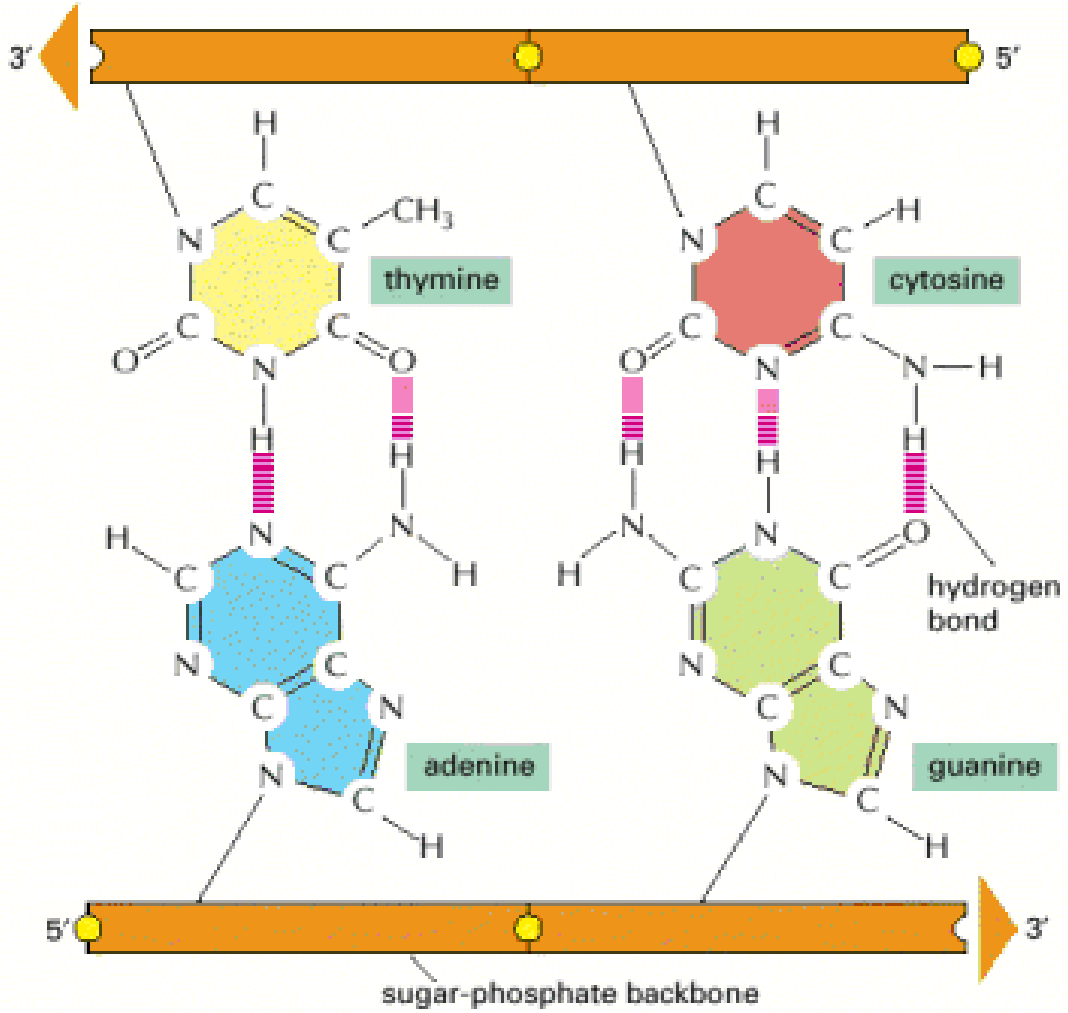
LECTURE 15

Complementary base pairs in the DNA double helix

The shapes and chemical structure of the bases allow hydrogen bonds to form efficiently only between A and T and between G and C, where atoms that are able to form hydrogen bonds can be brought close together without distorting the double helix.

Two hydrogen bonds form between A and T, while three form between G and C.

The bases can pair in this way only if the two polynucleotide chains that contain them are antiparallel to each other.



