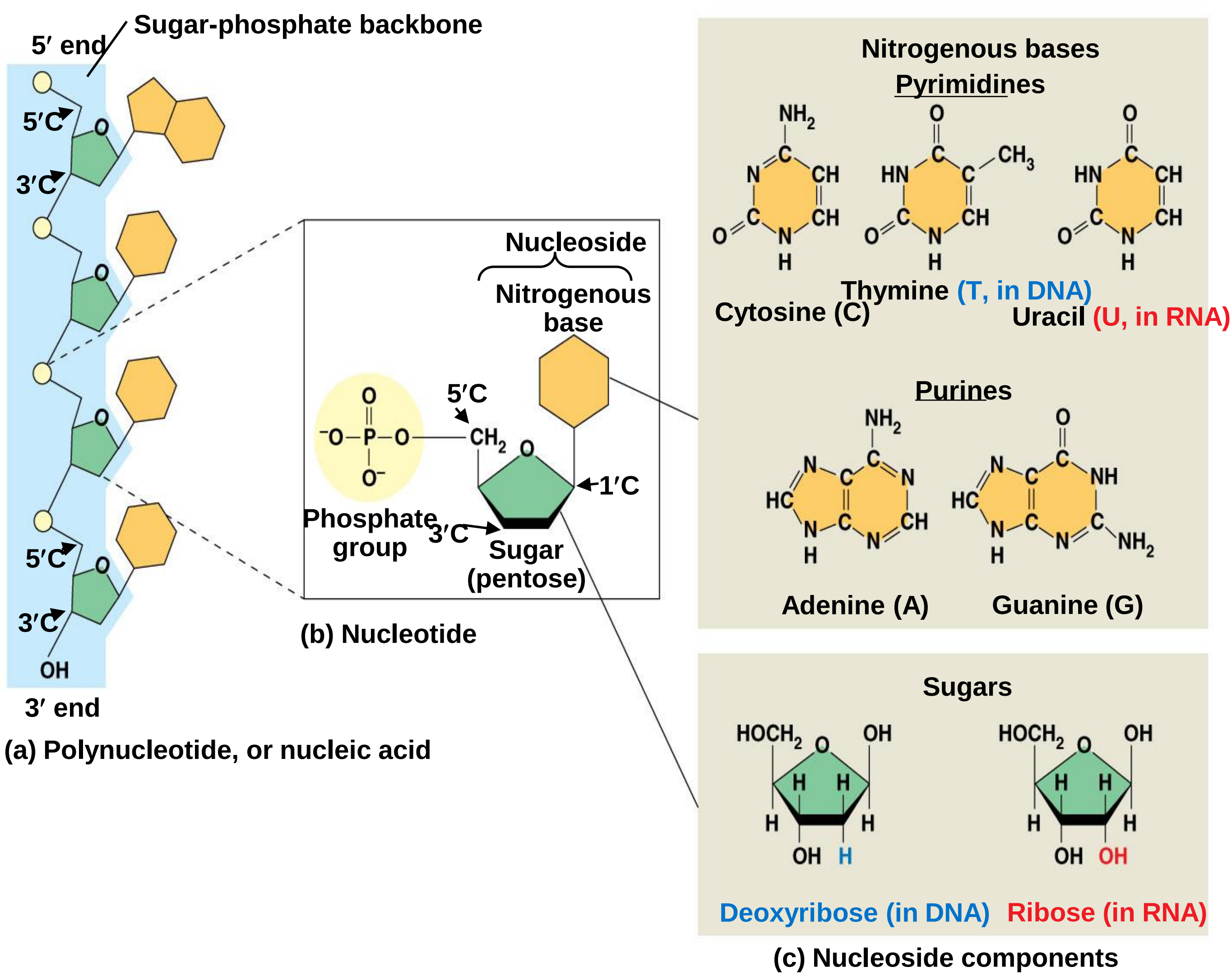
Today’s lecture

- Billion years ago, how did life begin?
- DNA, RNA & Proteins: ΔG and stability of molecules
- Central Dogma of Molecular Biology
- Proteins

DNA Structure

Macromolecule made from nucleotides

Figure 5.26



DNA is a linear polymer of nucleotides. Backbone is held together by covalent sugar-phosphate bonds.

DNA Backbone is negatively charge.
(One charge per nucleotide)

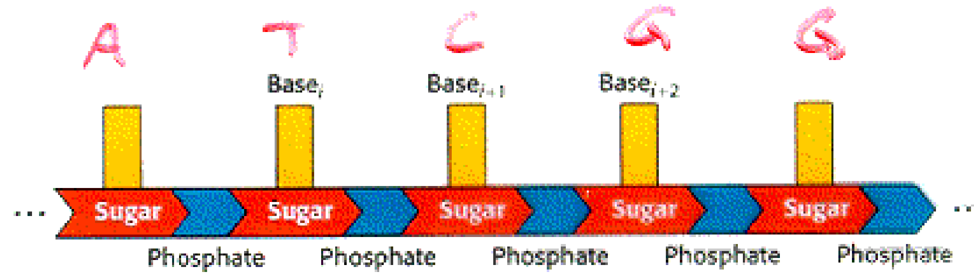
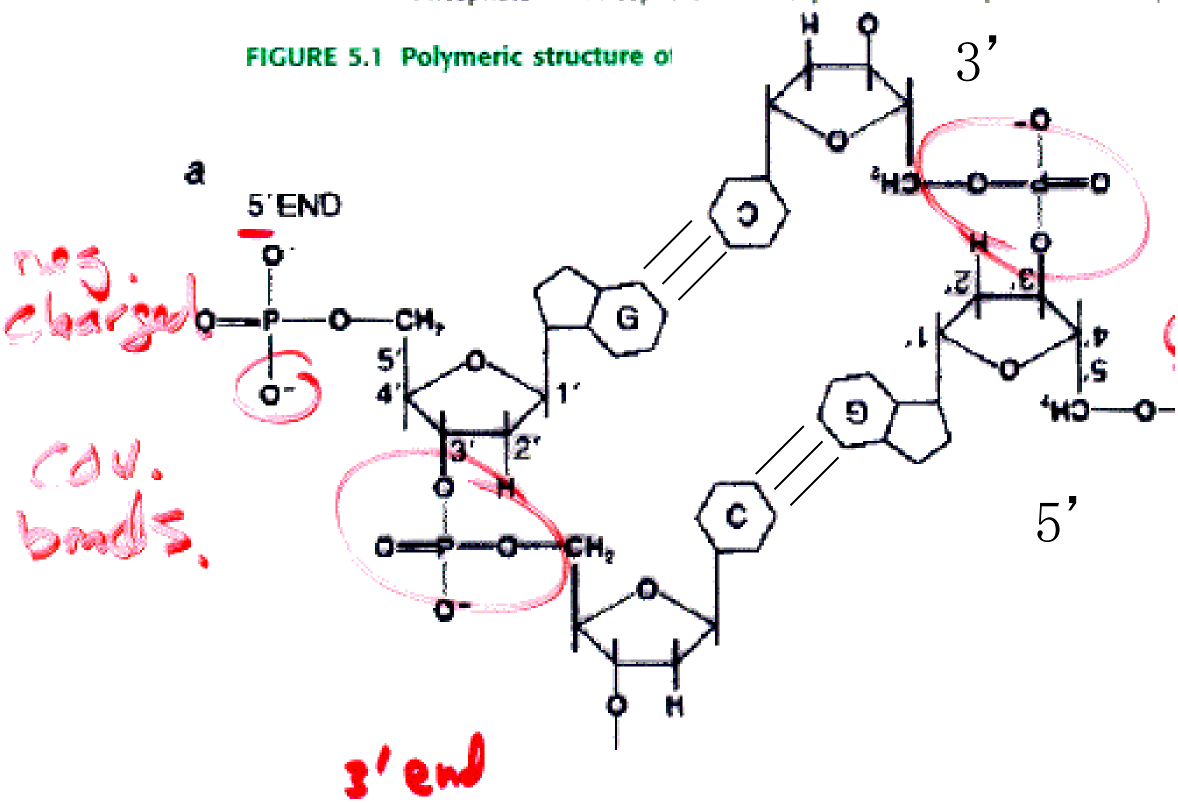


