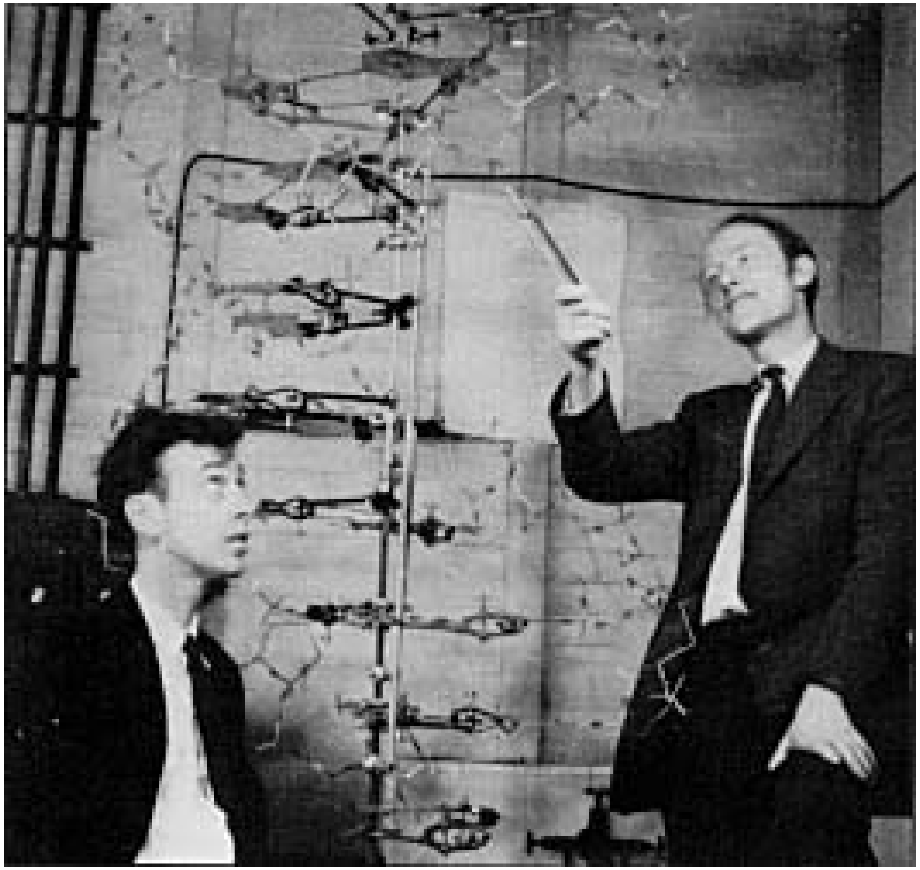
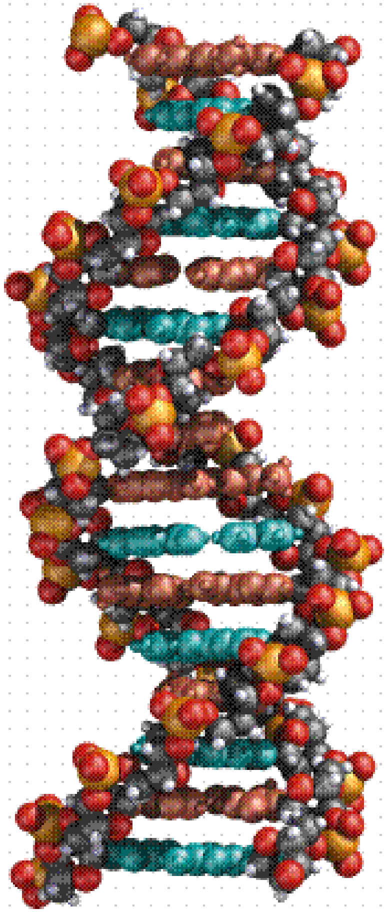
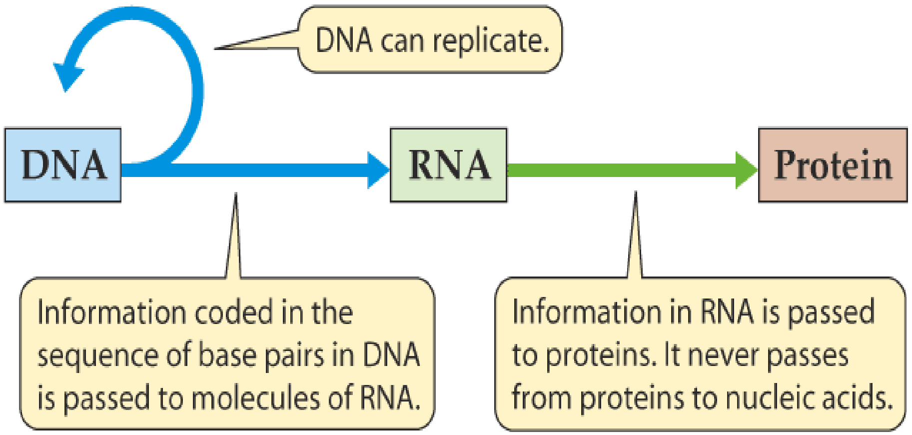
Nucleic Acid Structure

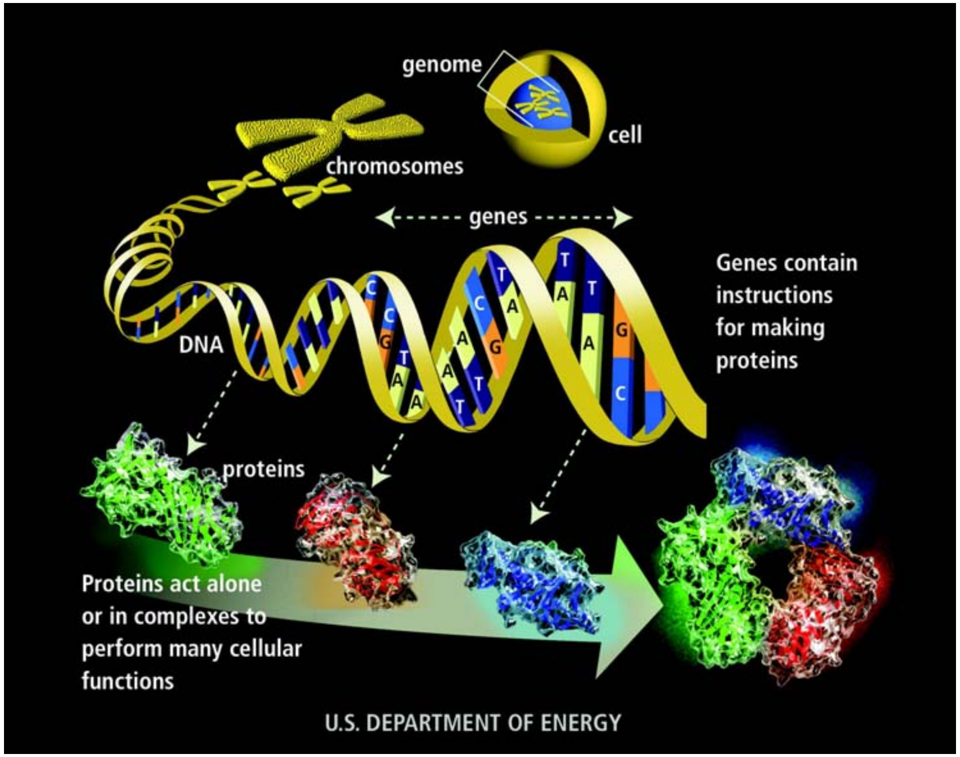




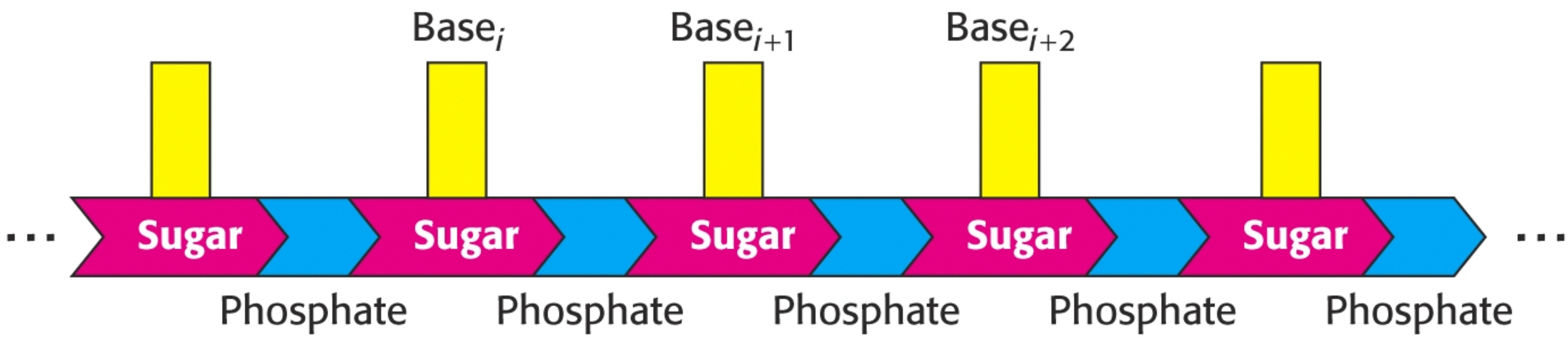
Many thanks to Dave Bevan for providing some of the material for this lecture.