Complementary base pairs in the DNA double helix

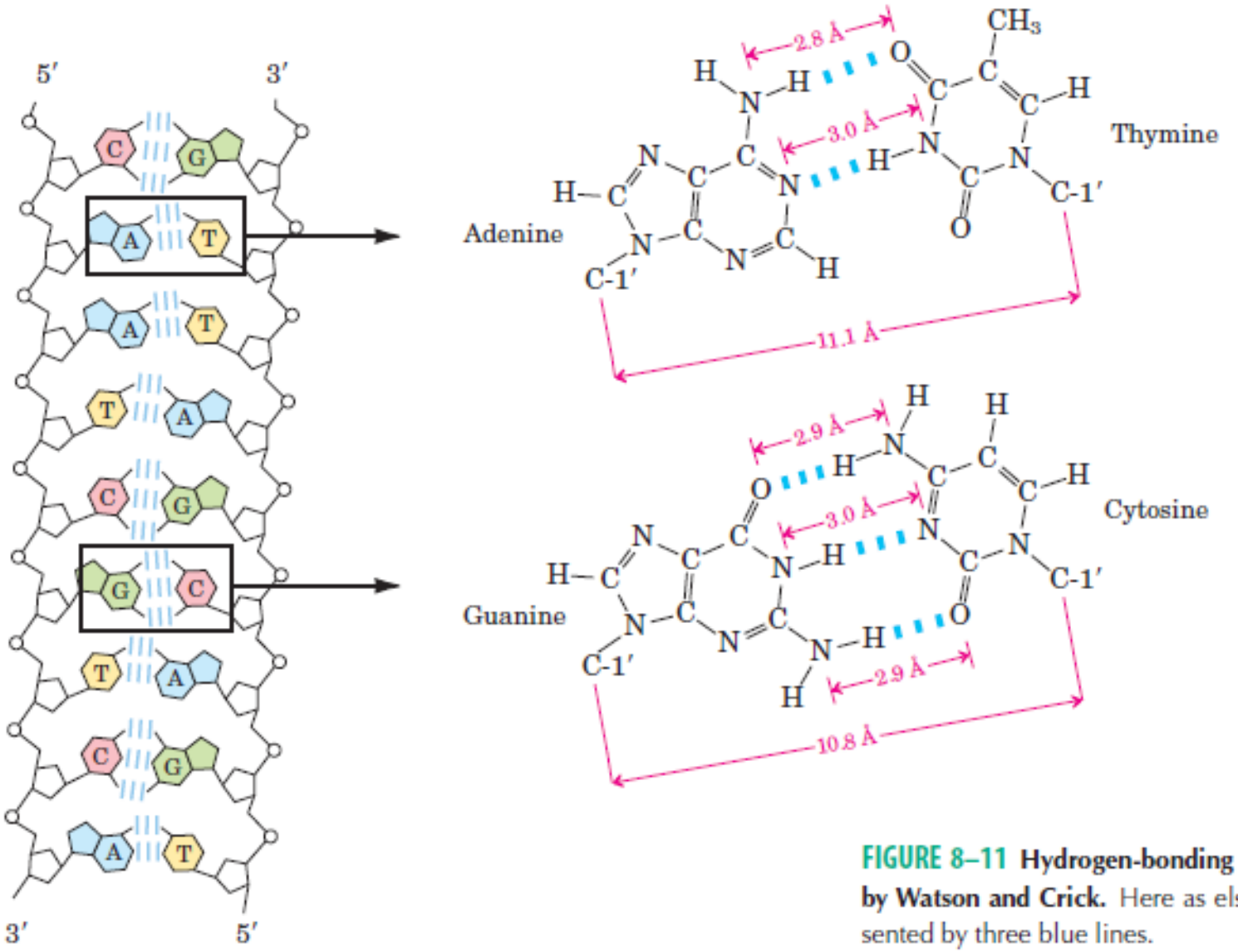
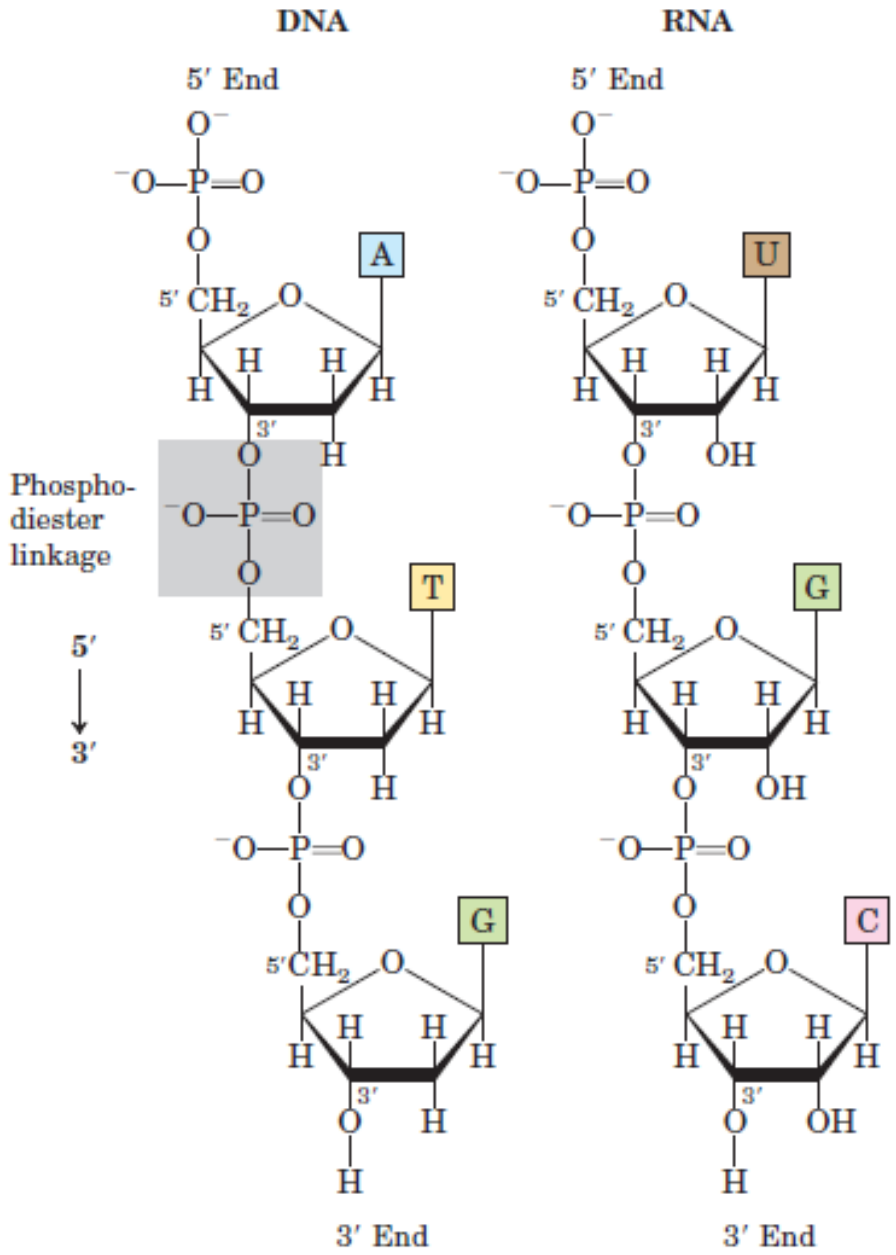


FIGURE 8–11 Hydrogen-bonding patterns in the base pairs defined by Watson and Crick. Here as elsewhere, hydrogen bonds are represented by three blue lines.

Phosphodiester bonds between successive nucleotides

Phosphodiester Bonds Link Successive Nucleotides in Nucleic Acids

The successive nucleotides of both DNA and RNA are covalently linked through phosphate-group “bridges,” in which the 5-phosphate group of one nucleotide unit is joined to the 3-hydroxyl group of the next nucleotide, creating a **phosphodiester linkage**



Hydrogen bonds – Complementary base pairing

Phosphodiester bond-
The phosphate residue forms a link between the 3-hydroxyl of one deoxyribose and the 5-hydroxyl of the next.

Van der walls forces –
The nitrogenous bases stacked upon one another are spaced based on their van der Waals distance.

Hydrophobic effects –
DNA has an interesting arrangement wherein the non-polar, uncharged bases are present in the interior of the structure, while the negatively charged phosphates are present on the outside.

As the cellular environment is aqueous and polar, the hydrophobic bases in the interior of the helix are kept away from the surrounding water and the hydrophilic heads are exposed and interact with the exterior water. This property increases the solubility of DNA in water.

N-glyosidic bond - nitrogenous base is linked to the 1 carbon of deoxyribose

Which of these is more stable?

