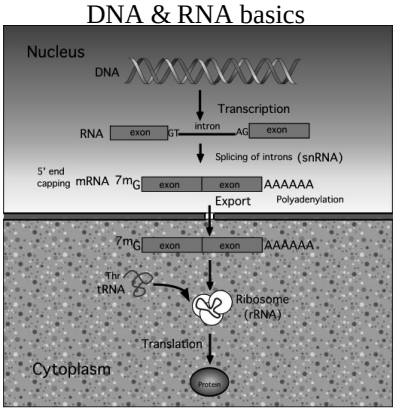
CH. 10 - Nucleotides & Nucleic Acids

- Repository of genetic information (DNA)
- Messenger - carries genetic instructions (mRNA)
- Energy currency of metabolism
- Second messengers (cAMP, cGMP)
- Coenzymes
- Metabolic intermediates

1

DNA & RNA basics



2

Multiple functions of RNA

- rRNA
  - Protein synthesis (ribosomes)
- mRNA
  - Carrier of genetic information to ribosomes
- tRNA
  - Translate mRNA information into specific αα's
- snRNA
  - Removal of introns from mRNA precursors
- Ribozymes
  - RNA catalysts (plant viruses)

3

Nucleotide structure

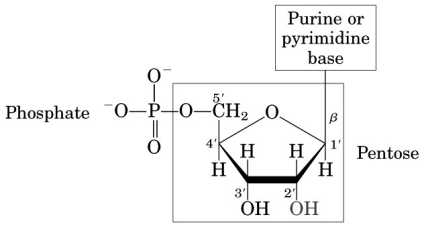
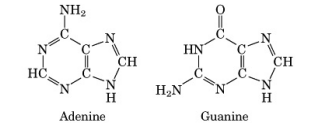


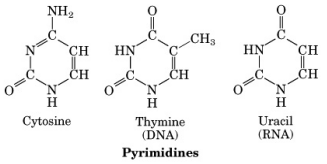
Fig 10.1

- Nitrogenous (N-containing) base
- Pentose (5C) sugar
- Phosphate

4

Nitrogenous bases - 2 parent compounds





Purines & Pyrimidines

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Base joined by *N*-β glycosyl bond to C1 of pentose sugar

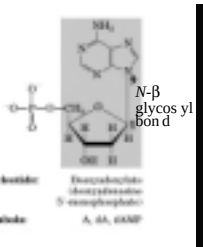

Fig 10.4

Phosphate esterified to C5 of pentose

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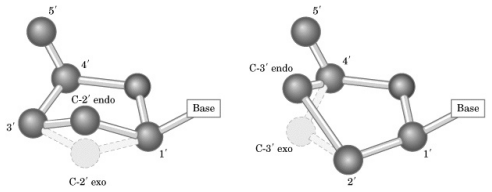
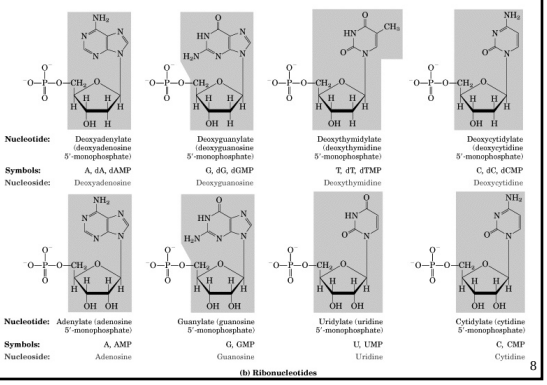
The pentose ring is "puckered"



"exo" & "endo" conformations important determinants of nucleic acid (NA) 3D structure

7

Major deoxyribo- and ribonucleotides



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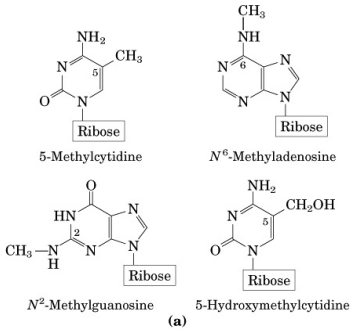
Minor purine & pyrimidine bases