The Central Dogma





Nucleic Acids are Linear Polymers



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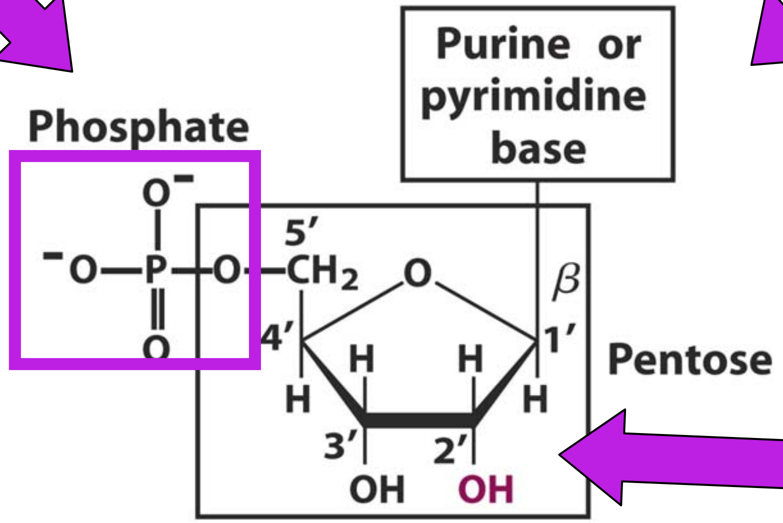
Structure of nucleotides

Nucleotides have three characteristic components:

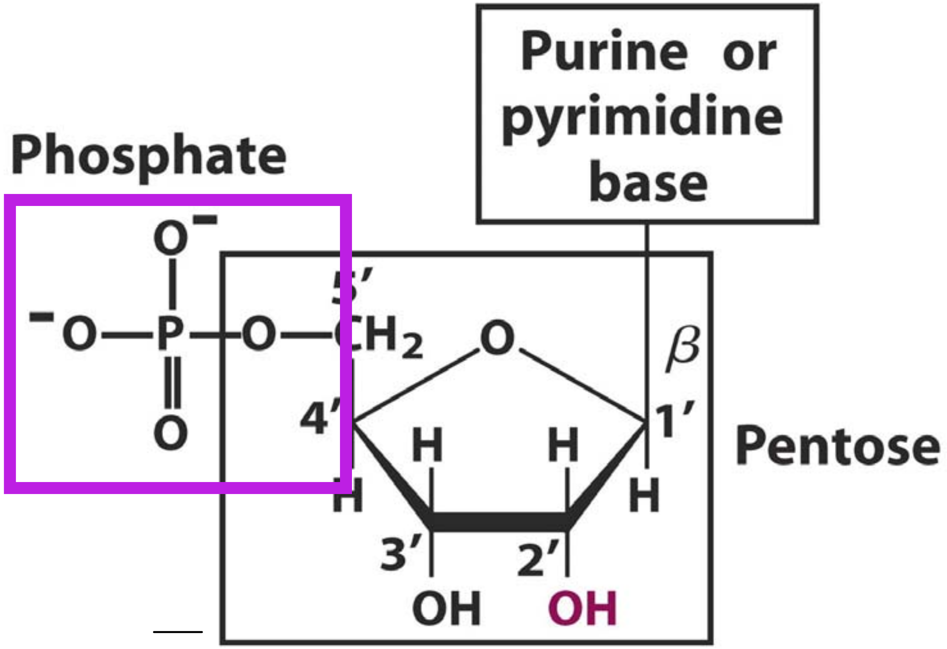
A phosphate group

A nitrogenous base
(pyrimidines or purine)



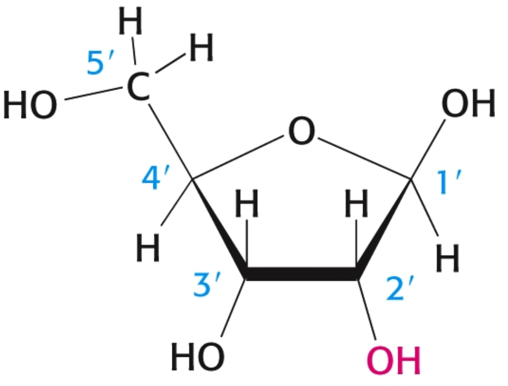
A pentose sugar

The phosphate

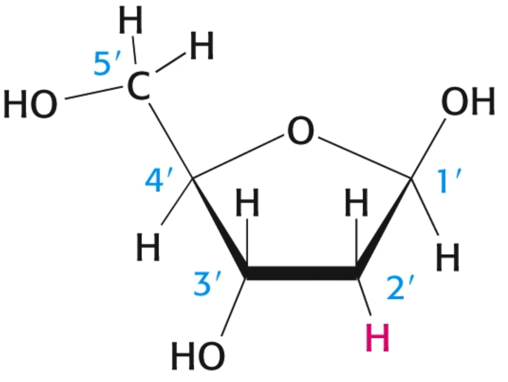


Carries a negative electric charge!

The Sugars of Nucleic Acids



Ribose



Deoxyribose

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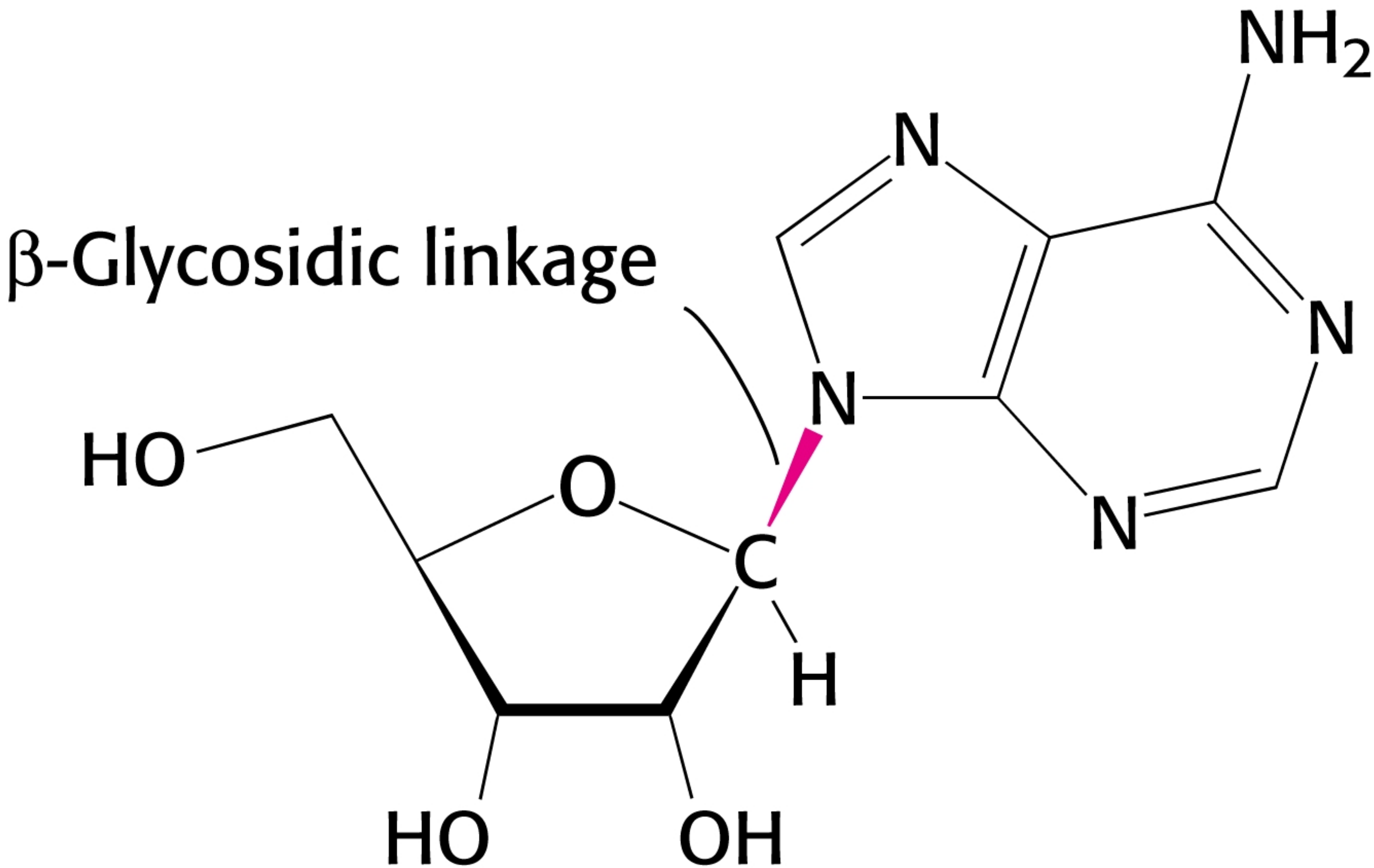

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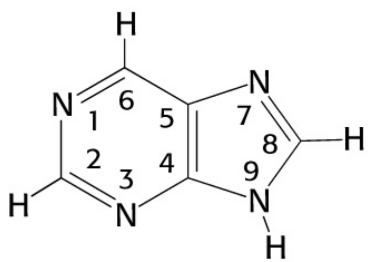
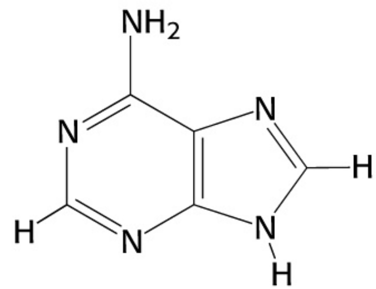
The Bases of Nucleic Acids