A. GACTTCAAATAT
B. GACTTCCGAT
C. GACTTCGACTCG
D. GACTTCAAATGC

Double-Helical DNA and RNA Can Be Denatured

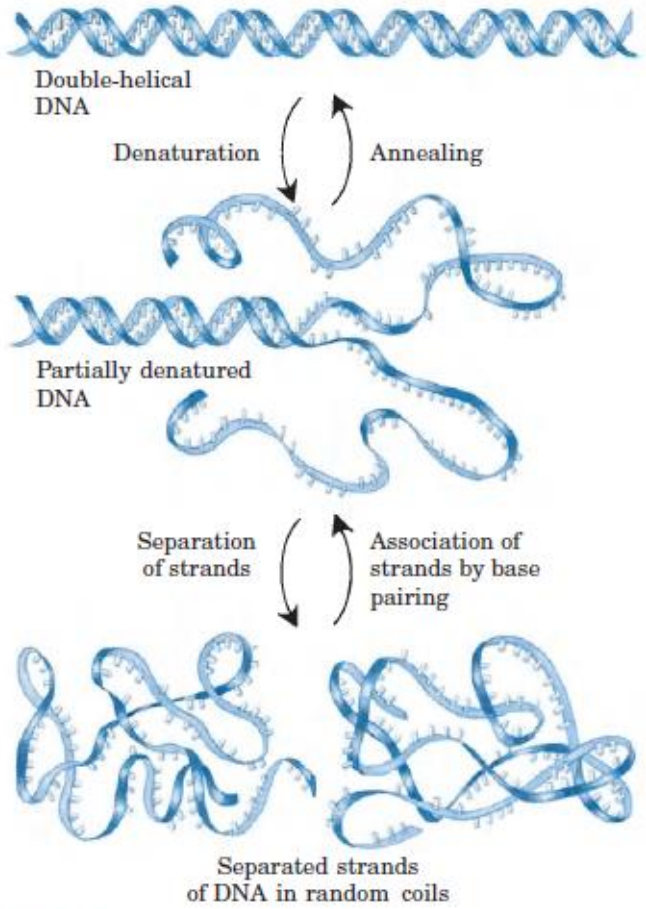


FIGURE 8–26 **Reversible denaturation and annealing (renaturation) of DNA.**

Hypochromic effect

The close interaction between stacked bases in a nucleic acid has the effect of decreasing its absorption of UV light relative to that of a solution with the same concentration of free nucleotides, and the absorption is decreased further when two complementary nucleic acid strands are paired.

Denaturation of a double-stranded nucleic acid produces the opposite result: an increase in absorption called the hyperchromic effect.

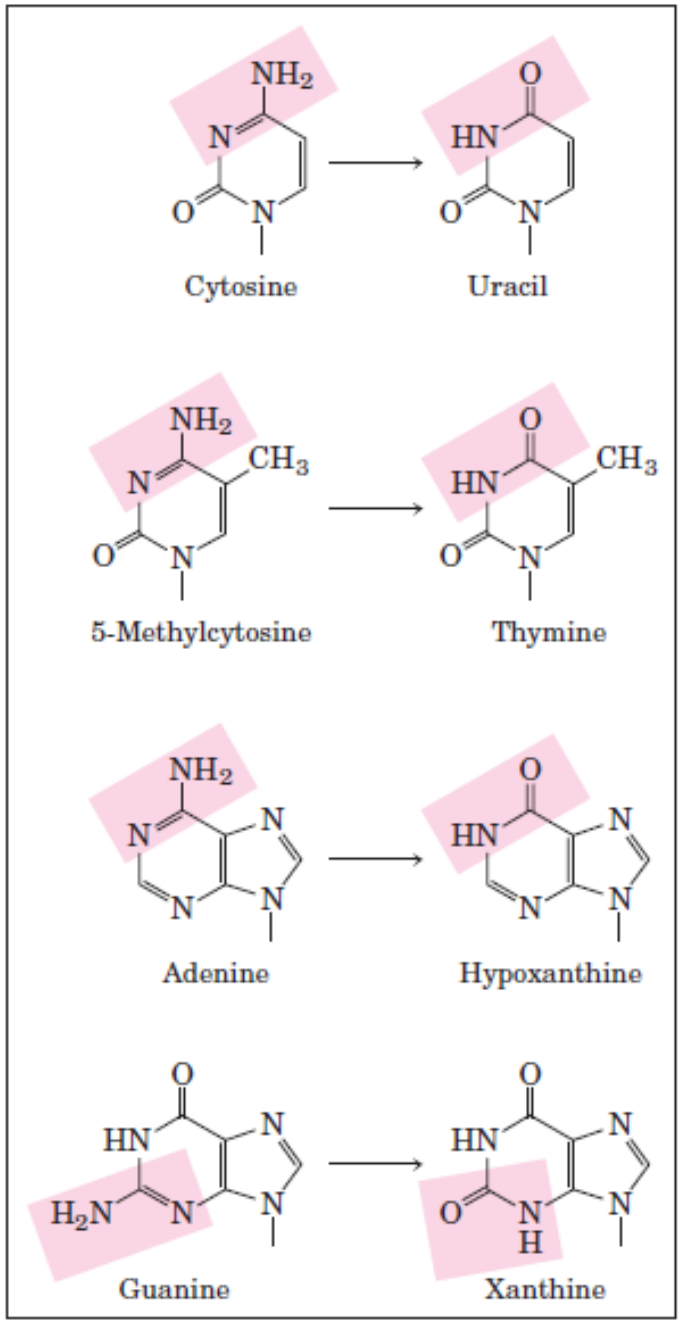
The transition from double-stranded DNA to the single-stranded, denatured form can thus be detected by monitoring UV absorption at 260 nm.

Nucleotides and Nucleic Acids Undergo Nonenzymatic Transformations

Purines and pyrimidines, undergo spontaneous alterations in their covalent structure.

The rate of these reactions is generally *very slow*, but they are physiologically significant because of the cell's very low tolerance for alterations in its genetic information.

Alterations in DNA structure that produce permanent changes in the genetic information encoded are called **mutations**



(a) Deamination

Deamination of cytosine (in DNA) to uracil occurs in about one of every 10_7 cytidine residues in 24 hours.

This corresponds to about 100 spontaneous events per day, on average, in a mammalian cell.

Deamination of adenine and guanine occurs at about 1/100th this rate.

The slow cytosine deamination reaction seems innocuous enough, but is almost certainly the reason why DNA contains thymine rather than uracil.

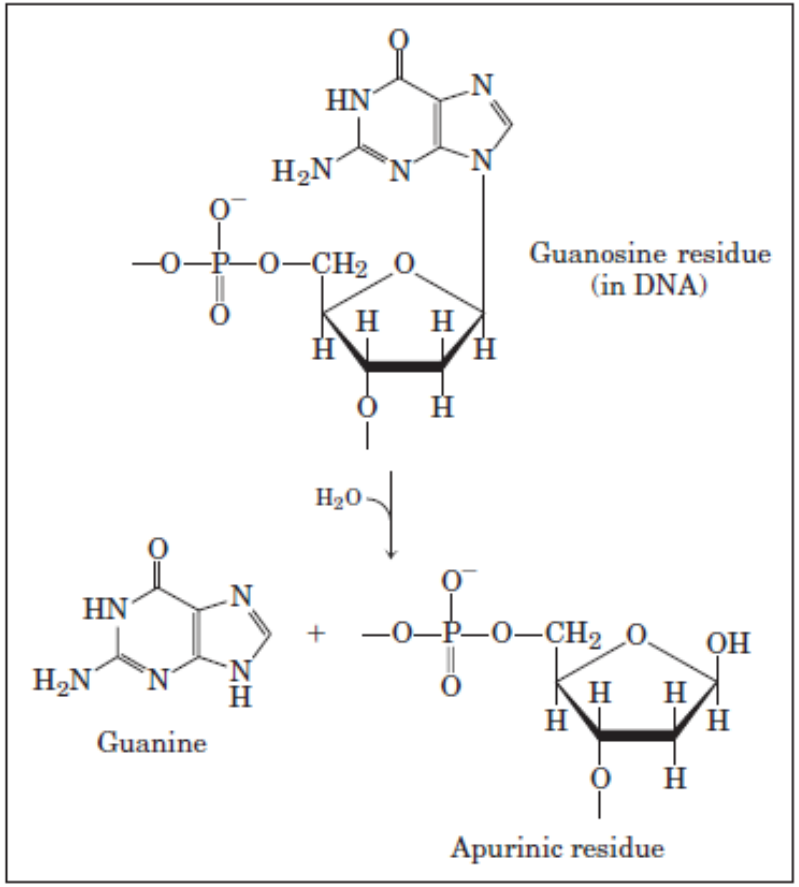
The product of cytosine deamination (uracil) is readily recognized as foreign in DNA and is removed by a repair system