Roles in regulating & protecting genetic information

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Phosphodiester bonds link nucleotides in Nucleic Acids (NA's)

Fig 10.7

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DNA & RNA subject to nonenzymatic hydrolysis

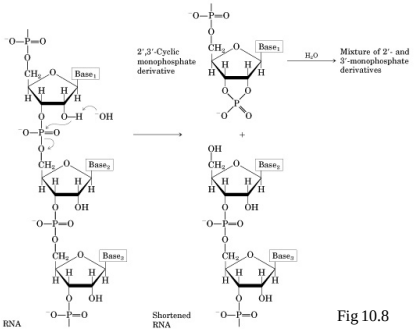

Fig 10.8

RNA more sensitive to alkaline conditions

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Nucleotide bases affect NA 3D structure

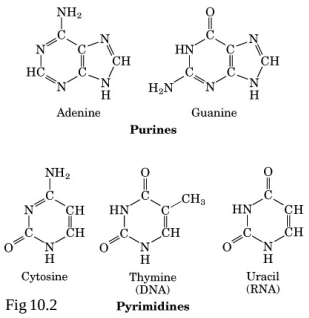

Fig 10.2

Highly conjugated (UV Absorption) and nearly planar

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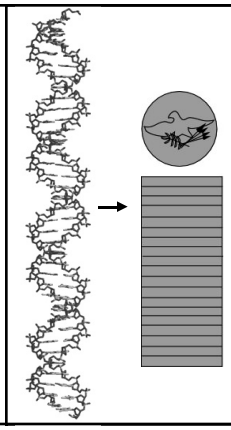
Stacking interactions stabilize DNA double helix

hydrophobic, van der Waals & dipole interactions



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H-bonding between amino & carbonyl groups 2nd important mode of interaction

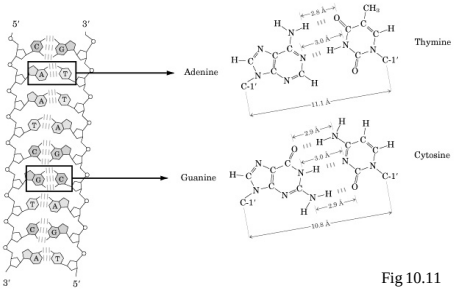

Fig 10.11

Permits complementary association of strands in double helix

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How was DNA determined to be the genetic material?

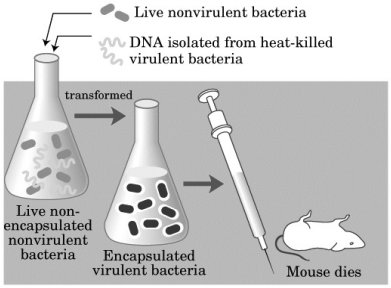

Fig 10.12

(e)

Avery-MacLeod-McCarty experiment (1944)

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The determination of DNA structure

- Chargaff & colleagues (1940's)
  - A+ G = T+ C
- Franklin & Wilkins (early 1950's)
  - DNA molecules are helical
- Watson & Crick (1953)
  - Modern model of double helix structure

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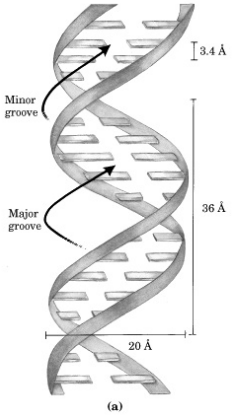
Watson-Crick model of DNA structure



(a)

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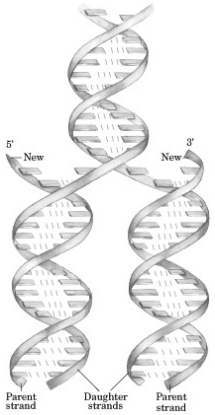
DNA model suggests mechanism for transmission of genetic information