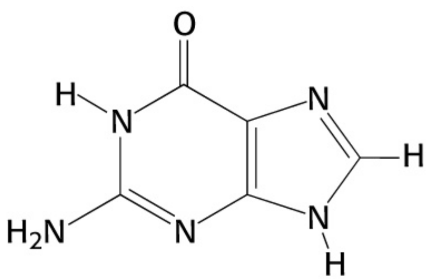
PURINES



Purine

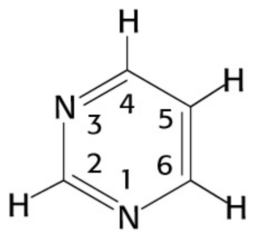


Adenine

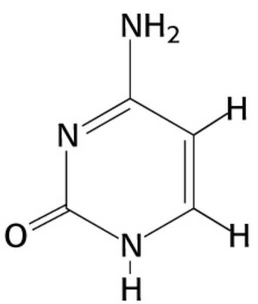


Guanine

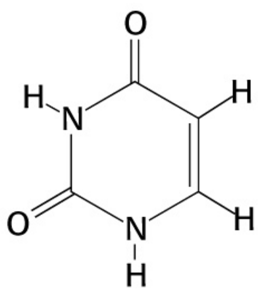
PYRIMIDINES



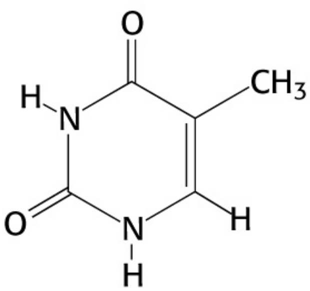
Pyrimidine



Cytosine



Uracil



Thymine

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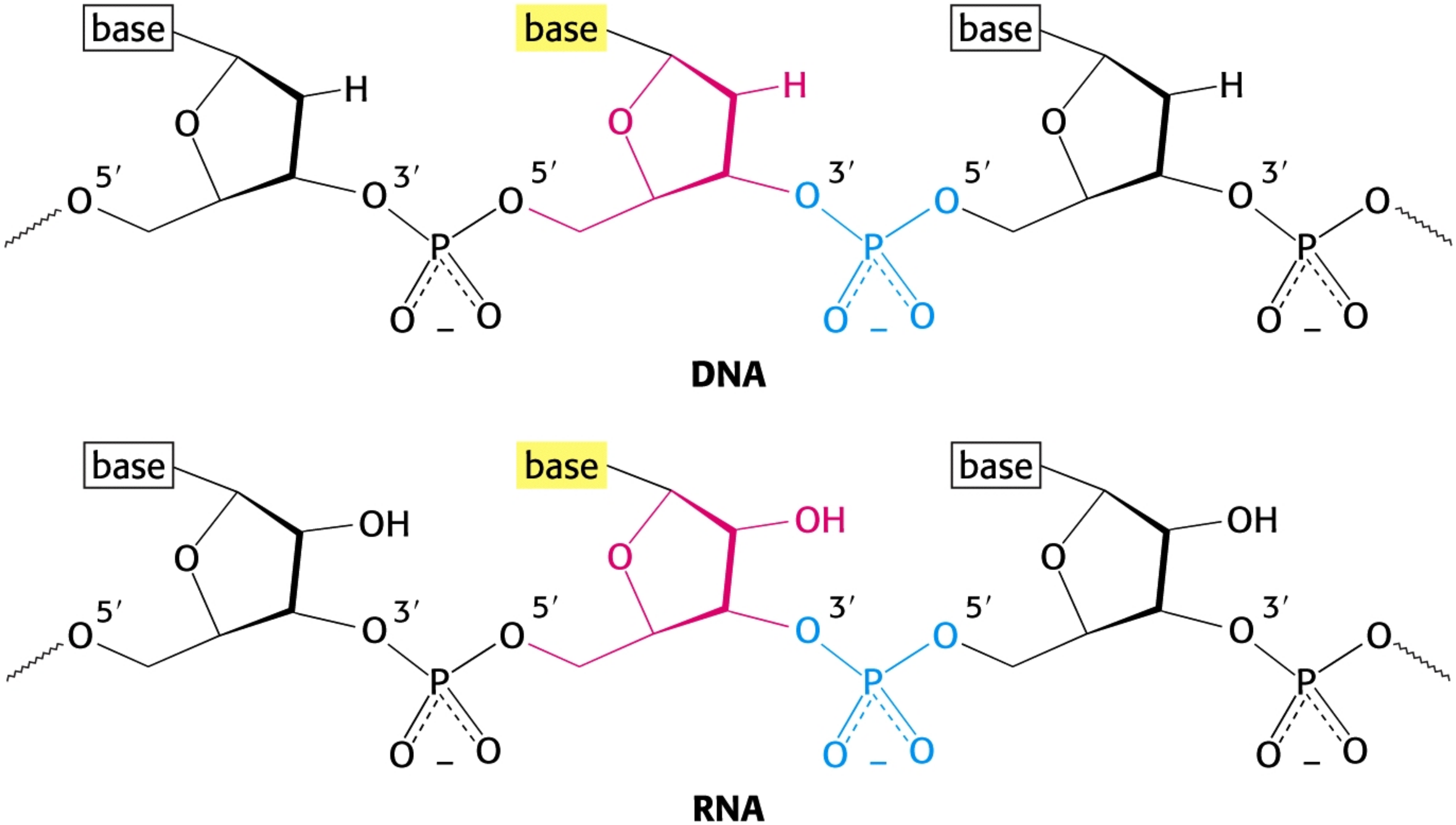
Backbones of DNA and RNA



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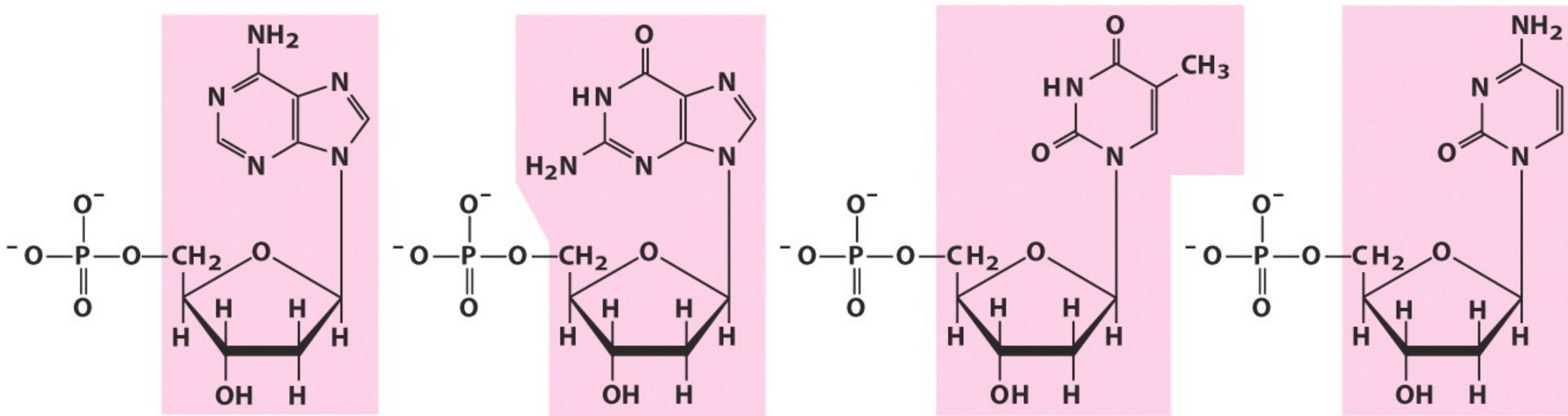
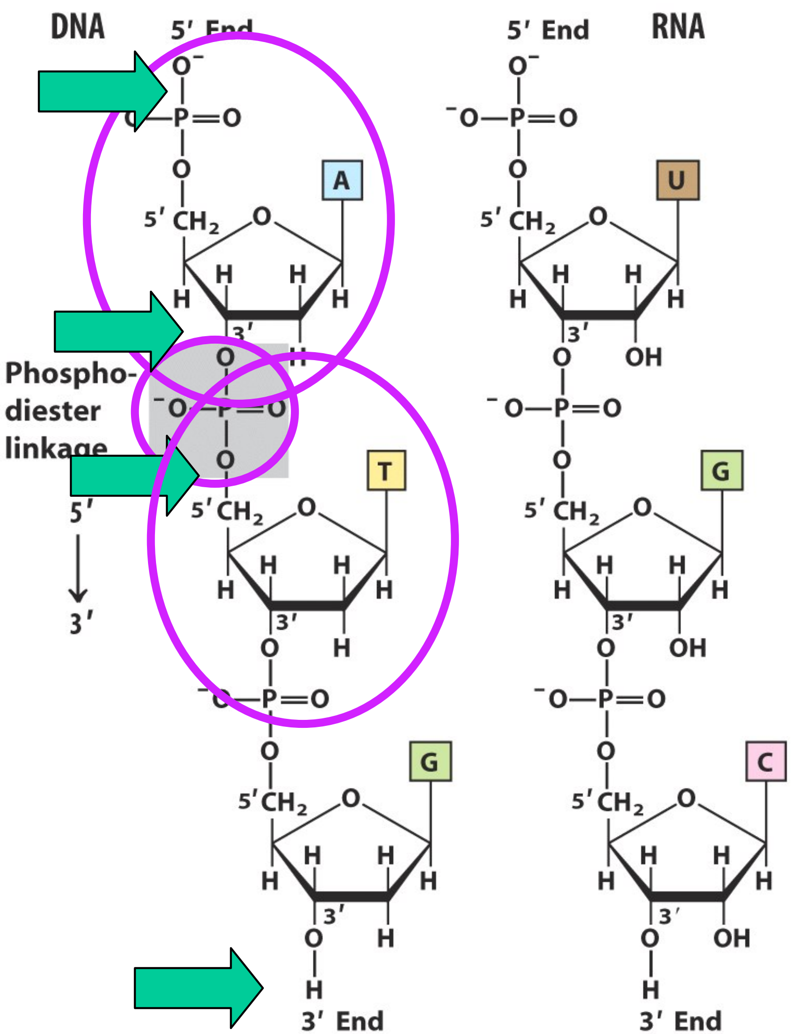
The major deoxyribonucleotides



Nucleotide:	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

(a) Deoxyribonucleotides

Nucleic acids



Nucleotide monomers
can be linked together via a phosphodiester linkage

formed between the 3' -OH of a nucleotide

and the phosphate of the next nucleotide.

Two ends of the resulting poly- or oligonucleotide are defined:

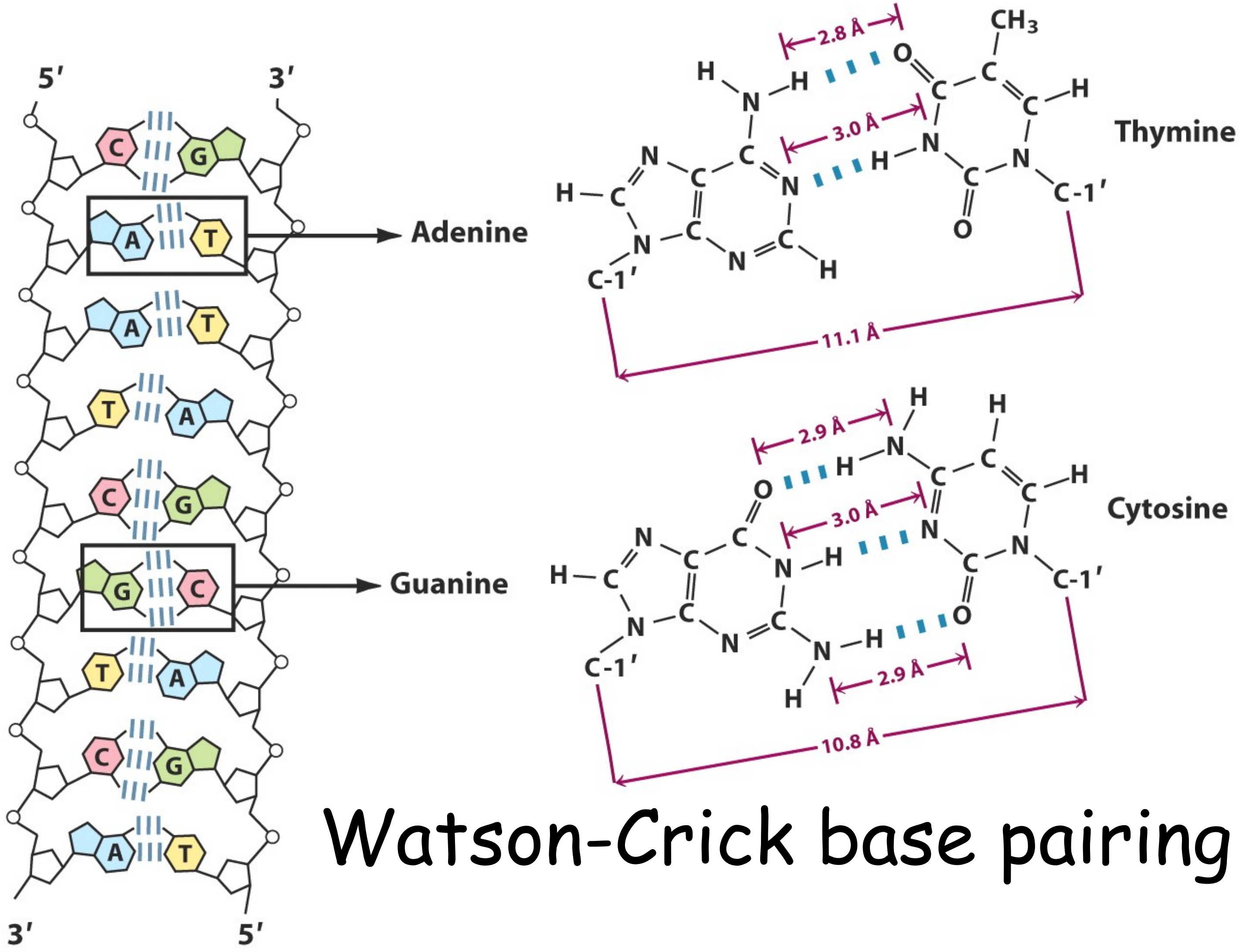
The 5' end lacks a nucleotide at the 5' position,