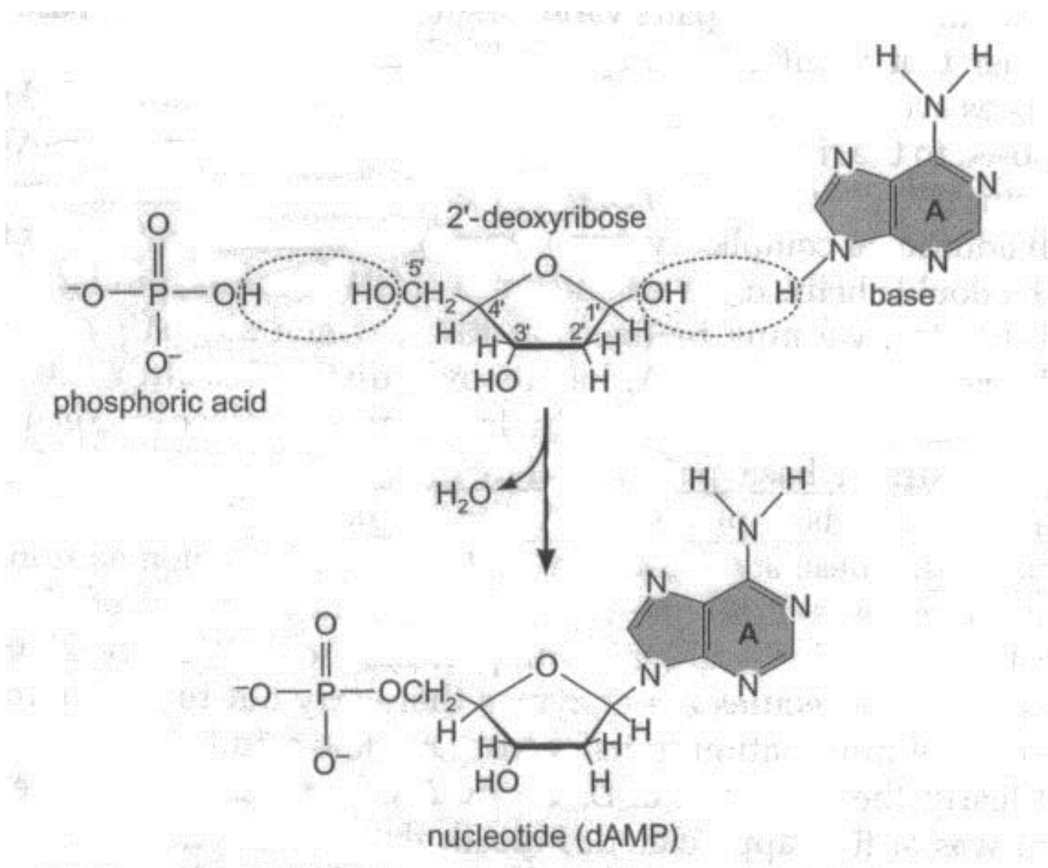
FIGURE 5.1 Polymeric structure of



The storage of information is in the linear arrangement of nucleotides.

How to make nucleotide

Another Example of condensation reaction



Free H_2O : lots of entropy gained

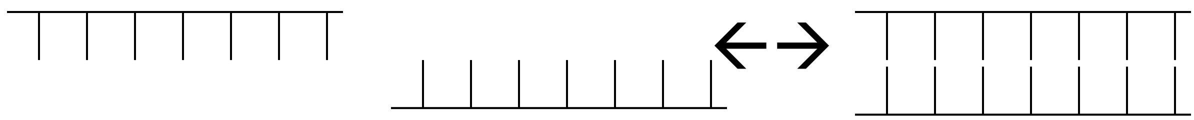
Reaction wants to go.

T_m & (ΔE) ΔG for DNA

Basic Problem:

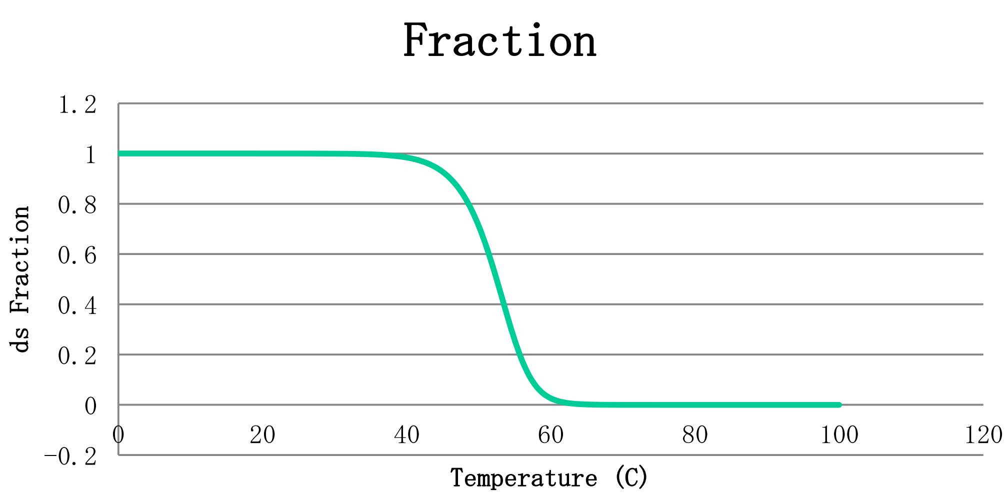
The reaction for forming Double-stranded nucleic acid D from Single-stranded nucleic acids S and C (Complementary strand):

S + C ←→ D



What is the “melting temperature” where ½ of DNA forms double stranded DNA?
How to calculate Tm?
When cold? When hot?

Talk to your neighbor and figure out a way!
(3 minutes)



Do as Homework…

(Will assign for next homework)

The equilibrium constant: K_{eq} = [D]/([S] [C])

Note: in the denominator is [S]+[C] because S and C are identical

The free energy: $\Delta G = -kT \ln K_{eq}$

What is ΔG?

Relate K_{eq} and Tm

DNA→ RNA→ Proteins
Central Dogma of Biology

DNA: series of 4 nucleotides (bases): A,T,G,C

↓ Transcription [DNA & RNA similar]

RNA: series of 4 nucleotides (bases): A,U,G,C

↓ Translation [RNA & Proteins different]

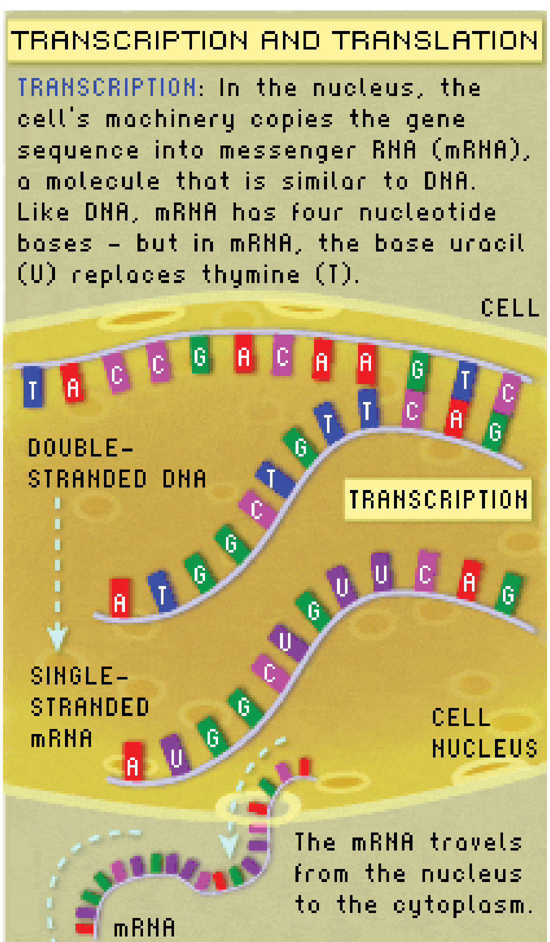
Proteins: series of 20 amino acids: Met-Ala-Val-…