Depurination

Another important reaction in deoxyribonucleotides is the hydrolysis of the *N*--glycosyl bond between the base and the pentose sugar, to create a DNA lesion called an AP (apurinic, apyrimidinic) site or abasic site

This occurs at a higher rate for purines than for pyrimidines.

As many as one in 10_5 purines (10,000 per mammalian cell) are lost from DNA every 24 hours under typical cellular conditions.



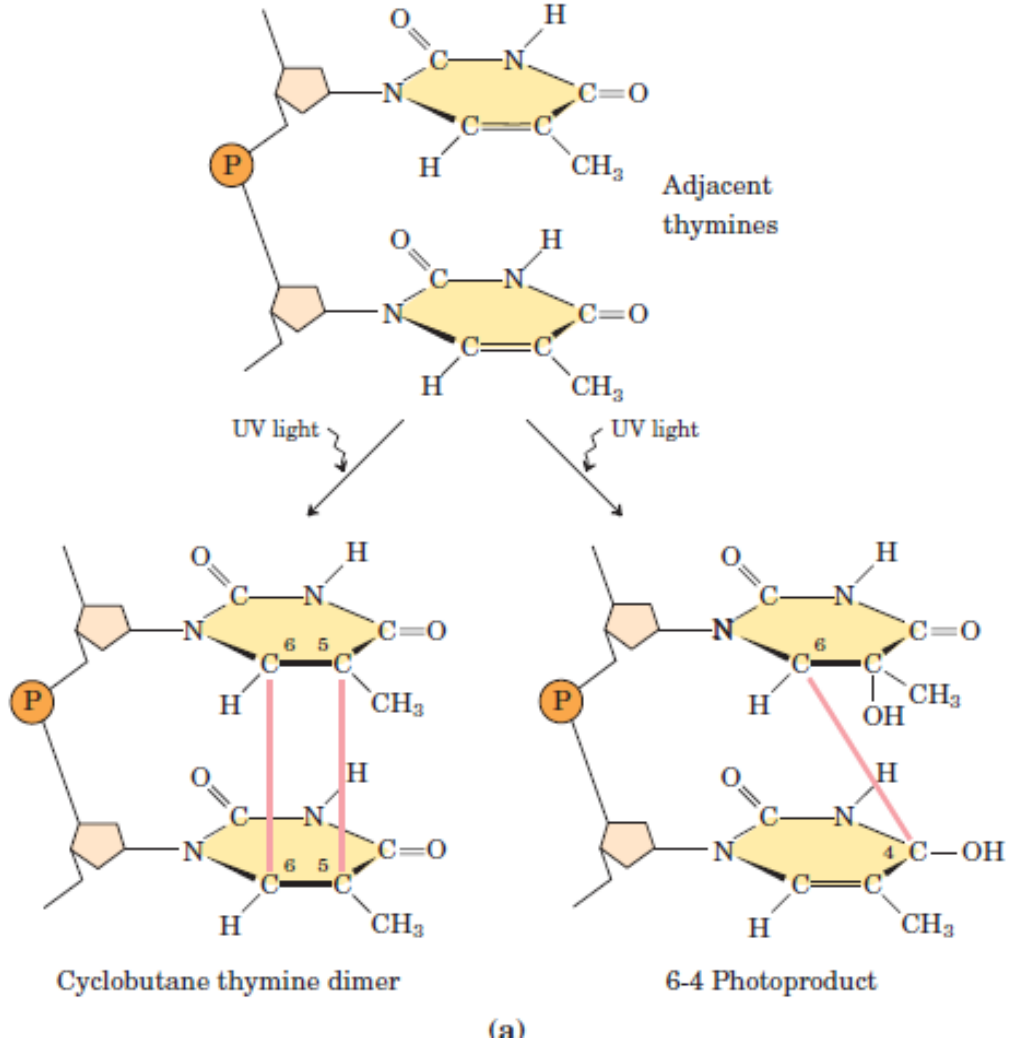
(b) Depurination

UV light exposure

In the cell, adjacent pyrimidine bases in nucleic acids forms cyclobutane pyrimidine dimers.

This happens most frequently between adjacent thymidine residues on the same DNA strand.

A second type of
pyrimidine dimer, called a 6-4 photoproduct, is also formed during UV irradiation.

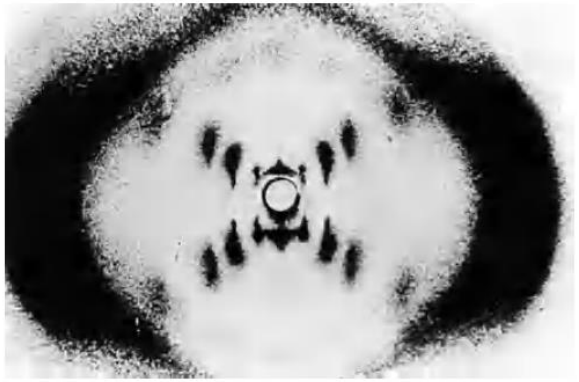


The DNA double helix, or duplex, is held together by two forces: hydrogen bonding between complementary base pairs and base-stacking interactions