and the 3' end lacks a nucleotide at the 3' end position.

Compare polynucleotides and polypeptides

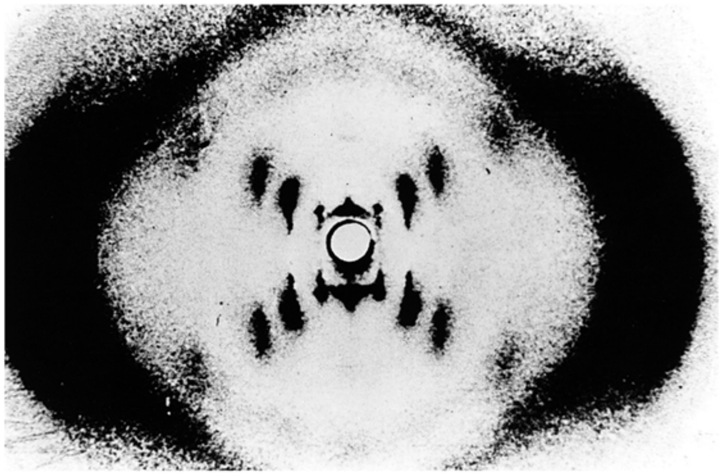
- As in proteins, the sequence of side chains (bases in nucleic acids) plays an important role in function.
- Nucleic acid structure depends on the sequence of bases *and* on the type of ribose sugar (ribose, or 2'-deoxyribose).
- Hydrogen bonding interactions are especially important in nucleic acids. Expectedly, weak bonds.

Interstrand H-bonding between DNA bases



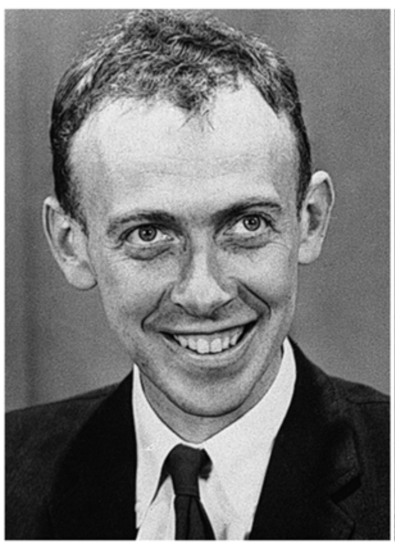
Watson-Crick base pairing

DNA structure determination

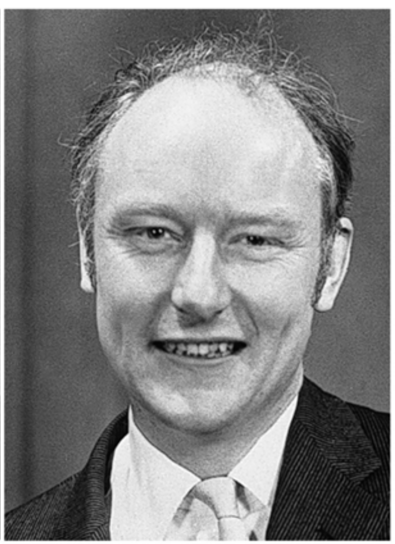


Rosalind Franklin,
1920–1958

Maurice Wilkins



James Watson

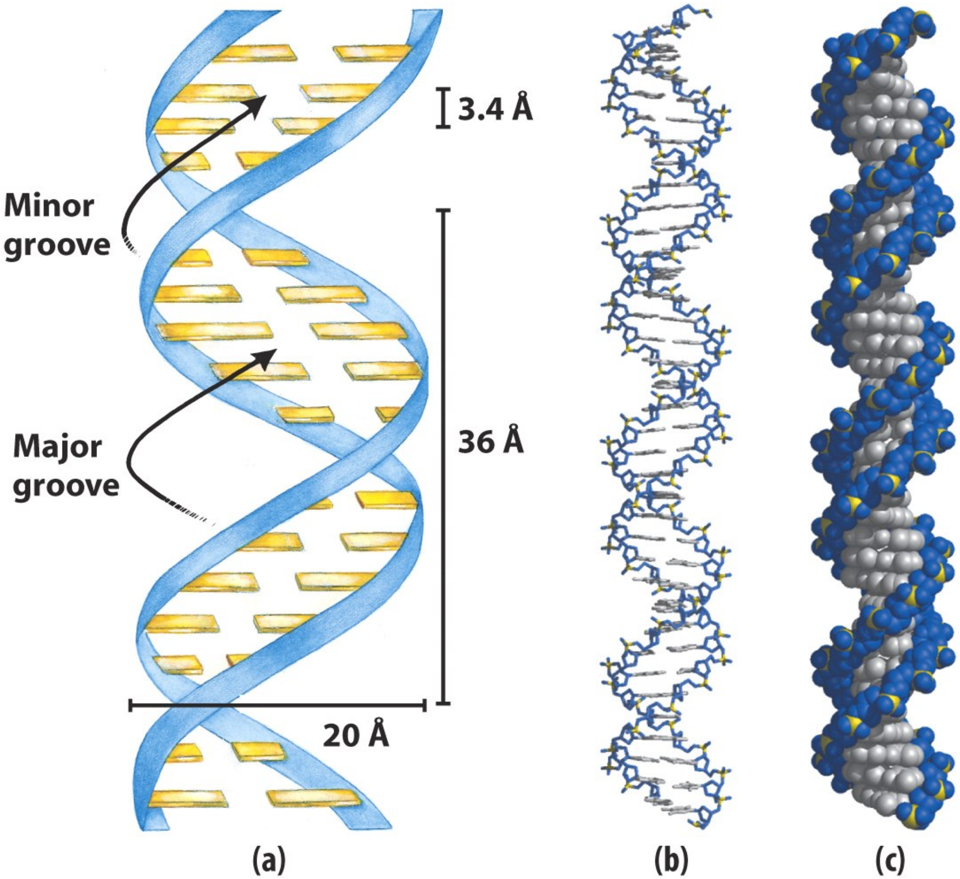


Francis Crick

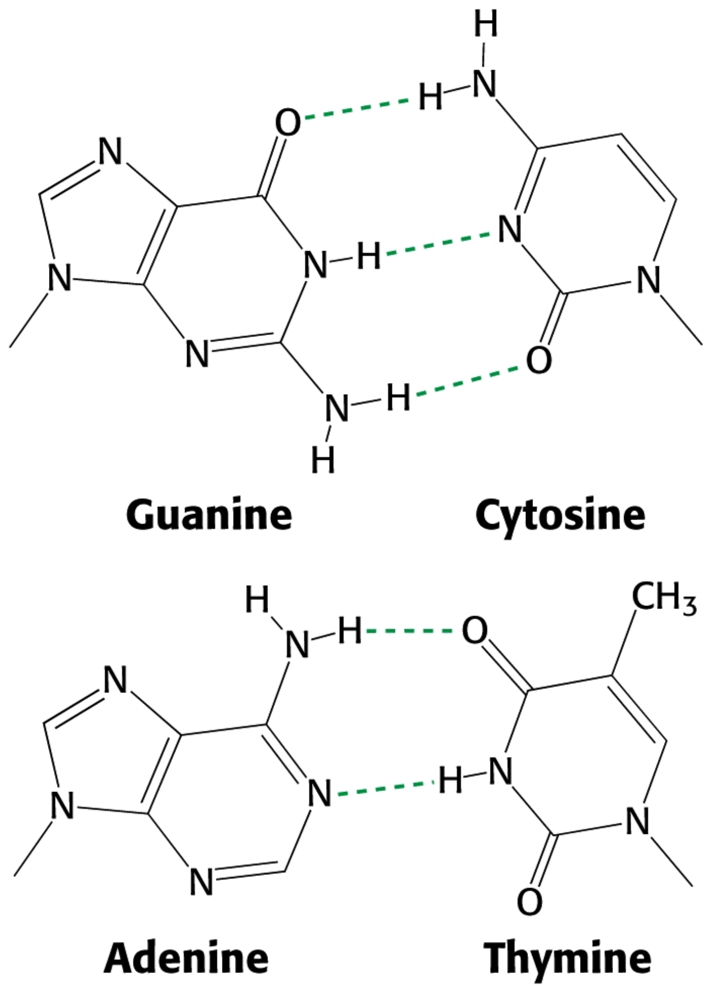
- Franklin collected x-ray diffraction data (early 1950s) that indicated 2 periodicities for DNA: 3.4 Å and 34 Å.
- Watson and Crick proposed a 3D model accounting for the data.

DNA structure

- DNA consists of two helical chains wound around the same axis in a right-handed fashion aligned in an antiparallel fashion.
- There are 10.5 base pairs, or 36 Å, per turn of the helix.
- Alternating deoxyribose and phosphate groups on the backbone form the outside of the helix.
- The planar purine and pyrimidine bases of both strands are stacked inside the helix.