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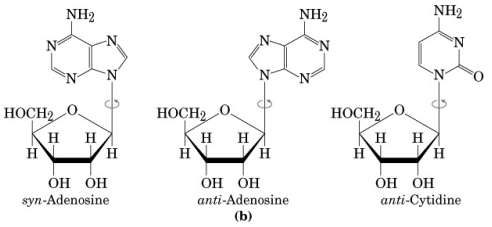
DNA can occur in different 3D forms



"syn" vs "anti" configurations of bases

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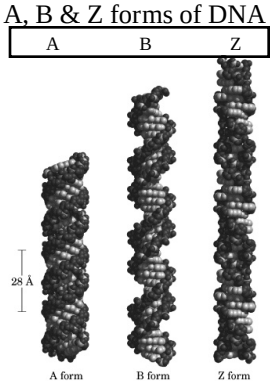
A, B & Z forms of DNA



B-form = Watson-Crick model

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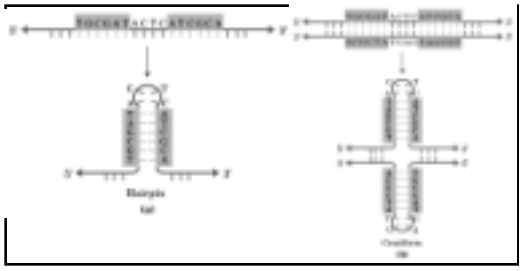
DNA sequences can also adopt unusual structures



Palindromes (inverted repeats)

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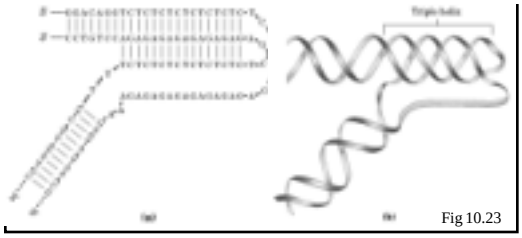
Unusual structures - triplex & tetraplex DNA's



Non-Watson-Crick Base pairing
(Hoogsteen pairing)

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Ribonucleic Acids have complex structures

- mRNA - genetic messenger
- tRNA - amino acid adapter molecule
- rRNA - structural component of ribsomes
- snRNA - pre-mRNA processing
- Ribozymes - catalytic RNA's

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Product of transcription is single-stranded RNA

- ss RNA assumes right-handed helix
- Self-complementary sequences can base pair
- G = C, A = U base-pairing
  - G = U also common
- RNA base pairing in anti-parallel

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Variety of RNA 2° can result

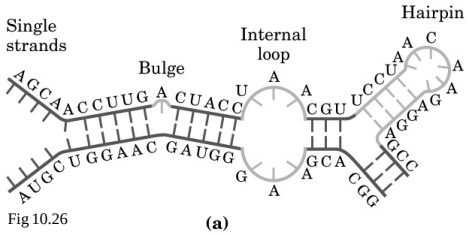

Fig 10.26

- Single strands
- Double strands ('A' form)
- Bulges
- Internal loops
- hairpins

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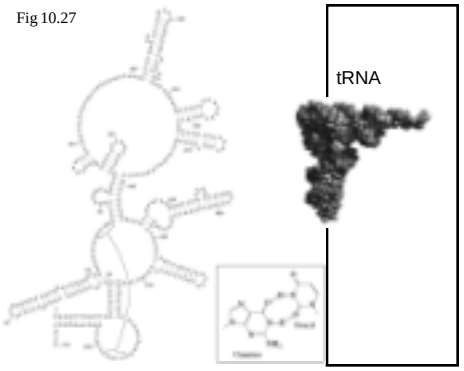
RNA 3° controls function and expression