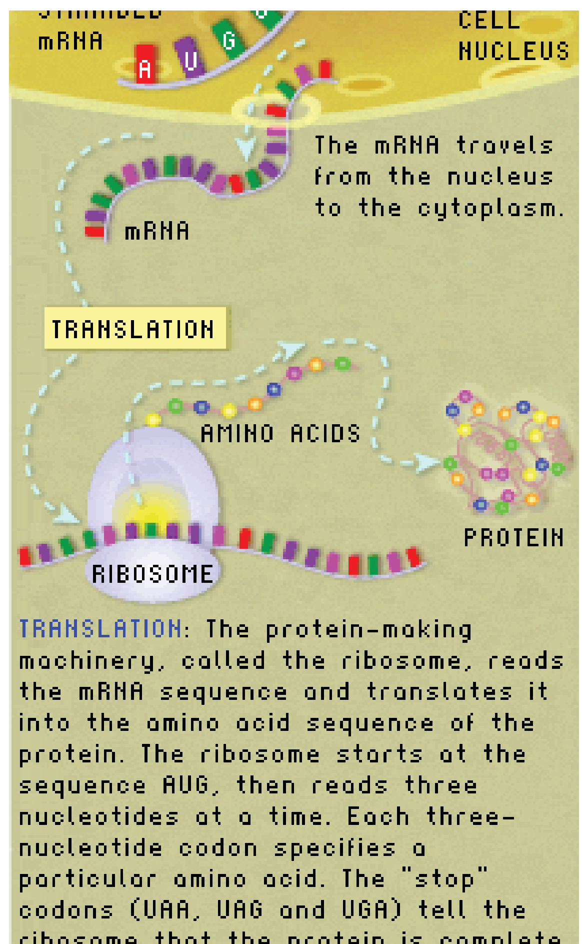
each coded by 3 bases → amino acid

AUG→ Methionine; GCU → Alanine; GUU→ Valine

Proteins are 3-D strings of linear amino acids

Do everything: structure, enzymes…





http://learn.genetics.utah.edu/units/basics/transcribe/

DNA Replication
Chicken & Egg Problem

Have already shown that

If DNA is long and therefore very stable,
how can it replicate itself without an enzyme
(to lower the activation energy)?

The answer won a Nobel prize!

Involves RNA…

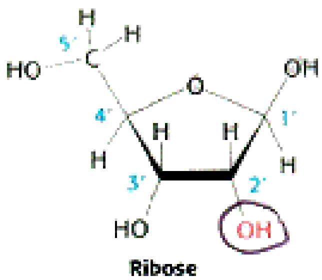
Difference between RNA and DNA is the Sugar + 1 Base

RNA is a string of nucleotides, just like DNA

Sugar: Pentose (5 membered ring)

= Ribose: ribonucleic acid (RNA)

= Deoxyribose (2' H)= deoxyribonucleic acid (DNA).

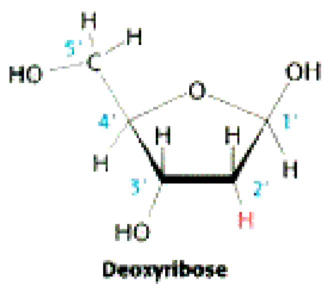


→ RNA → more diverse chemically + structurally

→ storage of info (short-term)

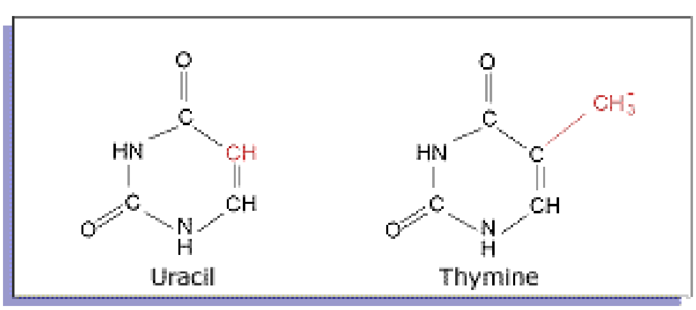
→ chemical rxns → ENZYME

→ Larger groove (than DNA)—more likely to be attacked by enzymes)



→ DNA is more chemically stable than RNA. Better for long-term high reliability storage of information

RNA substitutes Uracil for Thymidine

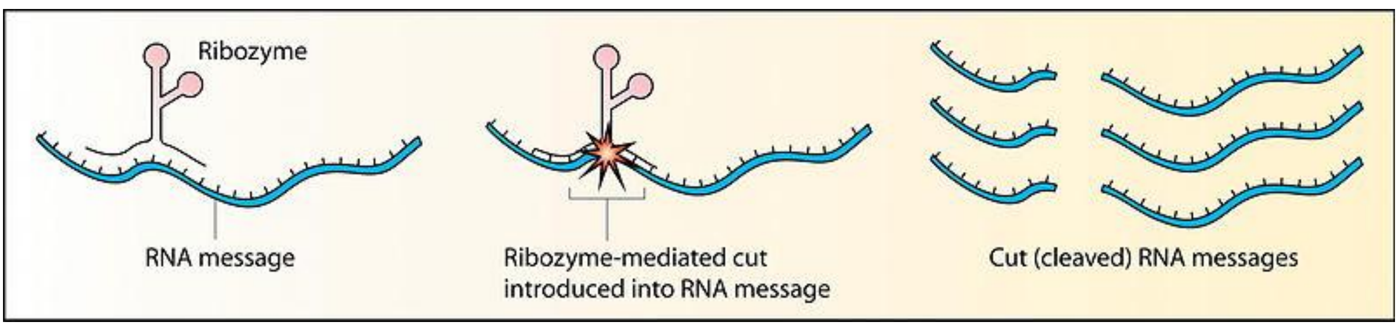


Uracil will base pair with many groups.
Methyl group restricts uracil (thymine) to pairing only with adenine.

This greatly improves the efficiency of DNA replication,
by reducing the rate of mismatches, and thus mutations

RNA can be it’s own enzyme!

RNA can be a **ribozyme** –a **ribo**nucleic acid and en**zyme**–is an RNA molecule with a well defined tertiary structure that enables it to catalyze a chemical reaction. It contains an active site made completely of RNA. Can cut either itself or another RNA.



http://en.wikipedia.org/wiki/Ribozyme

Used by nature! The ribosome, used to make proteins from RNA, is itself a ribozyme (involves RNA cutting by another RNA).
2009 Nobel Prize (Ramakrishnan, Cambridge; Steitz, Yale; Yonath; Weizmann)

RNA solves the chicken & egg problem

From Nobel Lecture

The discovery of catalytic properties in RNA also gives us a new insight into the way in which biological processes once began on this earth, billions of years ago. Researchers have wondered which were the first biological molecules. How could life begin if the DNA molecules of the genetic code can only be reproduced and deciphered with the aid of protein enzymes, and proteins can only be produced by means of genetic information from DNA? Which came first, the chicken or the egg? [Sid] Altman and [Tom] Cech have now found the missing link. Probably it was the RNA molecule that came first. This molecule has the properties needed by an original biomolecule, because it is capable of being both genetic code and enzyme at one and the same time.

Presentation Speech by Professor Bertil Andersson of the Royal Swedish Academy of Science, December 10, 1989

RNA can be catalytic!