Watson-Crick Base Pairing



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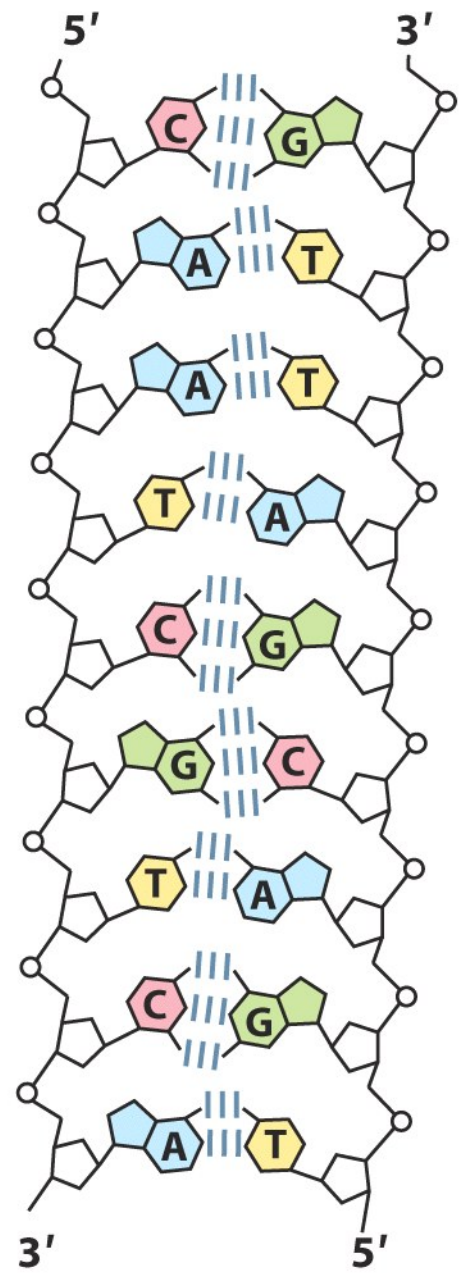
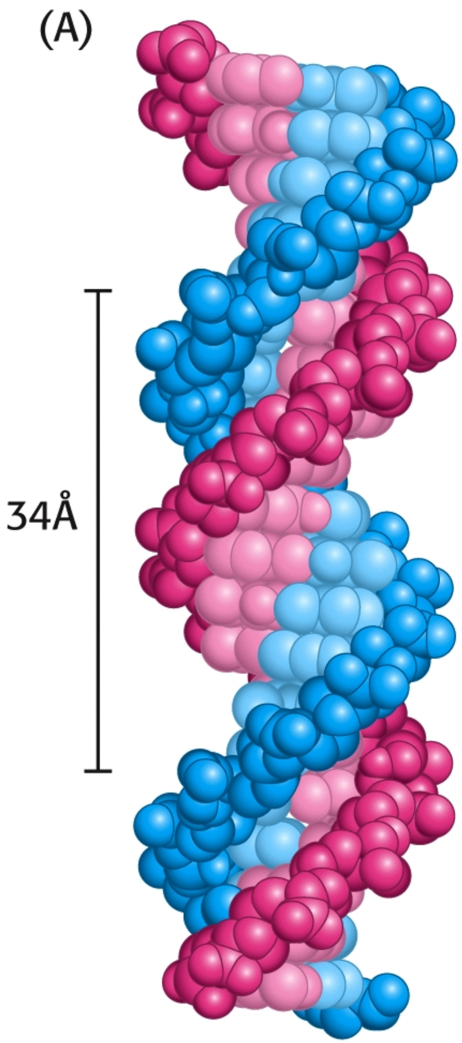
DNA strands

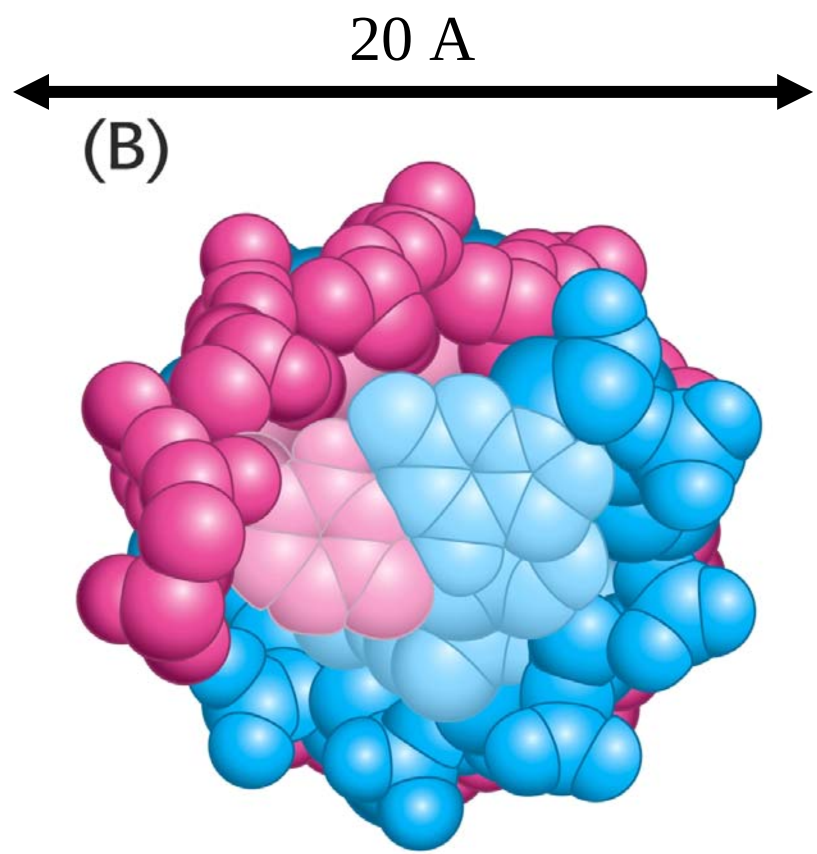
- The antiparallel strands of DNA are not identical, but are complementary.
- This means that they are positioned to align complementary base pairs: C with G, and A with T.
- So you can predict the sequence of one strand given the sequence of its complement.
- Useful for information storage *and* transfer!
- Note sequence conventionally is given from the 5' to 3' end



DNA Double Helix



Backbones in darker blue and red.
Bases in lighter blue and pink.



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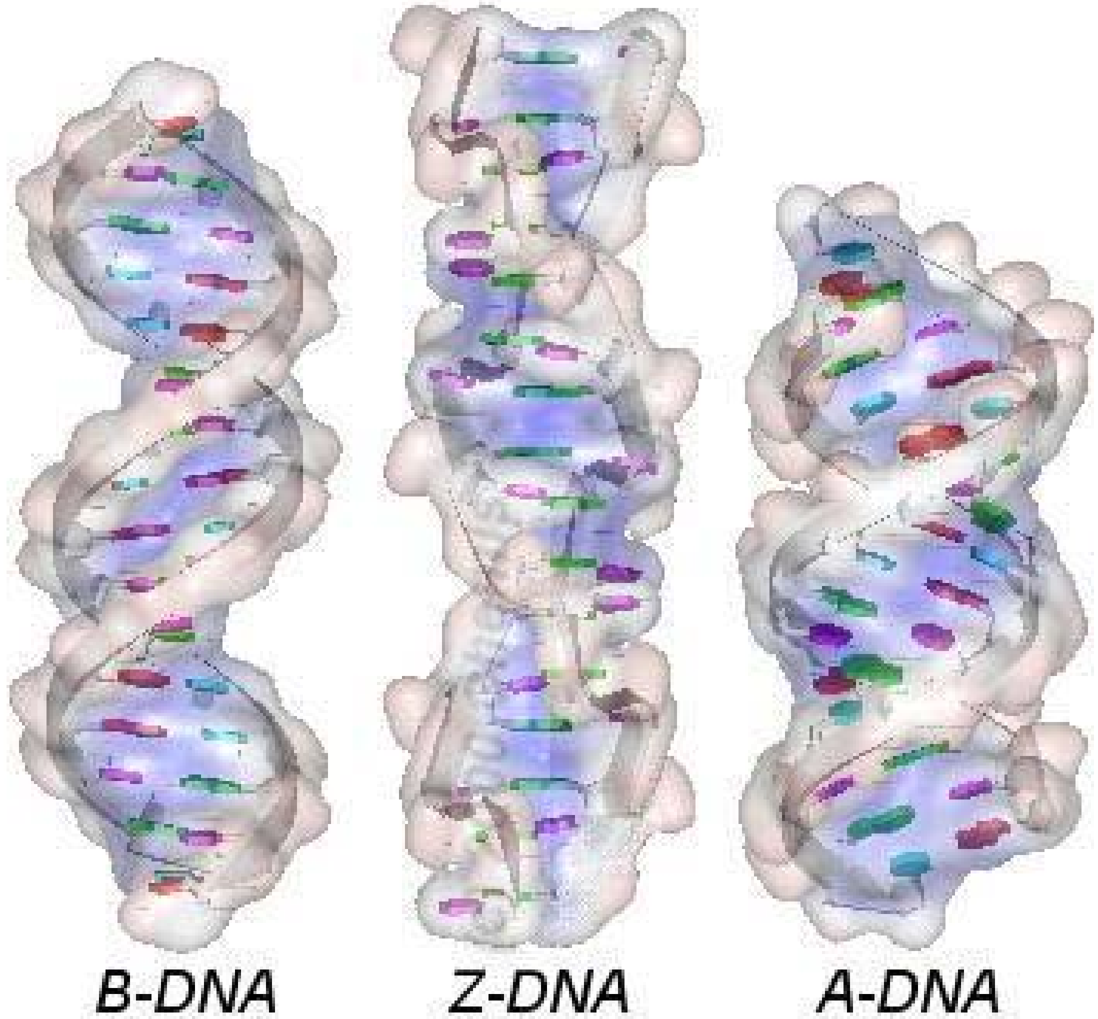
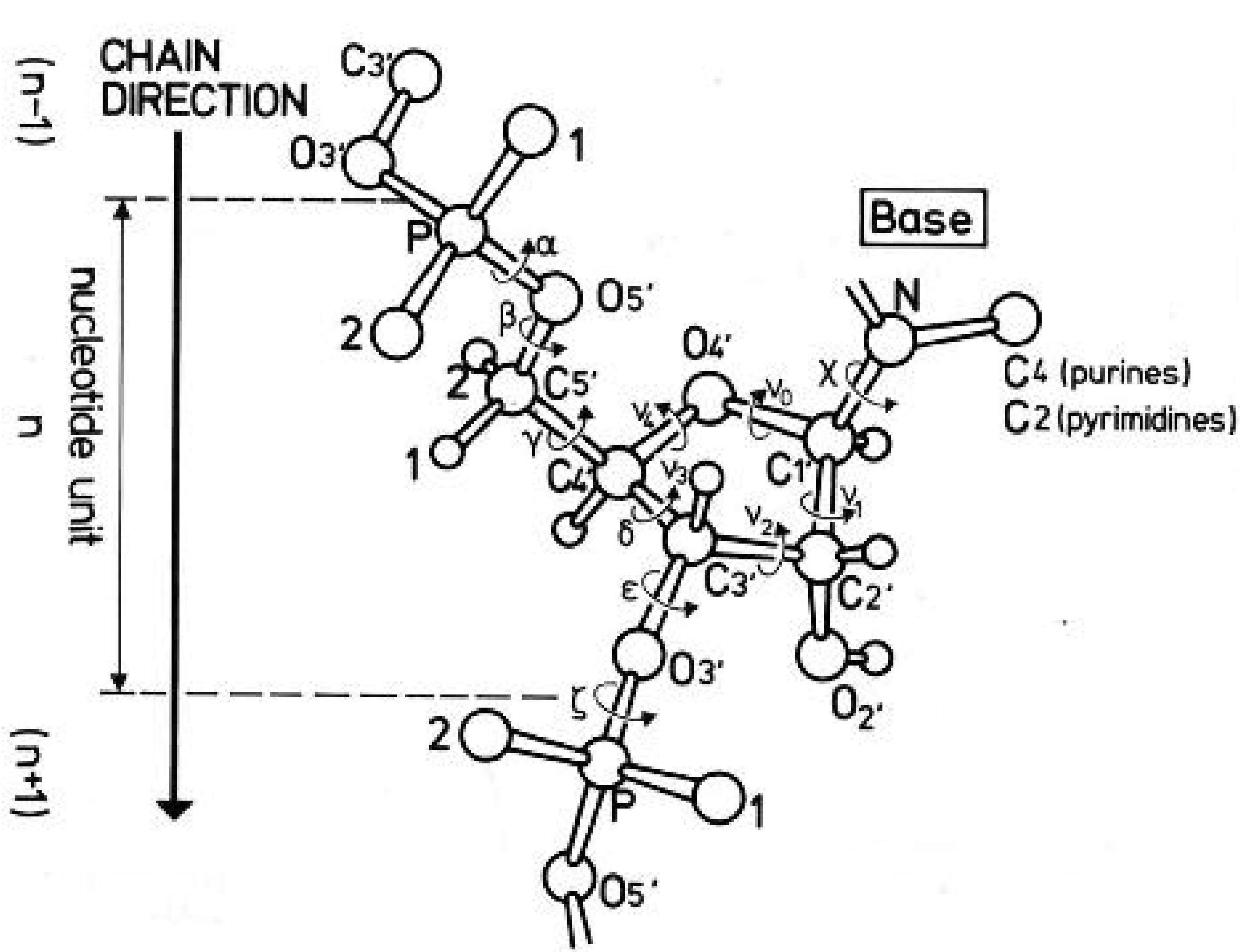
Forms of DNA