Fig 10.27



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Nucleic Acid chemistry & analysis

- Non-covalent transformation
  - Strand separation & renaturation
- Covalent transformation
  - Alterations to DNA structure (mutations)

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Strand separation & annealing

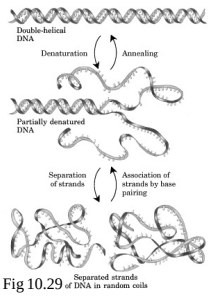

Fig 10.29

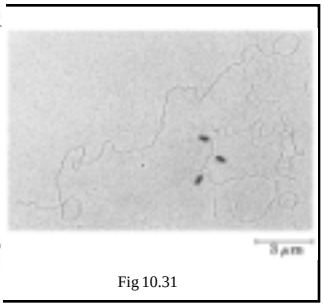

Fig 10.31

Strand separation often initiated at sites with high A+T content

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Covalent, nonenzymatic DNA transformations

- Deamination
- Hydrolysis of *N*-β-glycosyl bonds
- Formation of pyrimidine dimers
- Ring opening & base fragmentation
- Alkylation
- Oxidative damage

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Deamination reactions

Cytosine loss converts G-C to A-T base pair

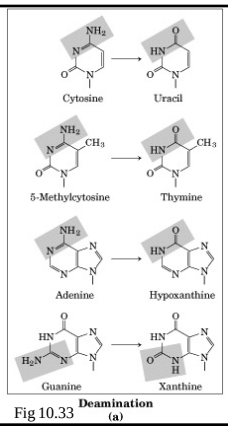

Fig 10.33

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Hydrolysis of *N*-β-glycosyl bonds

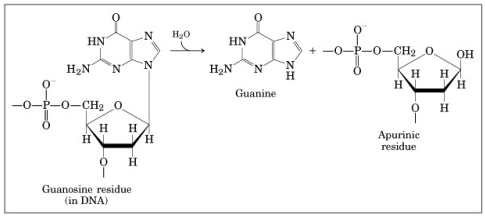


Fig 10.33b

"depurination" - more common among purines

Formation of pyrimidine dimers

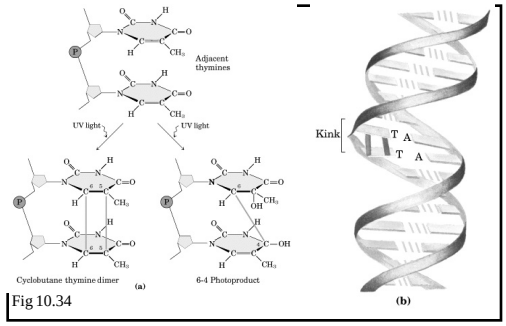
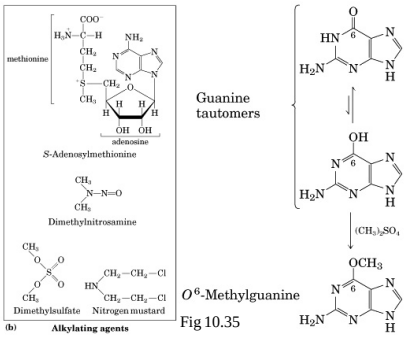


Fig 10.34

X-linking of adjacent thymine residues

Alkylation - addition of alkyl (methyl) groups



Guanine tautomers

O^6-Methylguanine

Fig 10.35

Prevents normal base-pairing

Oxidative damage to DNA

- Reactive metabolic byproducts: H_2O_2, O_2^-, etc.
- Variety of damaging reactions with DNA
  - Oxidation of deoxyribose
  - Strand breaks
- Catalases, peroxidases, superoxide dismutases
  - Enymzatic defense mechanisms

Non-damaging modification - methylation

- More common in Adenine & cytosine
- E.coli - primitive immune system
  - Self vs. foreign DNA
- Suppress migration of transposons (mobile DNA)
- "Silencing" regions of DNA
  - Prevent expression of genes
- All mediated via use of S-adenosylmethionine