Life probably started with RNA (not DNA)

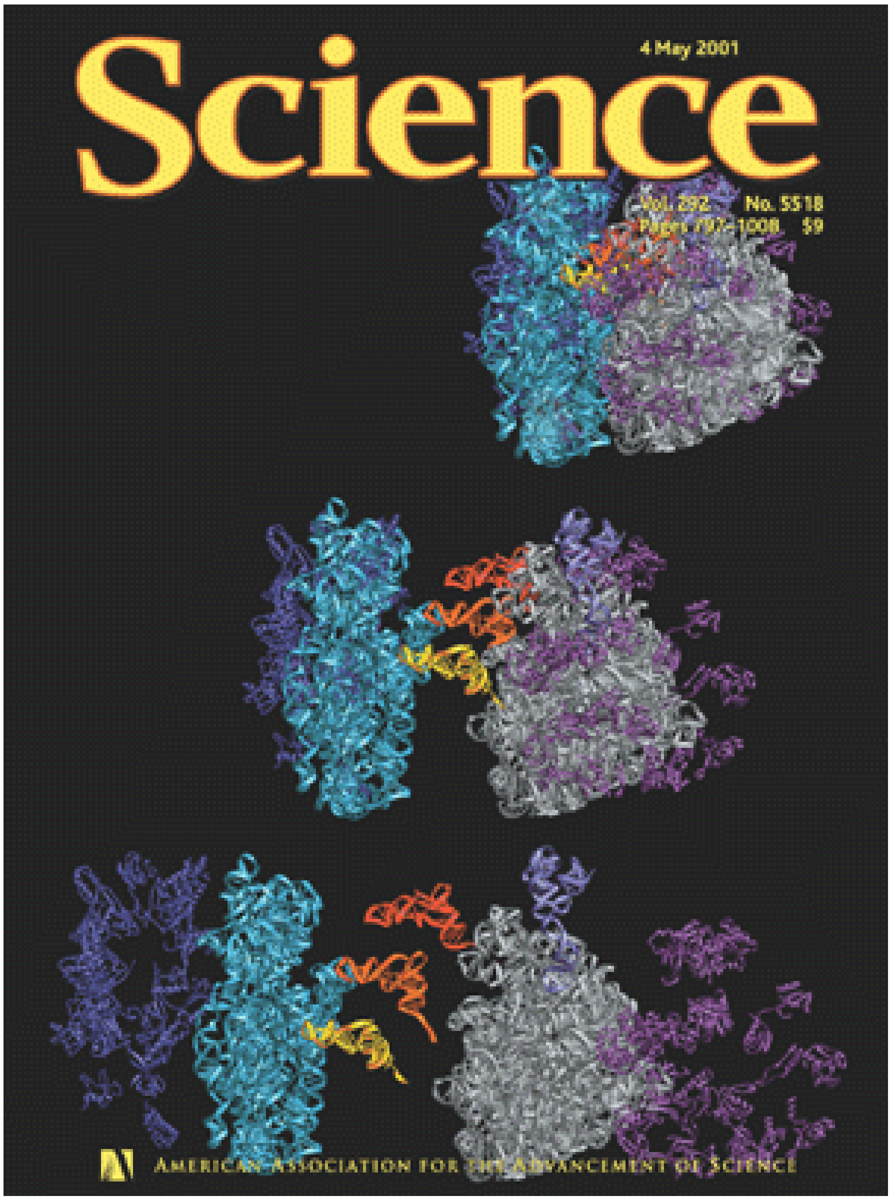
1989 Nobel Prize—Altman & Cech

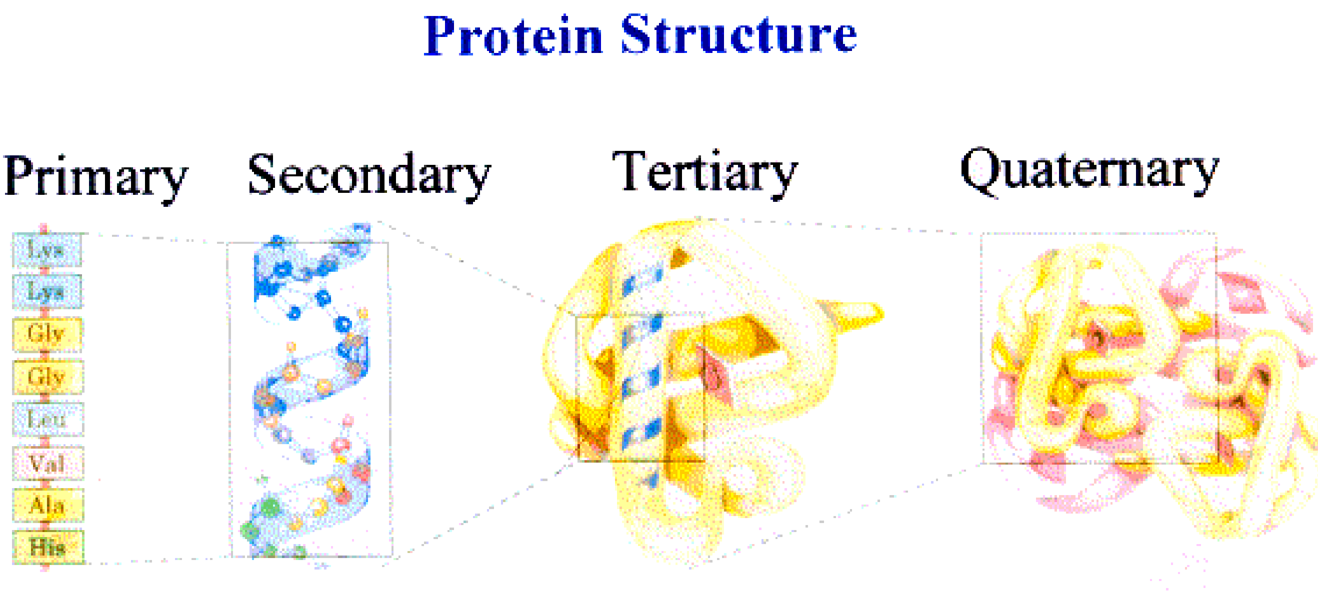
(1967 Carle Woese suggested RNA can be catalytic—won the equivalent of Nobel Prize)

It is now possible to make ribozymes that will specifically cleave any RNA molecule. These RNA catalysts may have pharmaceutical applications. For example, a ribozyme has been designed to cleave the RNA of HIV. If such a ribozyme was made by a cell, all incoming virus particles would have their RNA genome cleaved by the ribozyme, which would prevent infection.

Evidence that RNA have these properties?

The Ribosome is an RNA-based catalytic machine– Big surprise!





Primary = Linear sequence of ~ 20 amino acids
Secondary = local stable structural motifs
α-helix, β-sheet

Tertiary = 3-dimensional fold
(spatial arrangement of secondary structures)

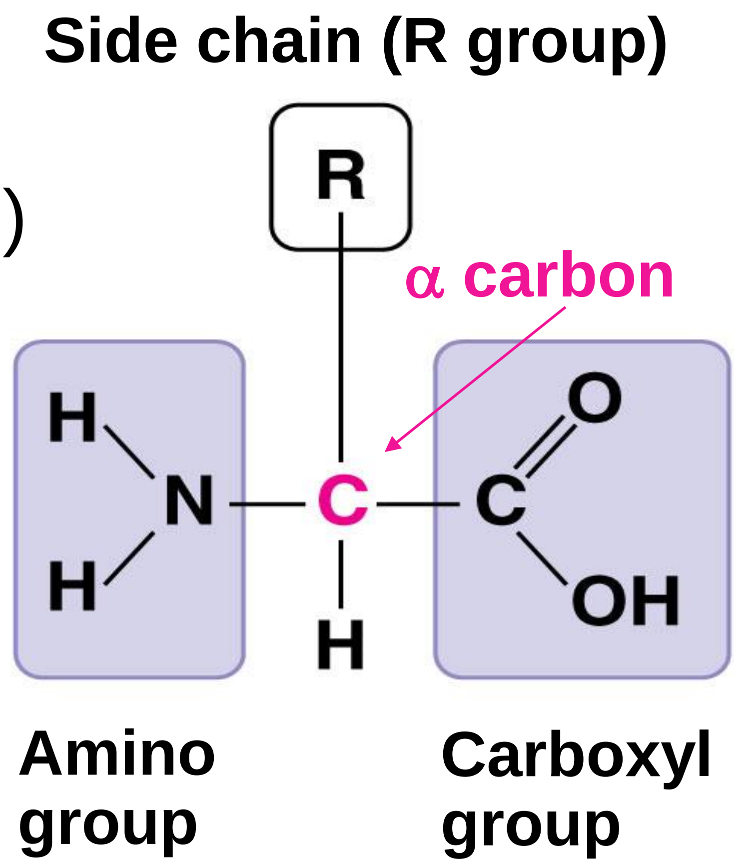
Quaternary = spatial arrangements of multiple (if present) polypeptides to make a protein.