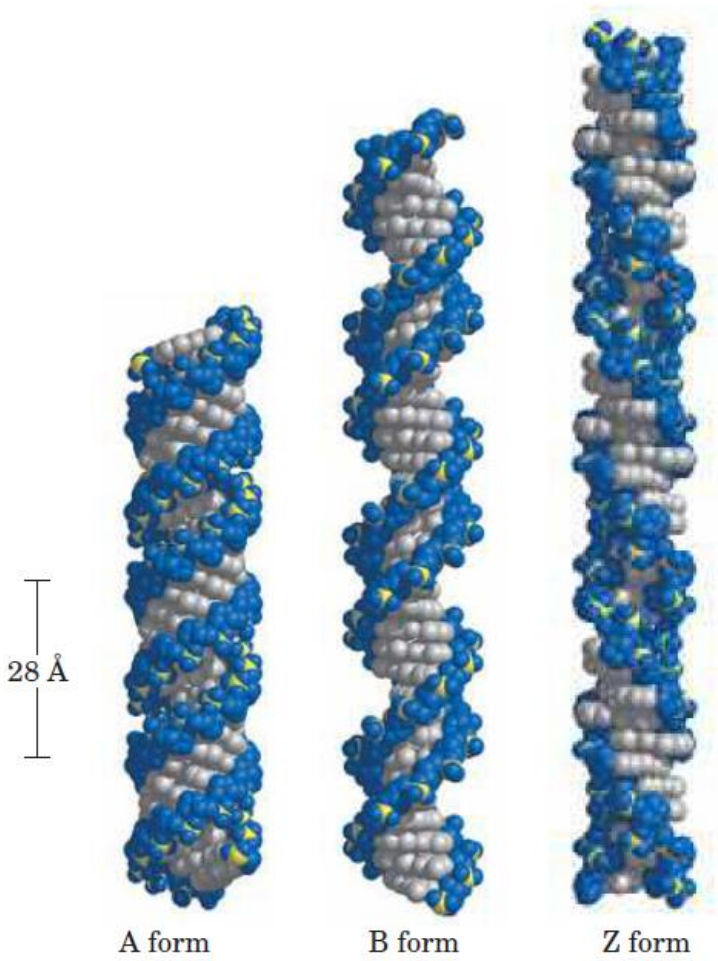
The Watson-Crick structure is also referred to as **B-form DNA**, or B-DNA.

The B form is the most stable structure for a random-sequence DNA molecule under physiological conditions and is therefore the standard point of reference in any study of the properties of DNA.

Two structural variants that have been well characterized in crystal structures are the **A** and **Z forms**.



X-ray diffraction pattern of DNA.
The spots forming a cross in the center denote a helical structure.
The heavy bands at the left and right arise from the recurring bases.



	A form	B form	Z form
Helical sense	Right handed	Right handed	Left handed
Diameter	~26 Å	~20 Å	~18 Å
Base pairs per helical turn	11	10.5	12
Helix rise per base pair	2.6 Å	3.4 Å	3.7 Å
Base tilt normal to the helix axis	20°	6°	7°
Sugar pucker conformation	C-3′ endo	C-2′ endo	C-2′ endo for pyrimidines; C-3′ endo for purines
Glycosyl bond conformation	Anti	Anti	Anti for pyrimidines; syn for purines

Certain DNA Sequences Adopt Unusual Structures

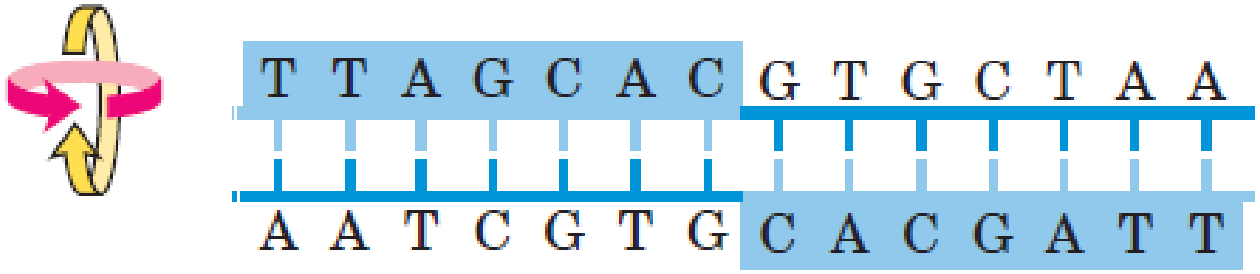
Bends occur in the DNA helix wherever four or more adenosine residues appear sequentially in one strand.

Six adenosines in a row produce a bend of about 18.

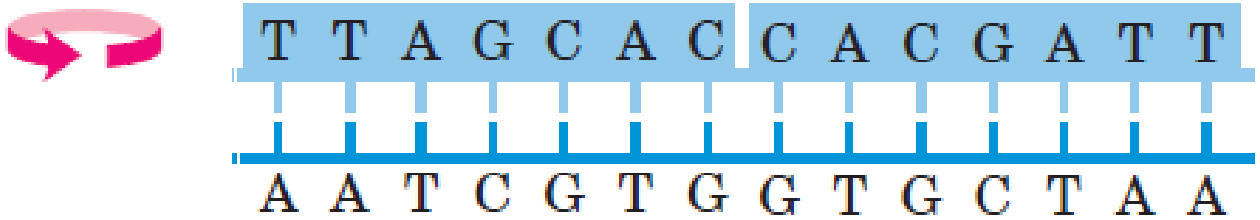
The bending observed with this and other sequences may be important in the binding of some proteins to DNA.