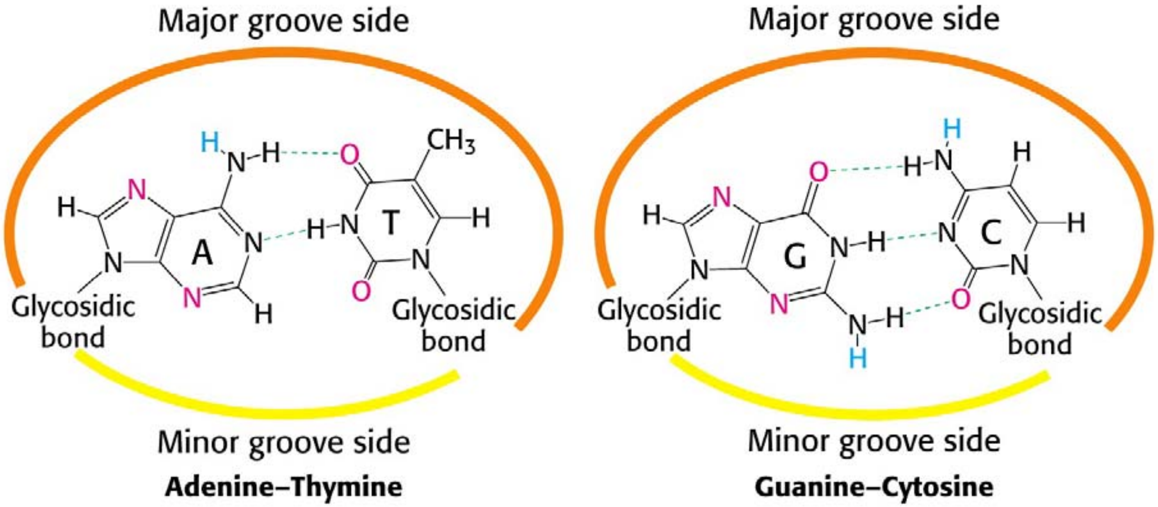
Most prevalent

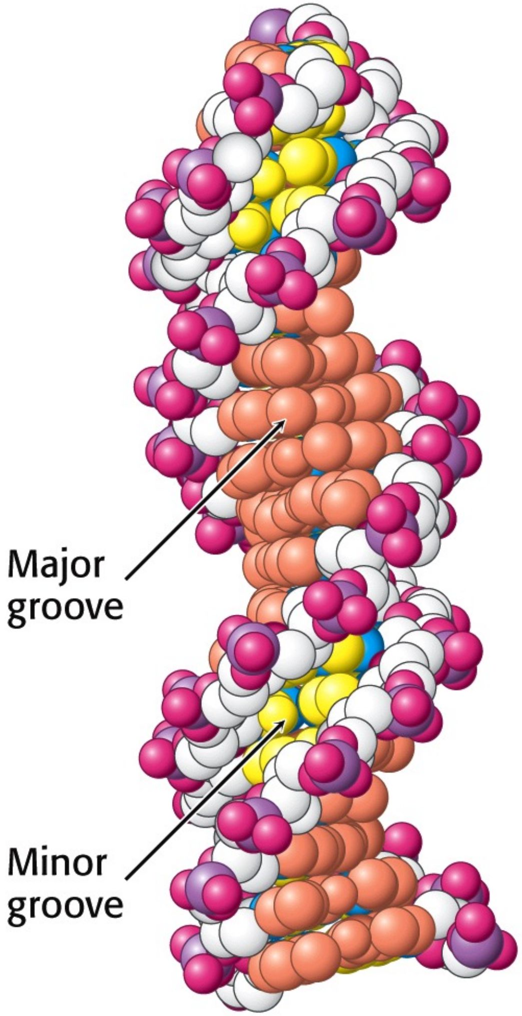


DNA Backbone Parameters



DNA Grooves





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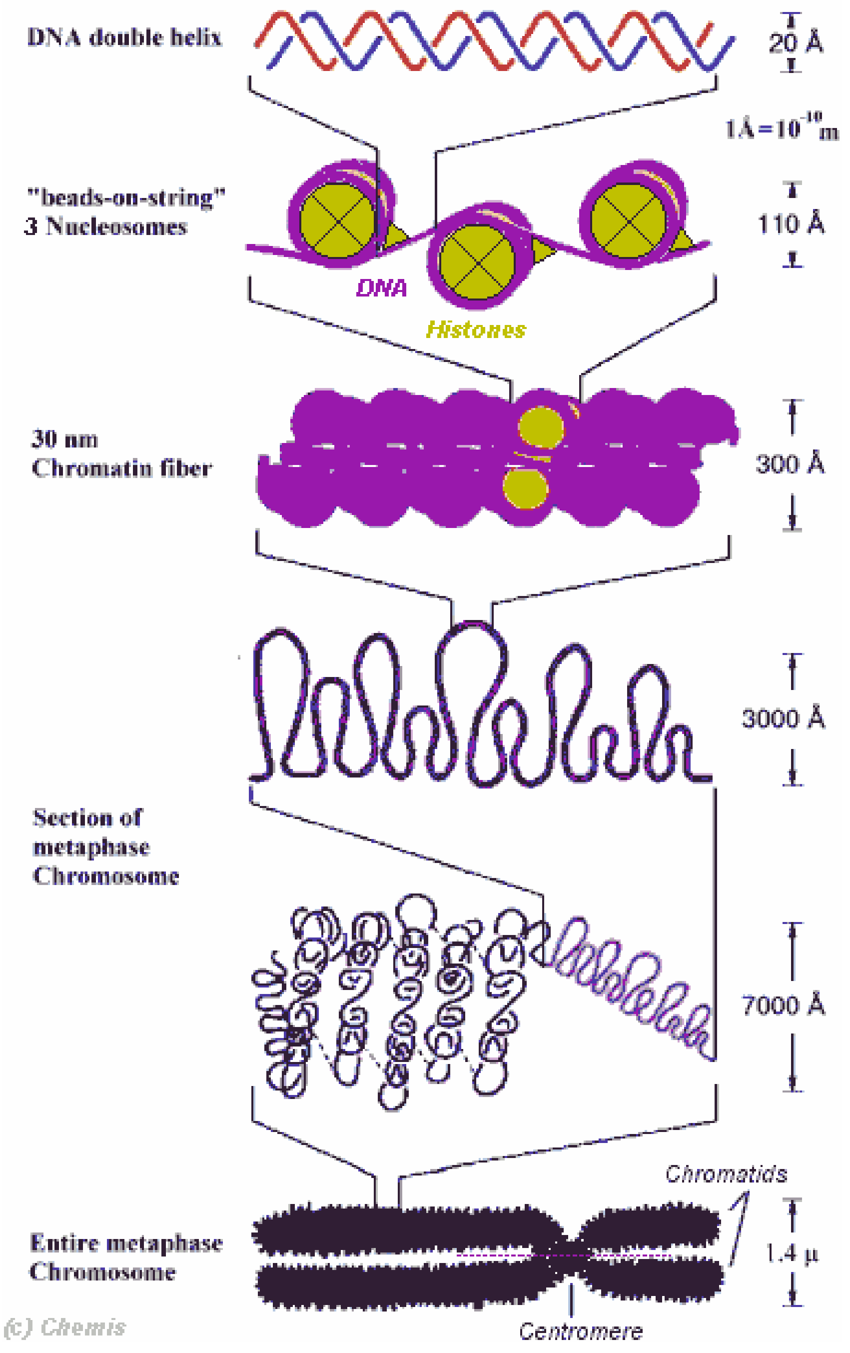
DNA Packing



DNA double helix
20 Å
1Å=10^{-10}m
"beads-on-string"
3 Nucleosomes
110 Å
DNA
Histones
30 nm
Chromatin fiber
300 Å
3000 Å
Section of
metaphase
Chromosome
7000 Å
Chromatids
Entire metaphase
Chromosome
1.4 µ
(c) Chemis
Centromere

The DNA is flexible. It is important to understand how it bends.