DNA analysis - Hybridization & Sequencing

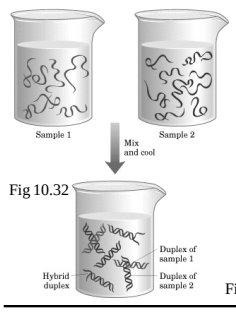


Fig 10.32

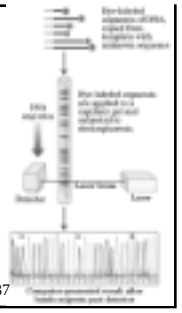
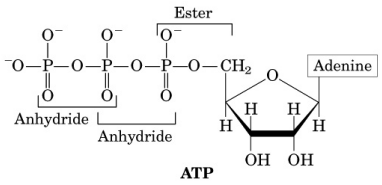
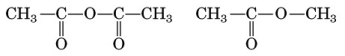


Fig 10.37

Basis of various genome projects (human, animal, plant, etc.)

Other functions of nucleotides





Acetic anhydride, a carboxylic acid anhydride

Methyl acetate, a carboxylic acid ester

Fig 10.40

Carriers of chemical energy

Enzyme cofactors

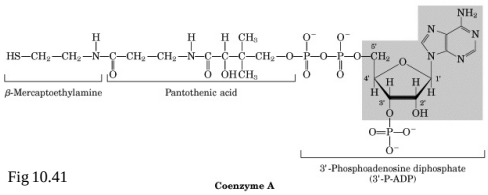
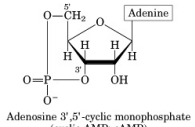


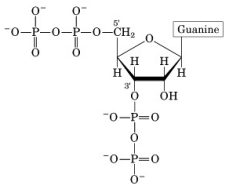
Fig 10.41

Multiple functional groups increase opportunities for forming favorable weak interactions

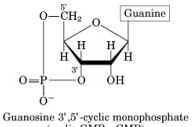
Nucleotides as regulatory molecules



Adenosine 3',5'-cyclic monophosphate (cyclic AMP; cAMP)



Guanosine 3'-diphosphate,5'-diphosphate (guanosine tetraphosphate) (ppGpp)



Guanosine 3',5'-cyclic monophosphate (cyclic GMP; cGMP)

Fig 10.42

Second messengers

CH. 10 Summary

Nucleotide roles

- Carry & store genetic information (RNA,DNA)
- Carry chemical energy
- Coenzymes
- Cellular 2nd messengers

Components

- Nitrogenous base (purines=A,G; pyrimidines=C,T,U
- Pentose sugar
- Phosphate group

Watson-Crick model of DNA structure

- 2 anti-parallel chains
- Right-handed double-helix
- Complementary base-pairing (A = T, G ≡ C)
- Hydrophilic sugar-phosphate backbone on outside
- Base pairs stacked perpendicular to long axis
- Nucleotides 3.4 A apart, ~ 10 nt's per turn of helix

DNA can exist in different structural forms

- A - short & wide
- B - Watson-Crick form
- Z - "zig-zag" left-handed helix

Sequence-dependent structural variation

- Bends (multiple A residues)
- Hairpins/cruciforms (inverted repeats)
- Triplex or tetraplex DNA
  - Polypyrimidine or polypurine stretches

RNA roles & structure

- mRNA, rRNA, tRNA, ribozymes, etc.
- Structurally more complex
  - Single stranded regions
  - Double stranded regions (A form)
  - Hairpins
  - Internal loops
  - Bulges

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DNA undergoes noncovalent & covalent modification

- Noncovalent - separation & annealing
  - DNA replication, repair, transcription
- Covalent
  - Deamination
  - depurination
  - Alkylation
  - irradiation
  - Oxidative damage
  - Methylation
- Hybridization & sequencing
  - powerful methods of 1° analysis

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