ROTATOR and NURSES RUN

Palindrome



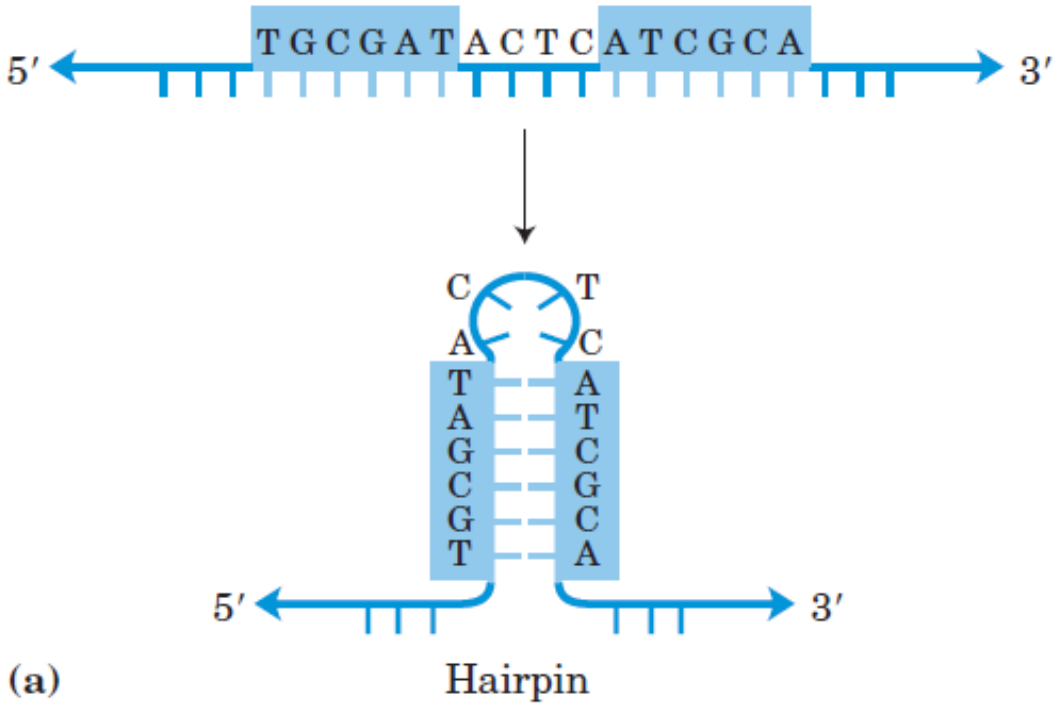
Mirror repeat

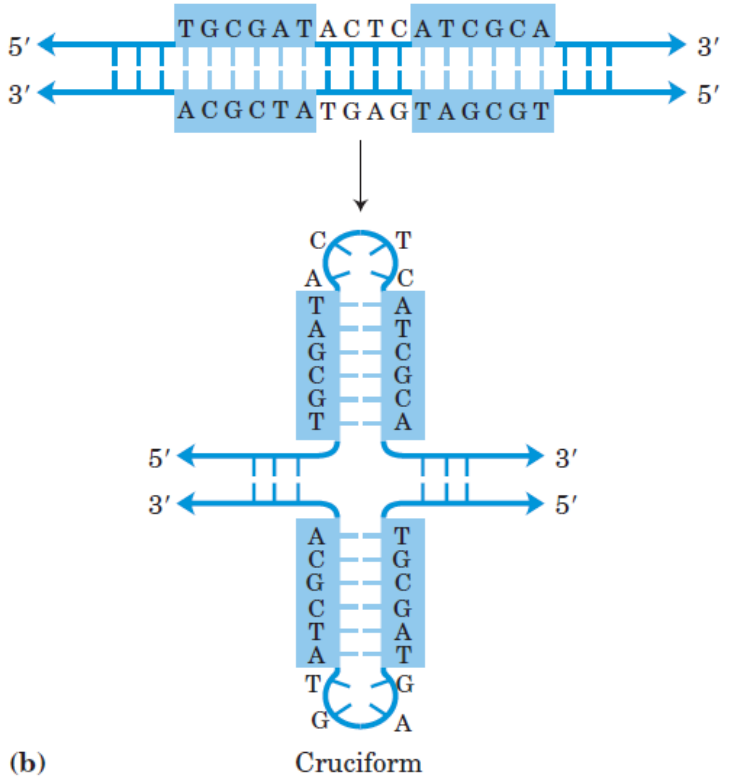


Palindromes and mirror repeats

Palindromes are sequences of double-stranded nucleic acids with twofold symmetry. In order to superimpose one repeat (shaded sequence) on the other, it
must be rotated 180 about the horizontal axis then 180 about the vertical axis, as shown by the colored arrows.

A mirror repeat, on the other hand, has a symmetric sequence within each strand. Superimposing one repeat on the other requires only a single 180 rotation about the vertical axis.





a) When only a single DNA (or RNA) strand is involved, the structure is called a **hairpin.**

b) When both strands of a duplex DNA are involved, it is called a **cruciform**

RNA

RNA has no simple, regular secondary structure that serves as a reference point, as does the double helix for DNA.

The three-dimensional structures of many RNAs, like those of proteins, are complex and unique.

Weak interactions, especially base-stacking interactions, help stabilize RNA structures, just as they do in DNA.

Messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA)—

Each form is involved in different functions and activities.

Messenger RNA is essentially a copy of a section of DNA and serves as a template for the manufacture of one or more proteins.

Transfer RNA binds to both mRNA and amino acids (the building blocks of proteins) and brings the correct amino acids into the growing polypeptide chain during protein formation, based on the nucleotide sequence of the mRNA.

Single-stranded RNA can also form many secondary structures in which a single RNA molecule folds over and forms hairpin loops, stabilized by intramolecular hydrogen bonds between complementary bases.

Such base-pairing of RNA is critical for many RNA functions, such as the ability of tRNA to bind to the correct sequence of mRNA during translation

mRNA

The minimum length of an mRNA is set by the length of the polypeptide chain for which it codes.

For example, a polypeptide chain of 100 amino acid residues requires an RNA coding sequence of at least 300 nucleotides, because each amino acid is coded by a nucleotide triplet

However, mRNAs transcribed from DNA are always somewhat longer than the length needed simply to code for a polypeptide sequence (or sequences).

The additional, noncoding RNA includes sequences that regulate protein synthesis.

The product of transcription of DNA is always single-stranded RNA.

The single strand tends to assume a right-handed helical conformation dominated by base stacking interactions which are stronger between two purines than between a purine and pyrimidine or between two pyrimidines.

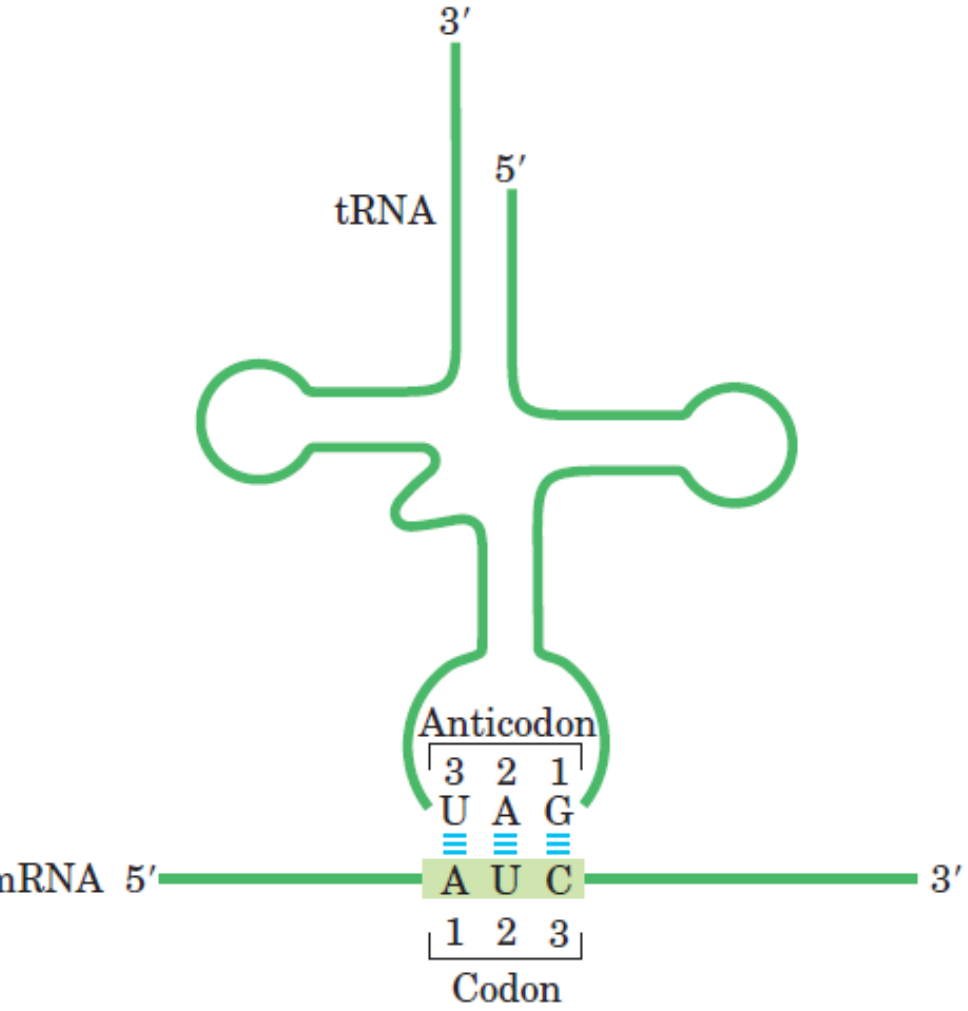
Any self-complementary sequences in the molecule produce more complex structures.