Can get enormous diversity and function with Proteins

Figure 5.UN01

Amino Acid Structure

(110 g/mole)

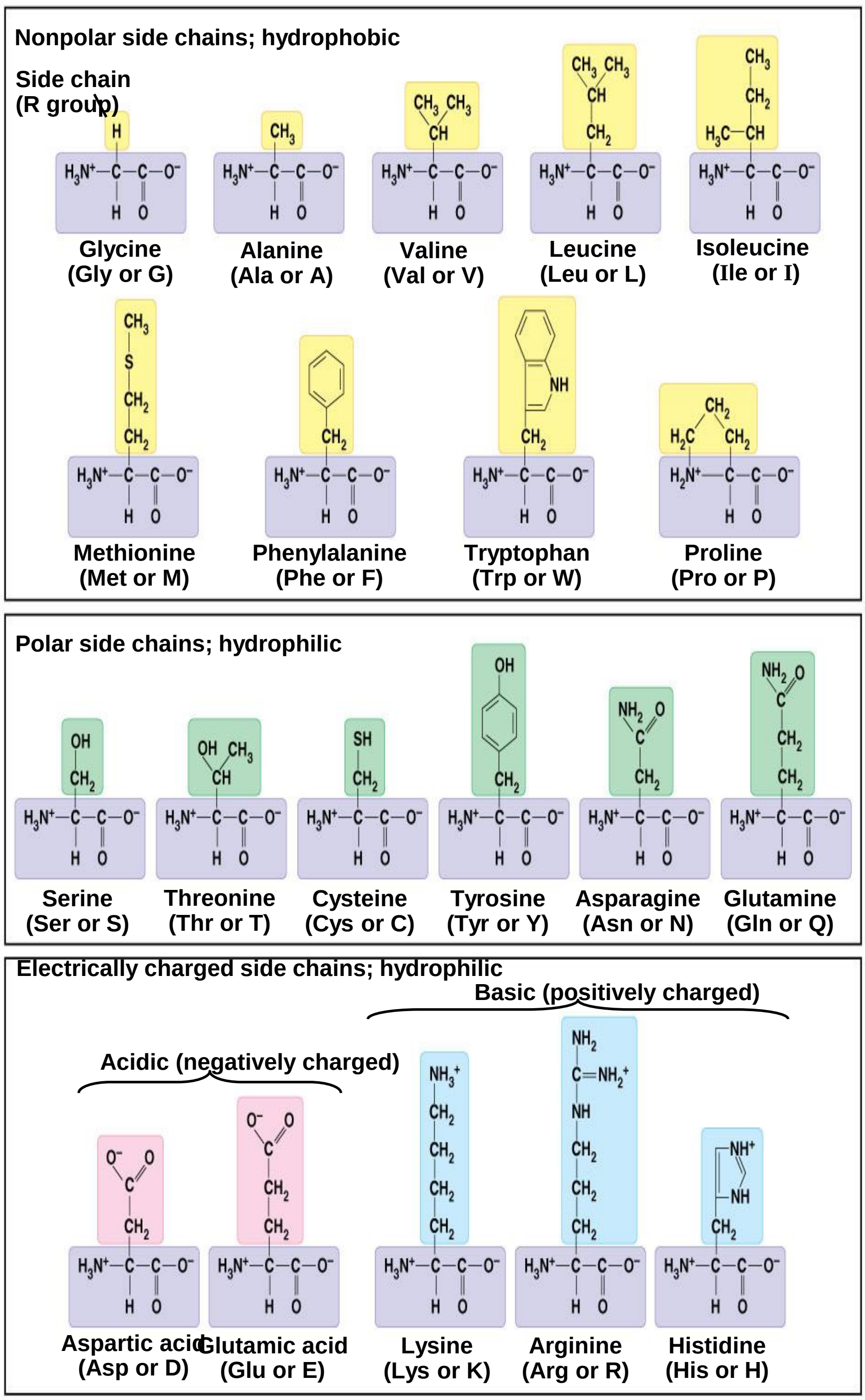


20 different R groups

Hydrophobic (non-polar; greasy)
Hydrophilic (polar; non-greasy)
Charge: positive, neutral, negatively

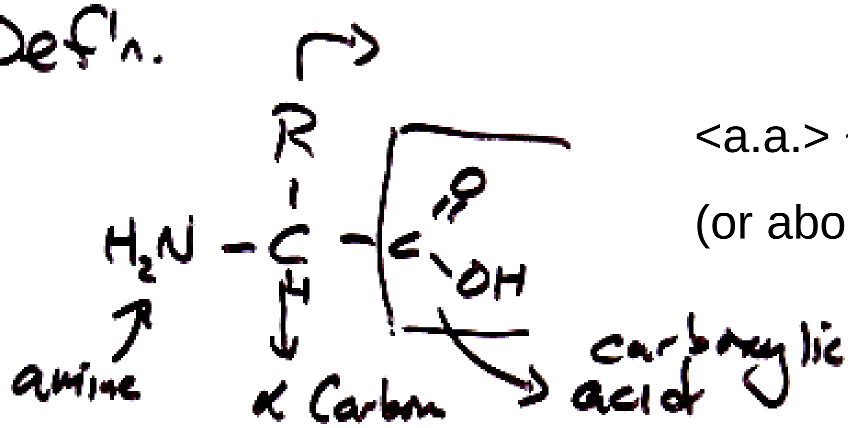
Figure 5.16

Amino Acid Structure—20 Diff. R



Amino acids

Def'n.



<a.a.> ~110 grams/mole

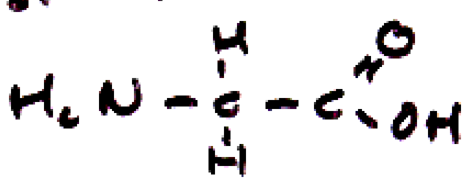
(or about 100g/mole)

R - general designation for some organic structure

= side group.

20 diff. type of a.a.
" " R groups.

