decreased by cations (e.g. Mg^{2+}) and cationic proteins

Absorption spectra of double-stranded and single-stranded DNA

- Double-stranded (DS)DNA (pH 7.0), absorbance max 260nm
- Denatured DNA absorbs12% -40% more than DS DNA



Melting curve for DNA

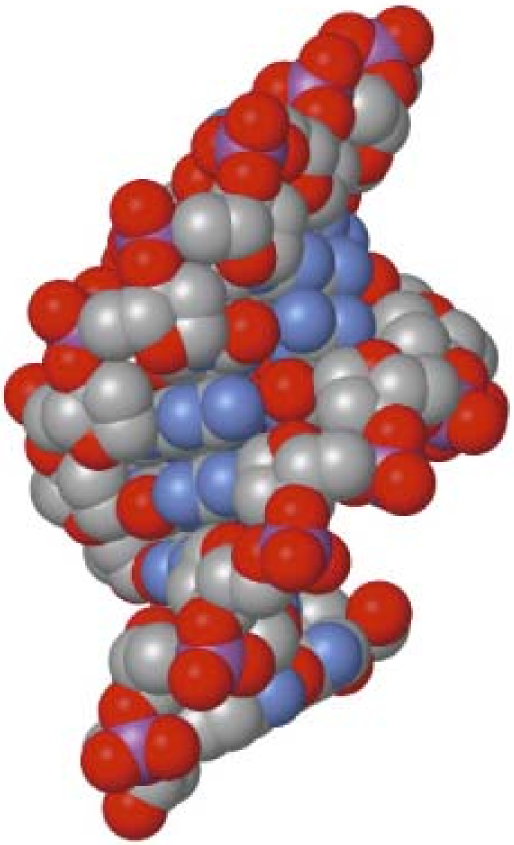


Conformations of Double-Stranded DNA

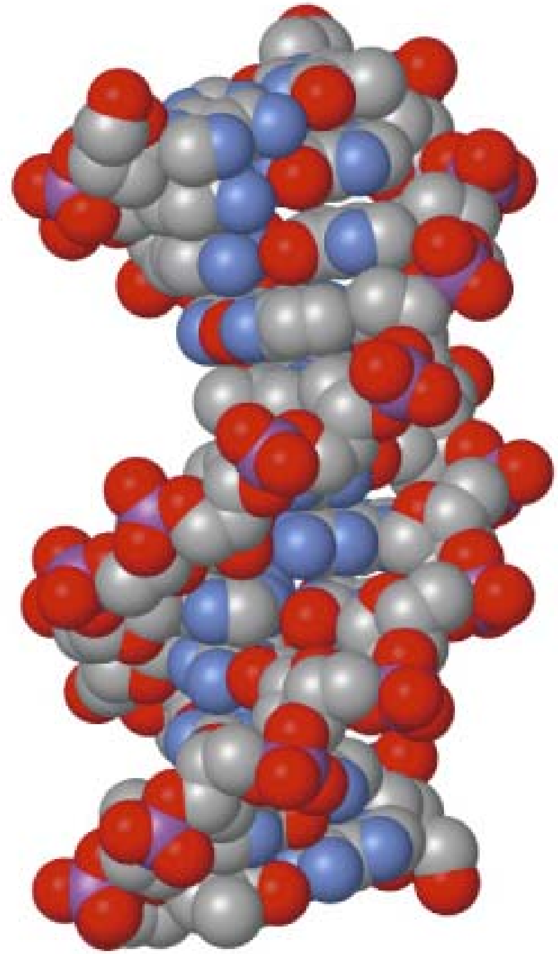
- Two alternative structures to B-DNA:
  A-DNA (forms when DNA is dehydrated)
  Z-DNA (when certain sequences are present)
- A-DNA is more tightly wound than B-DNA, and has minor grooves of similar width
- Z-DNA has no grooves and a left-handed helix
- Both A-DNA and Z-DNA exist in vivo in short regions of DNA

Forms of DNA

A



B



Z