RNA can base-pair with complementary regions of either RNA or DNA.

Base pairing matches the pattern for DNA: G pairs with C and A pairs with U (or with the occasional T residue in some RNAs).

One difference is that base pairing between G and U residues— unusual in DNA—is fairly common in RNA

tRNA



tRNAs can serve as adaptors in translating the language of nucleic acids into the language of proteins

Transfer RNAs are relatively small and consist of a single strand of RNA folded into a precise three-dimensional structure

The tRNAs in bacteria and in the cytosol of eukaryotes have between 73 and 93 nucleotide residues, corresponding to molecular weights of 24,000 to 31,000

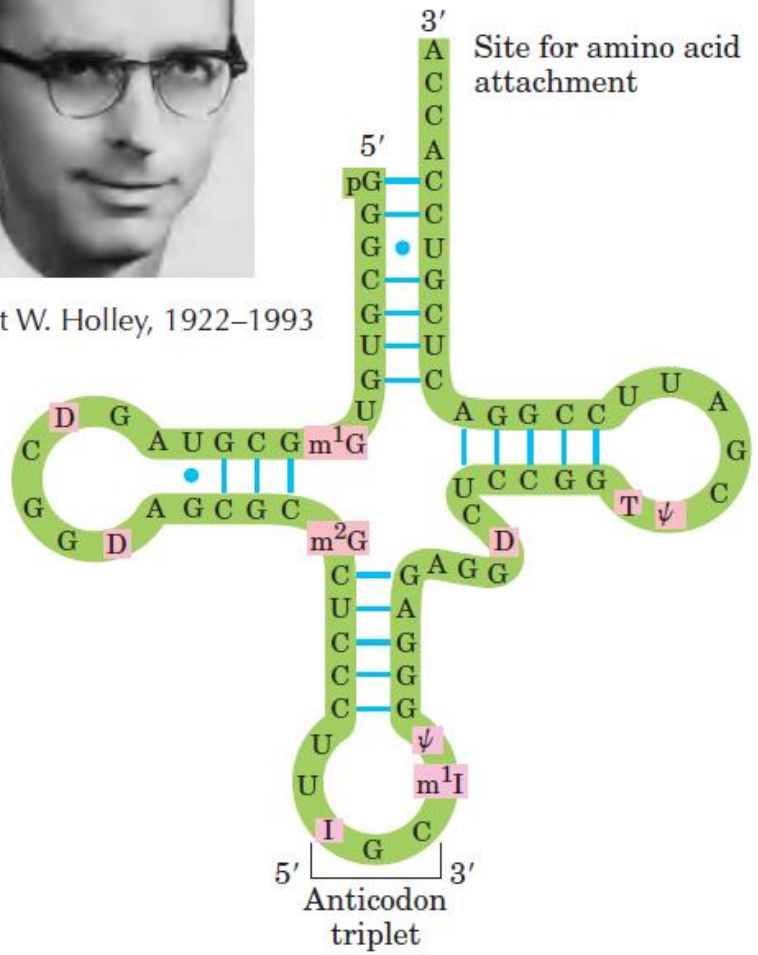
Mitochondria and chloroplasts contain distinctive, somewhat smaller tRNAs.

Cells have at least one kind of tRNA for each amino acid; at least 32 tRNAs are required to recognize all the amino acid codons (some recognize more than one codon), but some cells use more than 32.

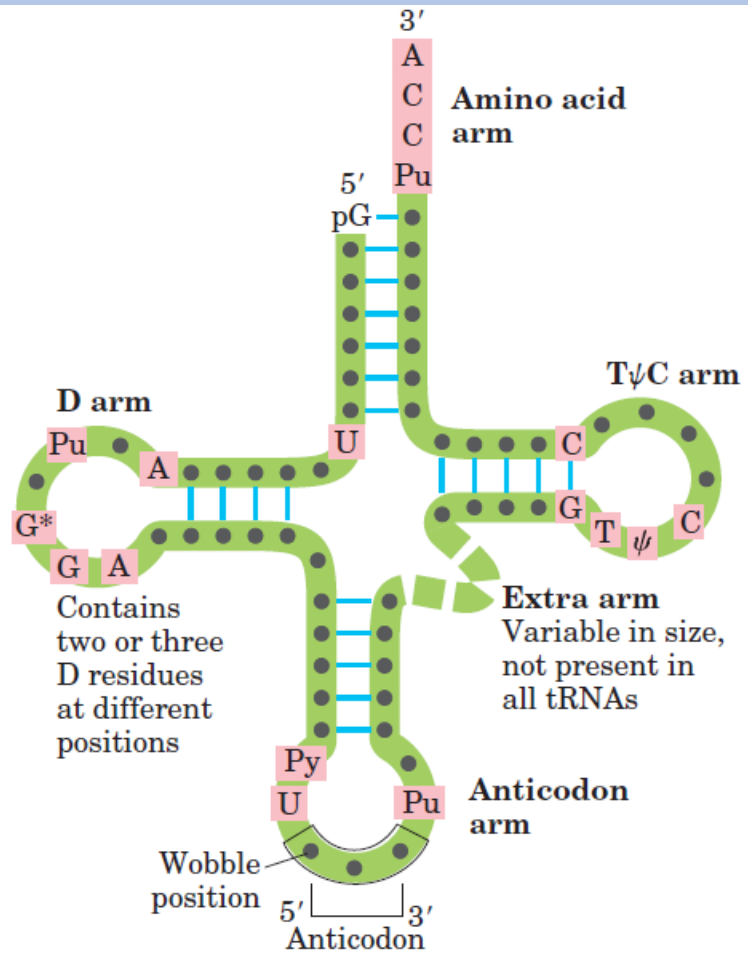
The genetic code, in effect, is defined by two elements:
(1) the anticodons on tRNAs (which determine where an amino acid is placed in a growing polypeptide) and

(2) (2) the specificity of the enzymes—the aminoacyl-tRNA synthetases—that charge the tRNAs, which determines the identity of the amino acid attached to a given tRNA.