Simplest R = H



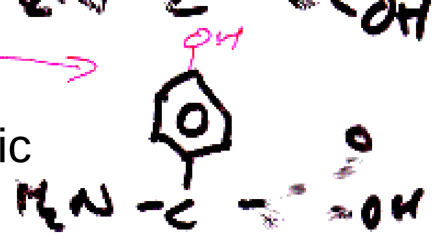
glycine

hydrophilic

alanine

Tyrosine →

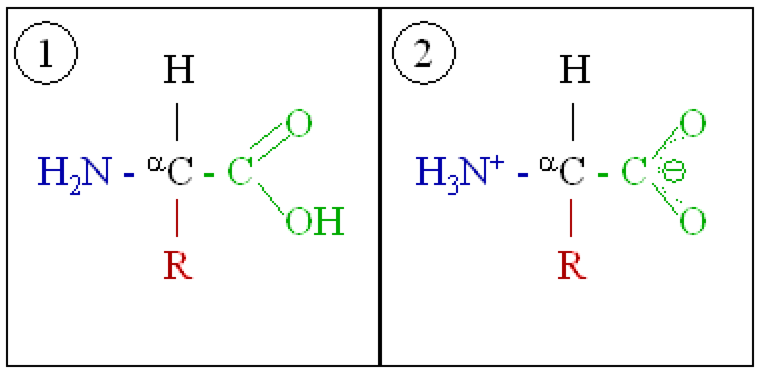
Fairly hydrophilic

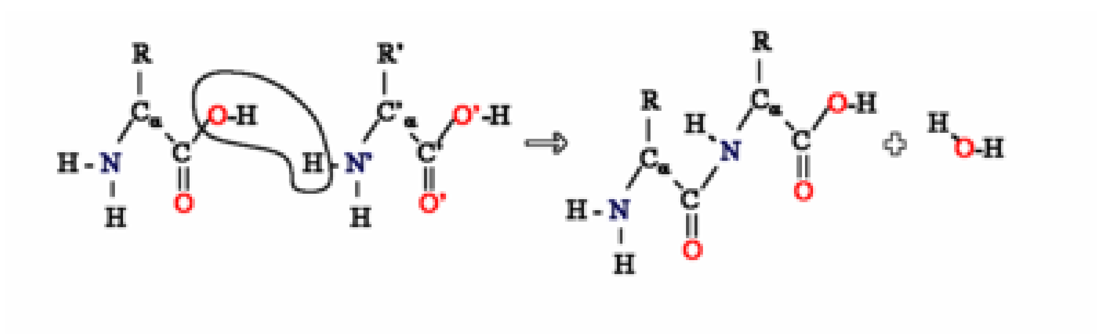


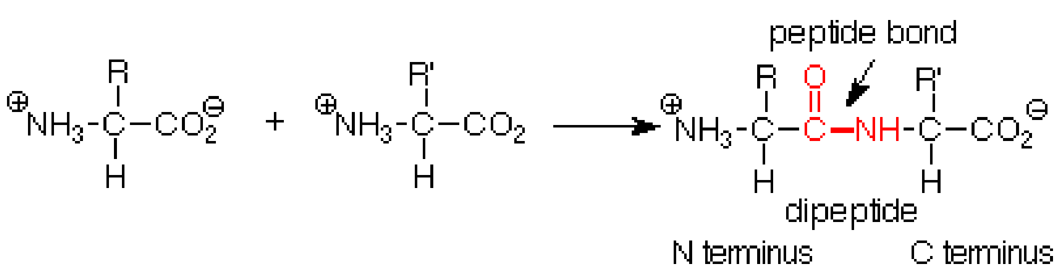
phenylalanine

Hydrophobic

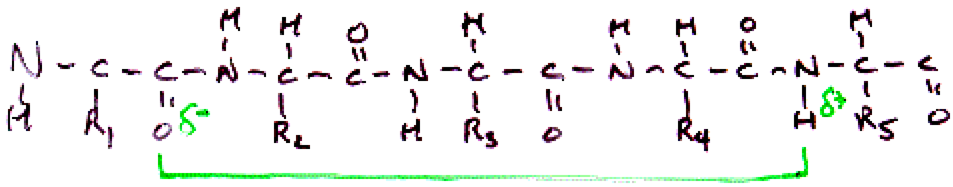
Amino Acids undergo condensation reaction to form peptides







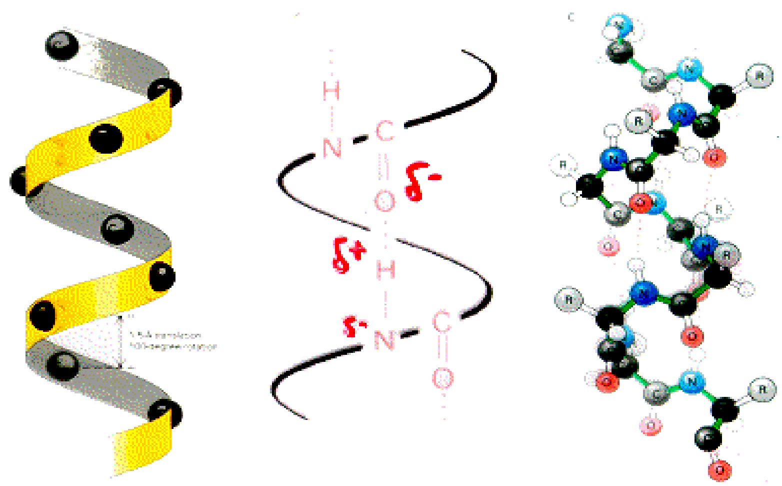
Secondary Structure
α-helix, β-sheets



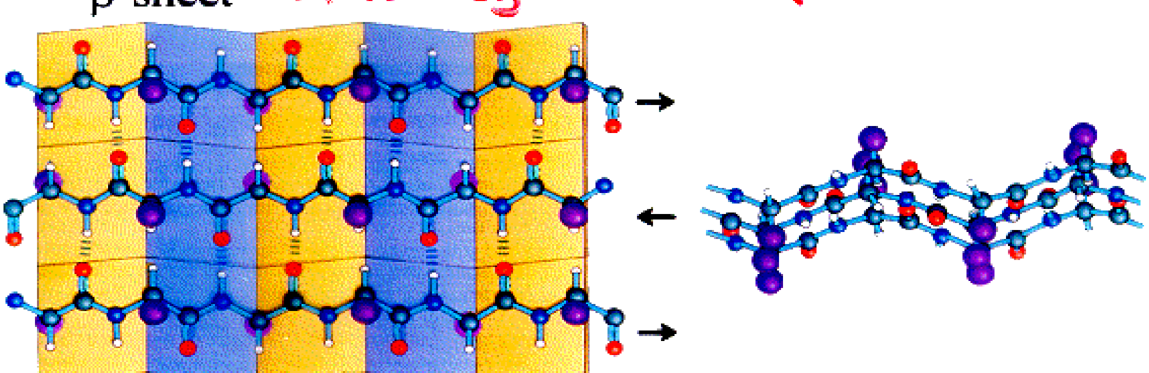
C=O of one a.a. can H-bond to NH gray of a.a. 4 a.a. away.

Stabilized by H-bond (about 2 H bond per a.a.)

α-helix



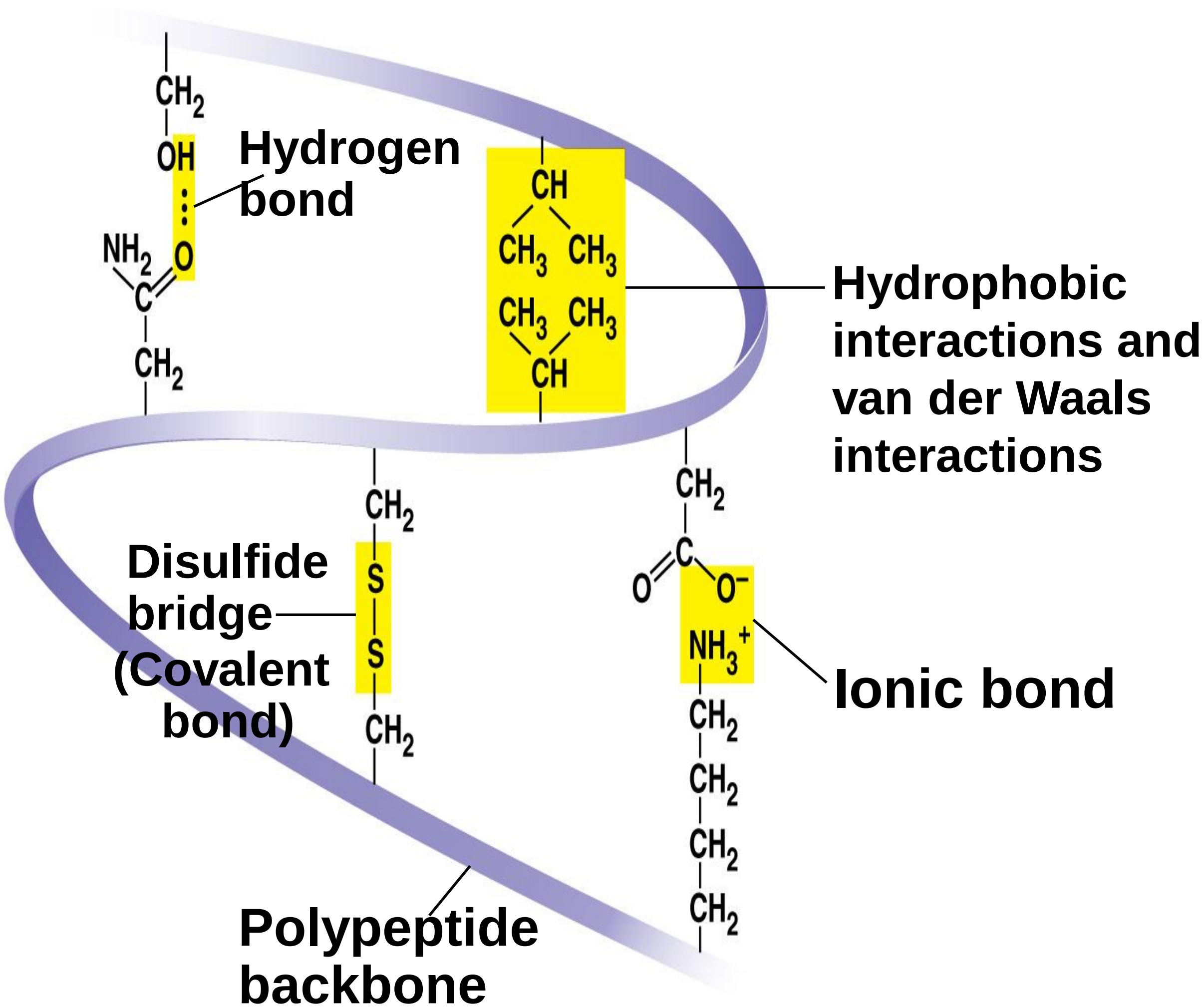
β-sheet - stab. by H-bonds.