Why is this important? Here is the one reason that is often cited:

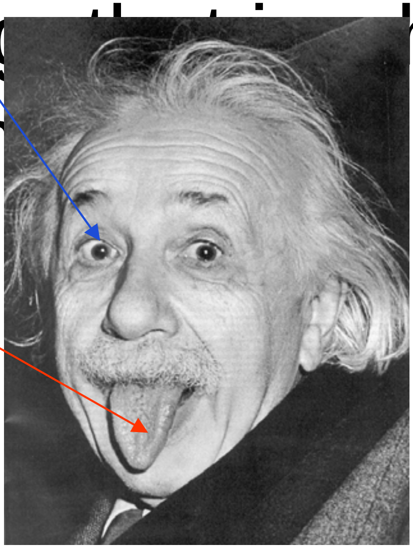
AN ANIMAL CELL

12 feet

So the DNA in the cell must be really bent.

One reason (out of many) why it is important to know how the DNA is folded up in the cell.

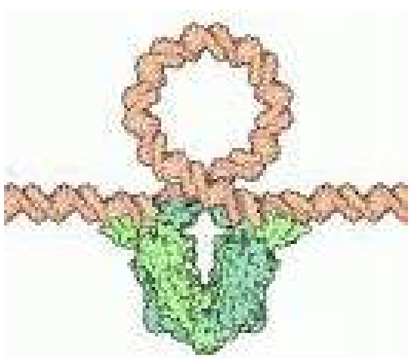
The DNA in all your cells is identical. Yet cells are different. For instance, the DNA in the eye cells is *exactly* the same as in the tongue cells. But it is packed differently, exposing different parts for reading by the cell when it develops and functions. Roughly speakin ... hat makes cells of the same organ ... nt from each other.



Obviously, the folding will depend on how flexible the DNA is.

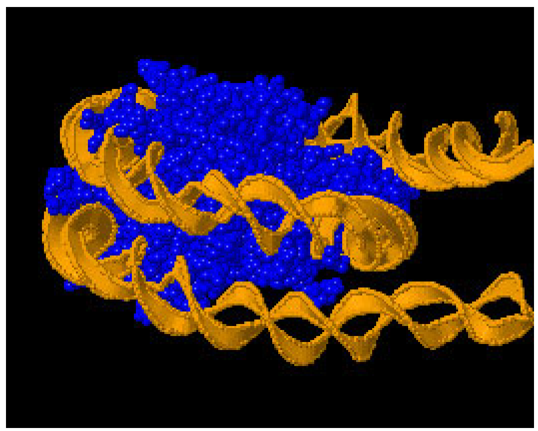
Tightly bent DNA is a fact of life:

~100A
~30 bp



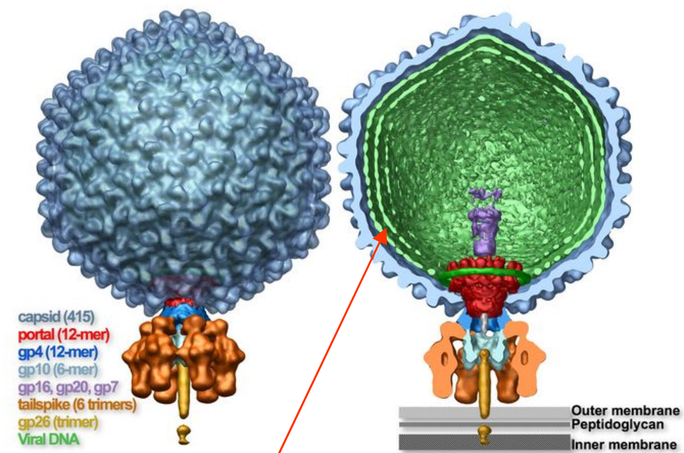
DNA looping
mediated by a
transcription factor

~ 80 A
~25 bp



DNA packing
in the nucleosome

~500A
~ 145 bp

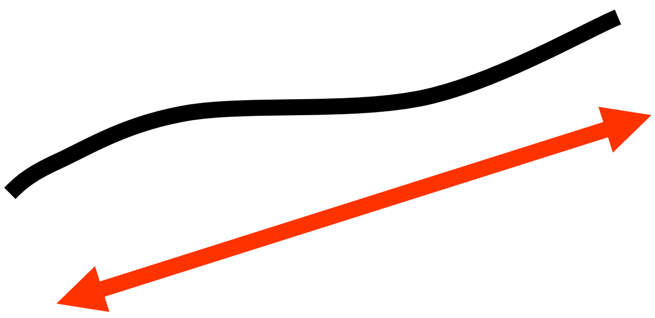


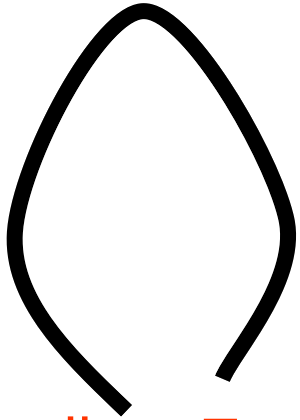
Assembly and infection of large dsDNA viruses

DNA packing
inside a virus

Weakly and Tightly bent DNA. Persistence length.

Weak bending. Energy << kT

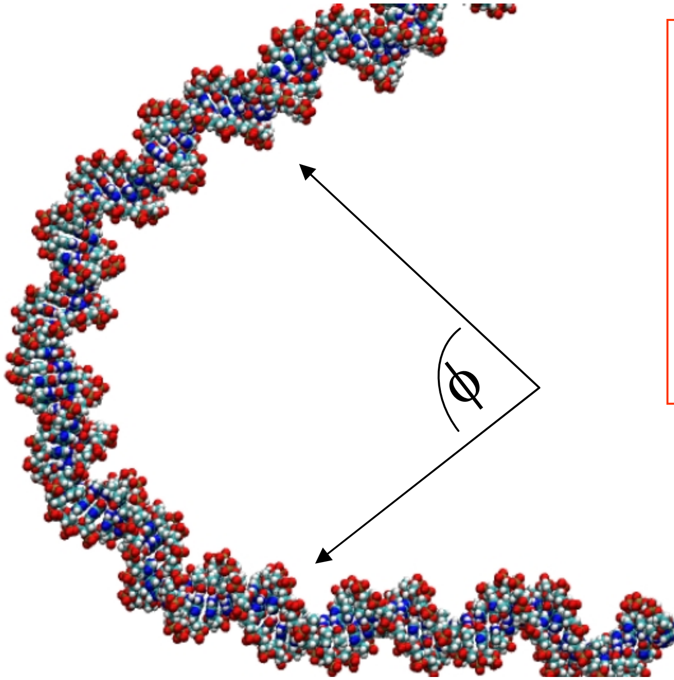




Tight bending, Energy >> kT

The key length scale of a polymer: persistence length.
Conventional value = ~145 pb or ~500A for DNA

Classical elastic rod theory (Landau)



Bending energy $\propto \phi^2$

Hooke's Law Harmonic WLC model.

$$E \approx kTL\int_0^C (\frac{\partial t}{\partial s})ds \geq kT\phi^2$$

(In our case, L = C ~ 500A.)

DNA flexibility depends on its sequence!

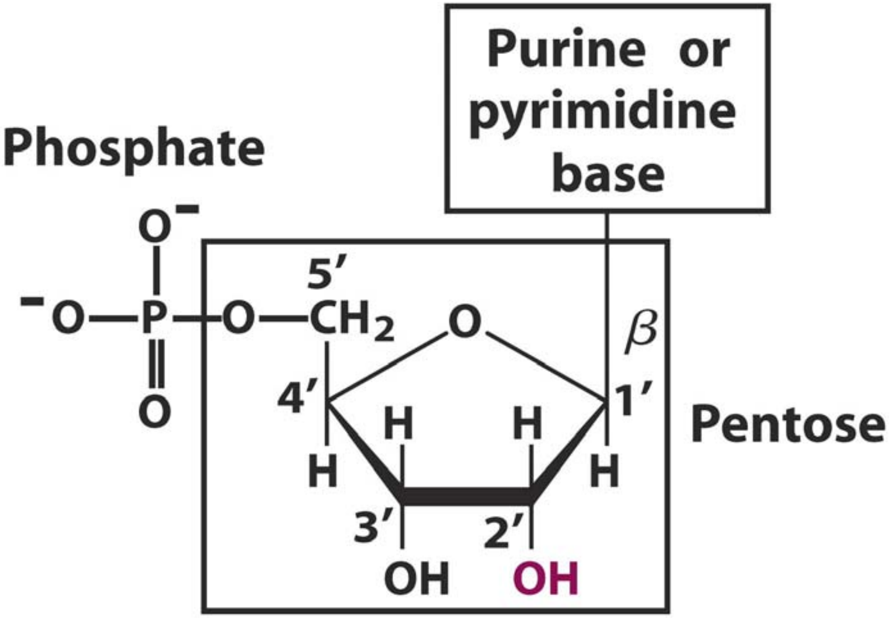
- It is very important to be able to predict this dependence (still not fully solved problem).
- What’s more flexible: AAAAA
  TTTTTT

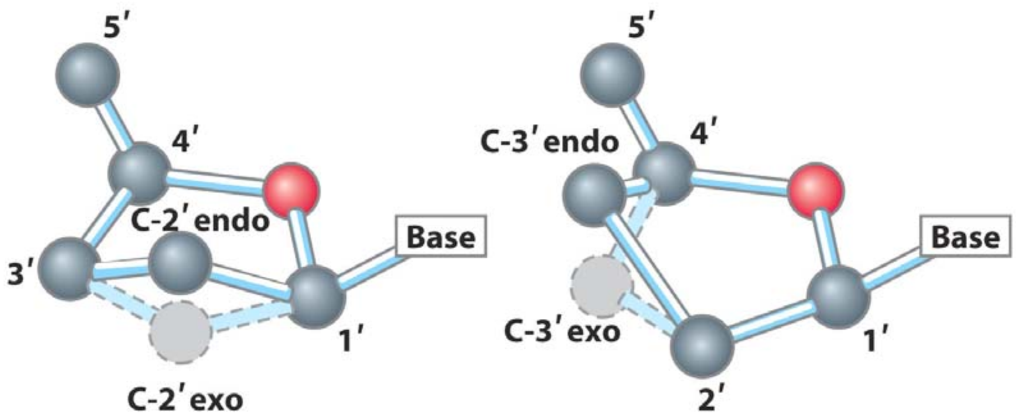
  Or: GGGGGG
  CCCCCC

A-T linked by 2 H-bonds, but G-C by 3.
Less room to wiggle, so less flexible.