Robert W. Holley, 1922–1993

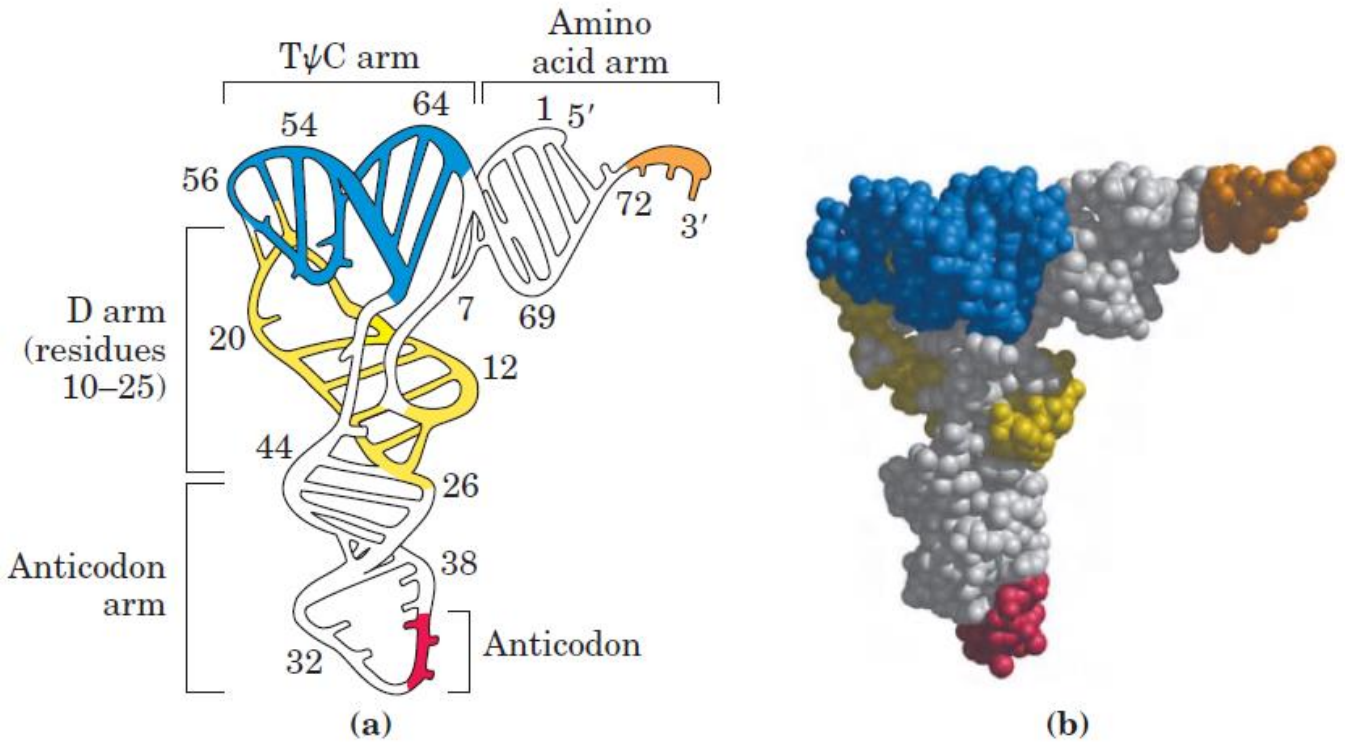


Nucleotide sequence of yeast $tRNA_{Ala}$. This structure was deduced in 1965 by Robert W. Holley and his colleagues; it is shown in the cloverleaf conformation in which intrastrand base pairing is maximal.

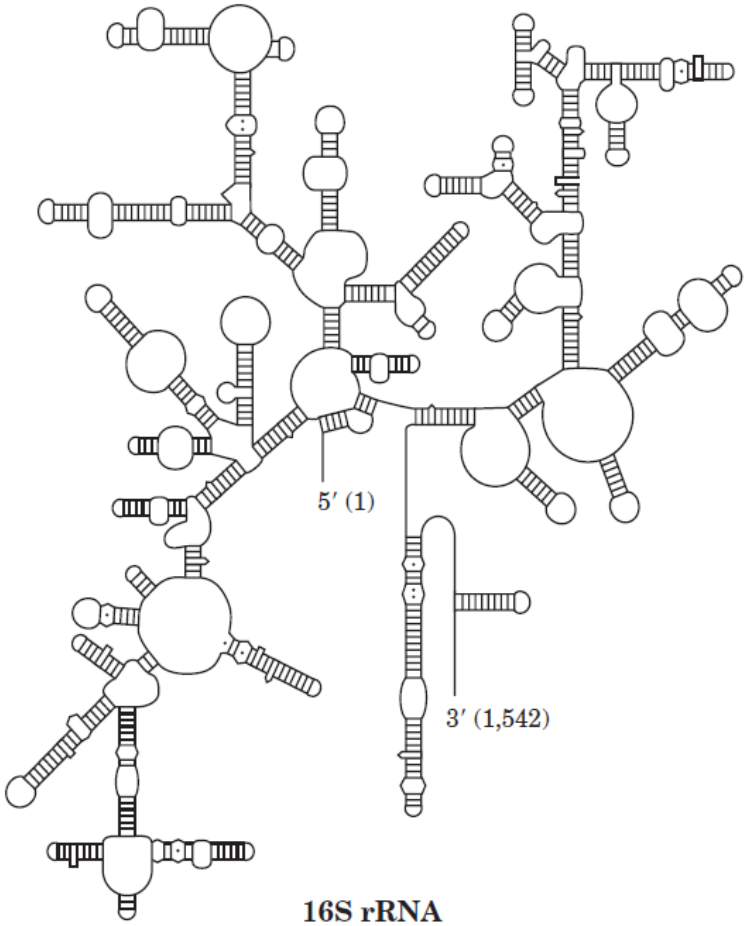


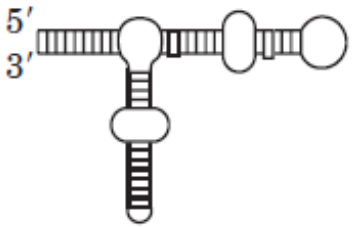
General cloverleaf secondary structure of tRNAs

In three dimensions, a tRNA has the form of a twisted L



rRNA





Bacterial rRNAs. Diagrams of the secondary structure of *E. coli* 16S and 5S rRNAs. The first (5 end) and final (3 end) ribonucleotide residues of the 16S rRNA are numbered