α-helix, β-sheets depends on specific amino acids

- **Tertiary structure** is determined by interactions between R groups, rather than interactions between backbone constituents
- These interactions between R groups include hydrogen bonds, ionic bonds, **hydrophobic interactions**, and van der Waals interactions
- Strong covalent bonds called **disulfide bridges** may reinforce the protein’s structure

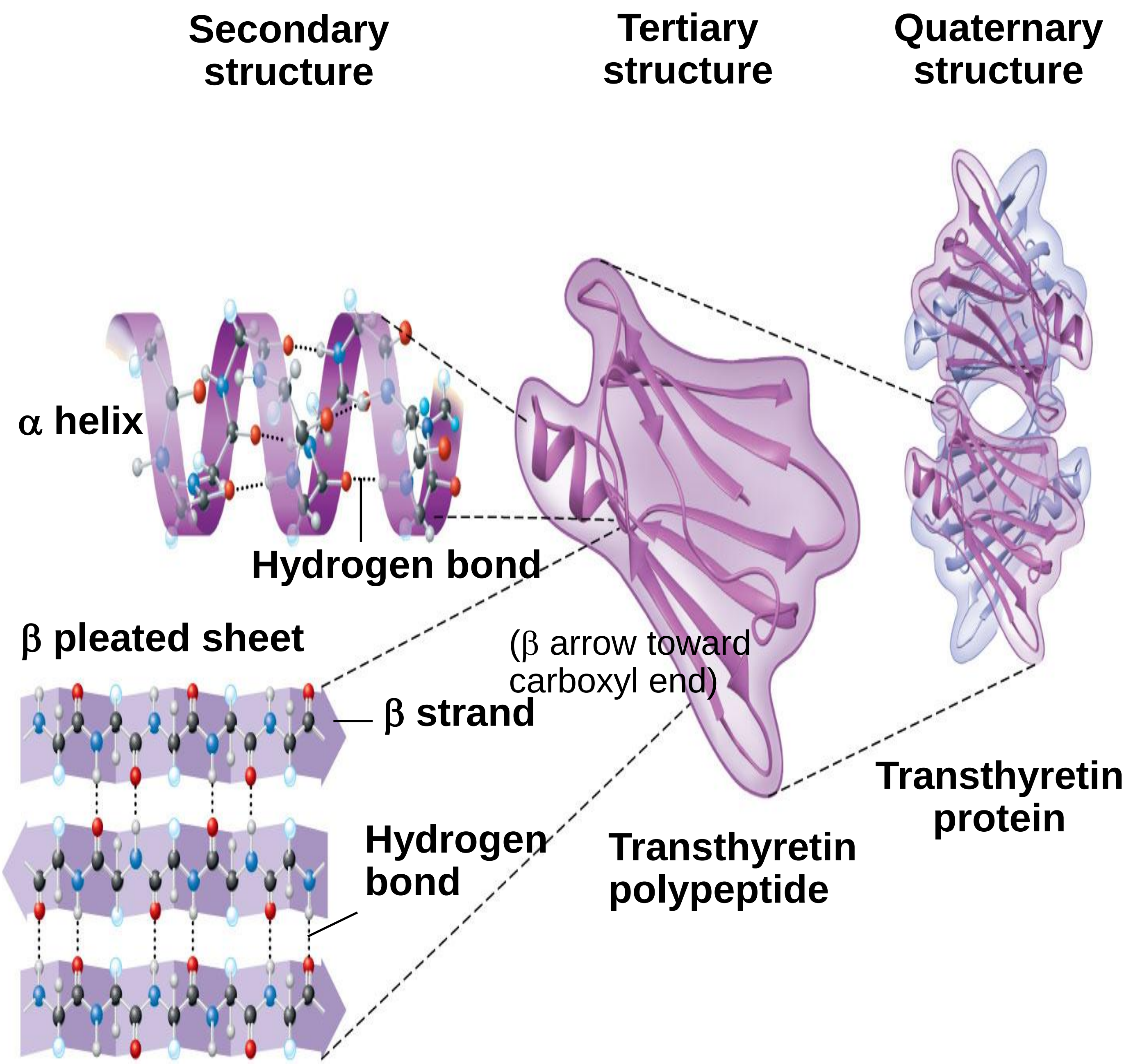
Figure 5.20f



(Not gone over in lecture but presented here.)

Figure 5.20b

4 Different layers of Protein Structure



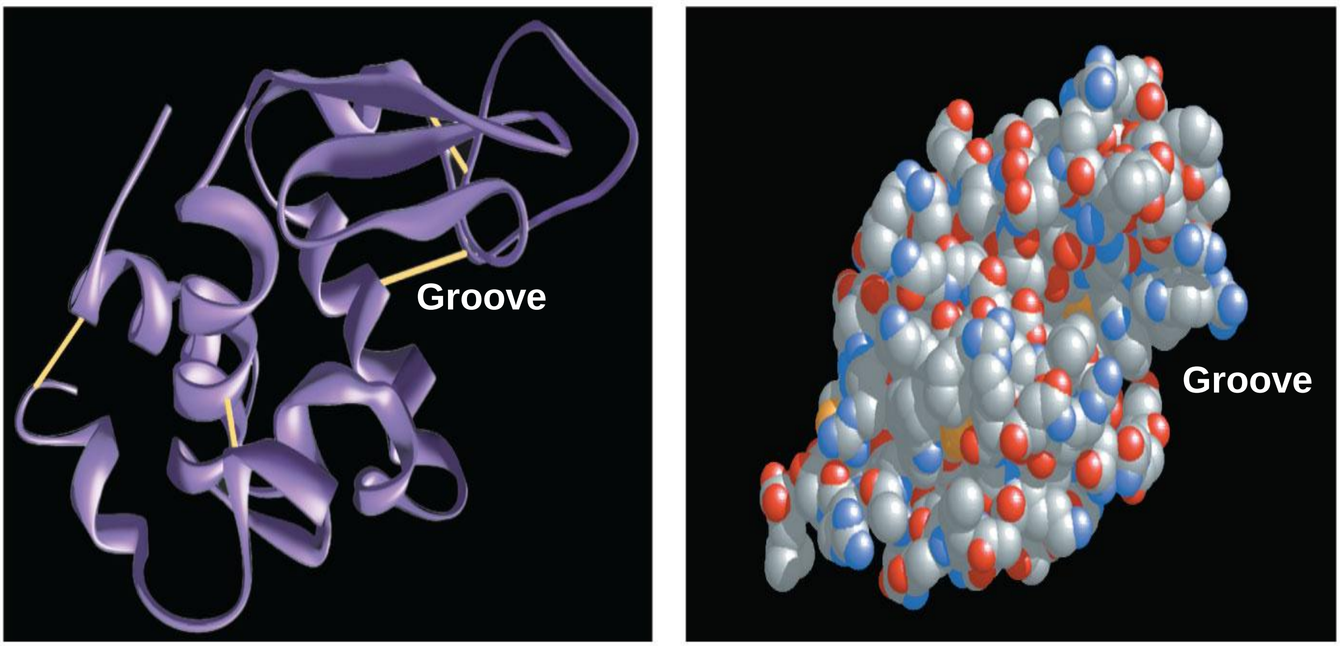
Size of proteins

10kD to 100kD to over a million

Recall aa = 110 D…say 100D
10kD=100aa

(Antibodies-100-250kD)

Figure 5.18



(a) A ribbon model

(b) A space-filling model

Protein Structure and Function

- A functional protein consists of one or more polypeptides precisely twisted, folded, and coiled into a unique shape

- The sequence of amino acids determines a protein’s three-dimensional structure
- A protein’s structure determines its function