Ribose

- An important derivative of ribose is 2'-deoxyribose, or just deoxyribose, in which the 2' OH is replaced with H.
- Deoxyribose is in DNA (deoxyribonucleic acid)
- Ribose is in RNA (ribonucleic acid).
- The sugar prefers different puckers in DNA (C-2' endo) and RNA C-3' endo).



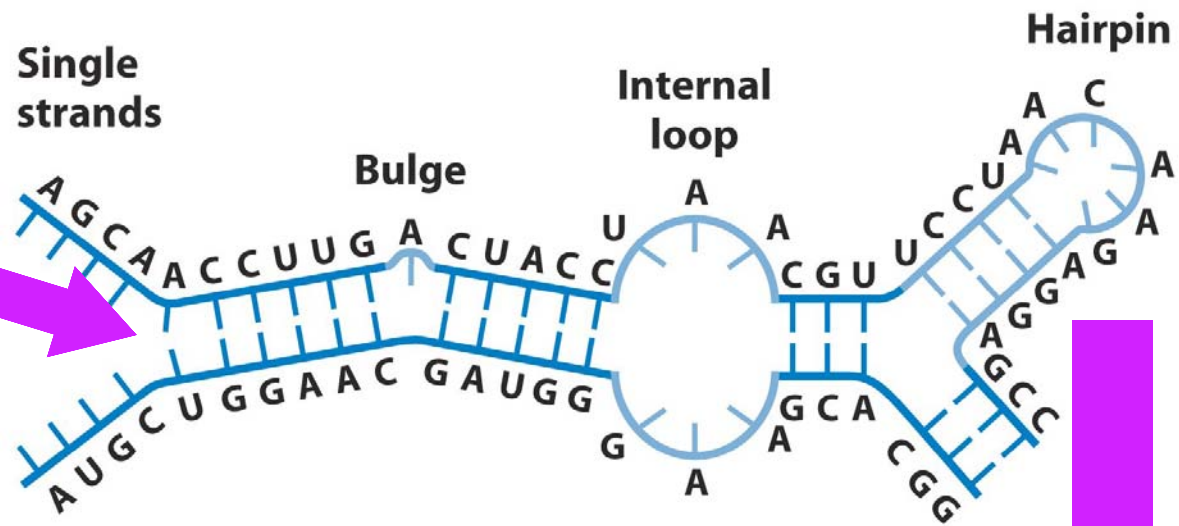


Types of RNA

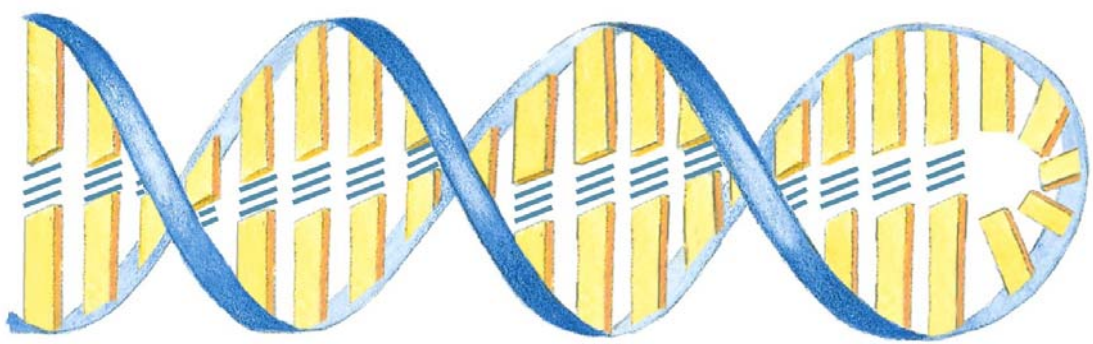
- mRNA (messenger RNA)
  - Template for protein synthesis (translation)
- tRNA (transfer RNA)
  - Carries activated amino acids to ribosome for protein synthesis
  - At least one kind of tRNA for each of the 20 amino acids
- rRNA (ribosomal RNA)
  - Major component of ribosomes

RNA has a rich and varied structure

Watson-Crick base pairs (helical segments; Usually A-form). Helix is secondary structure. Note A-U pairs in RNA.

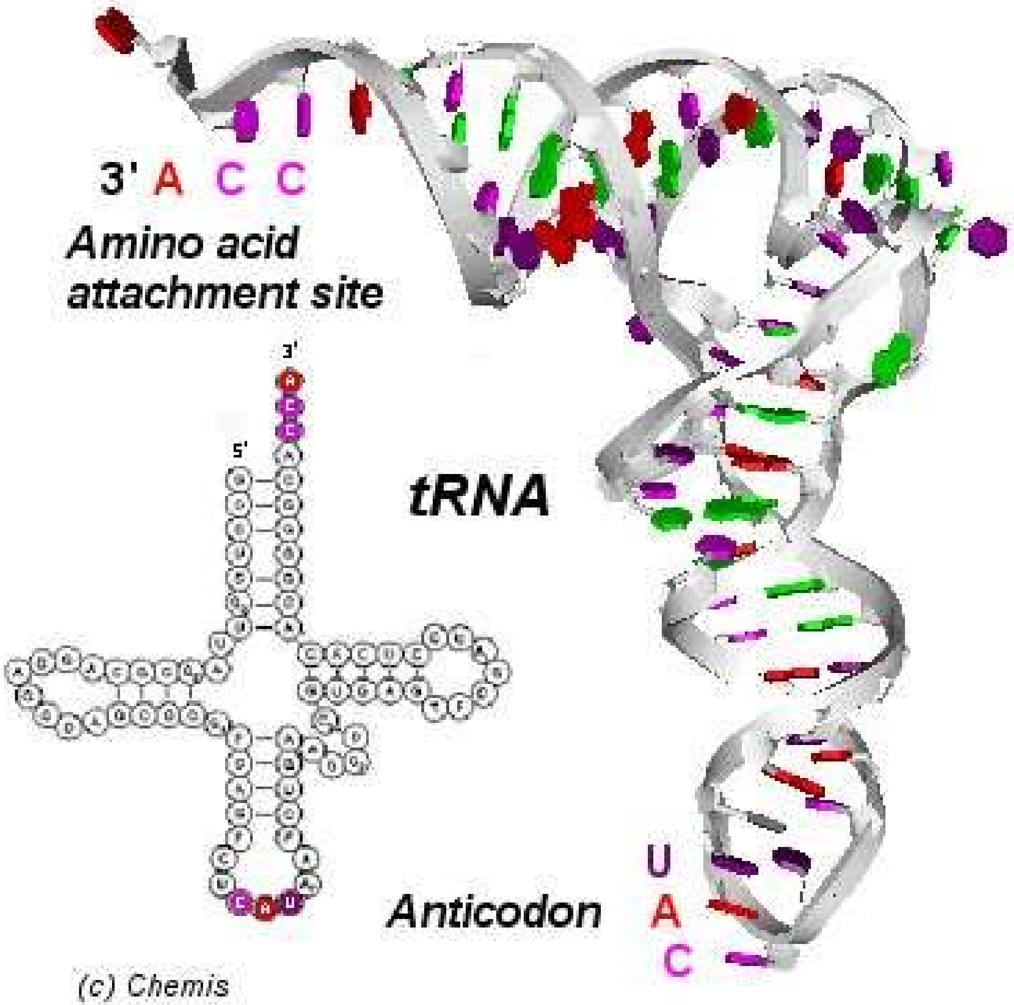


DNA can form structures like this as well.



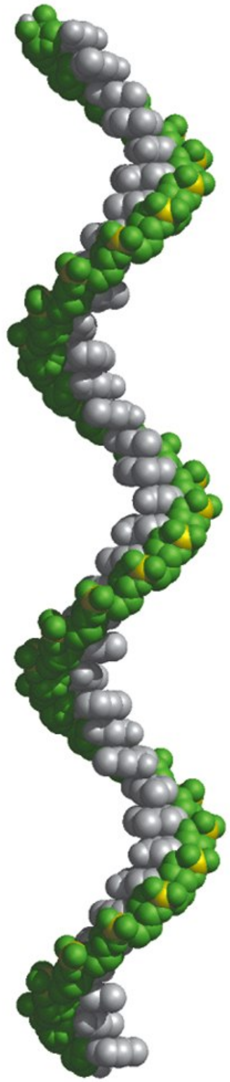
Hairpin double helix

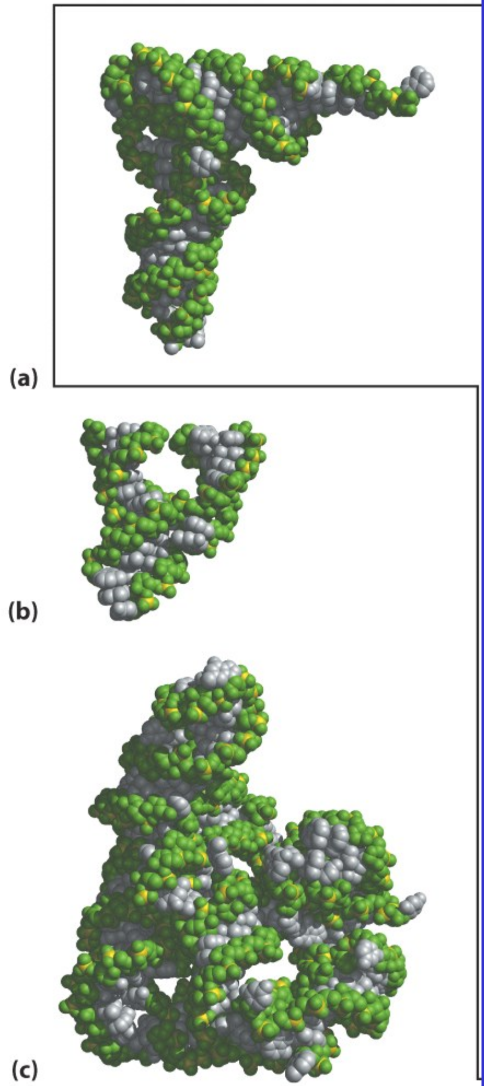
Structure of tRNA



RNA displays interesting tertiary structure

Single-stranded RNA right-handed helix





Yeast $tRNA^{Phe}$
(1TRA)

Hammerhead ribozyme
(1MME)

T. thermophila intron,
A ribozyme (RNA enzyme)
(1GRZ)

The mother of all proteins

Large subunit of the ribosome

Made of proteins and RNA.

1ffk

Function: protein sysnthesis