Figure 5.19

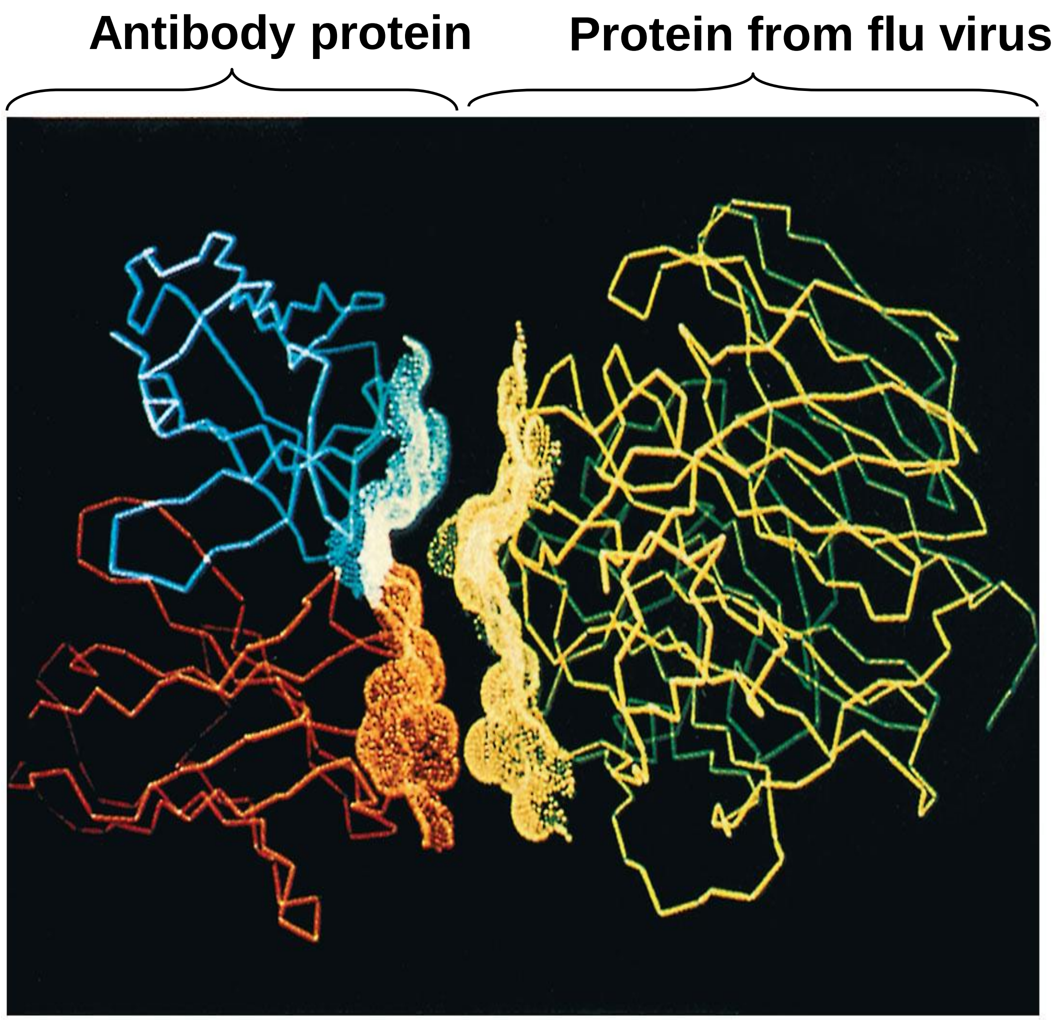


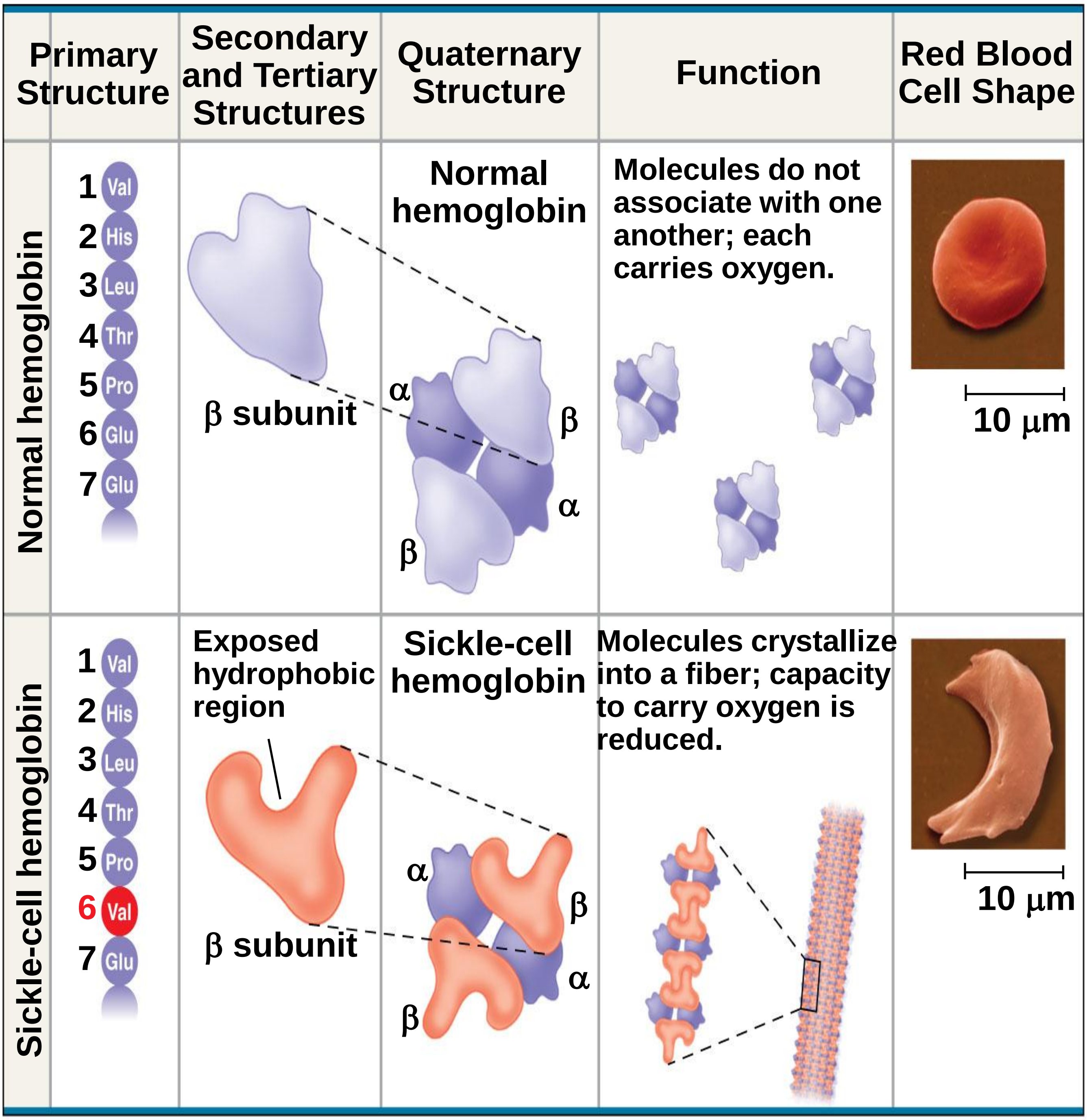
Figure 5.20d

Sickle-Cell Disease: A Change in Primary Structure

- A slight change in primary structure can affect a protein's structure and ability to function
- **Sickle-cell disease**, an inherited blood disorder, results from a single amino acid substitution in the protein hemoglobin

Figure 5.21

Sickle Cell Anemia



Why does sickle cell anemia still exist?

It is clearly disadvantageous to have disease; make probability of reproducing less likely.

Recall you're diploid—have two copies of each gene.

If have both SS, then you have anemia.

If both genes unmutated: "normal".

If heterozygote, (one "good", one "bad") then have certain advantages.

If mother/father have SS and NN, probability of kid having SS? NN? SN?

Advantage: More resistant to malaria.

Evaluate class

1. What was the most interesting thing you learned in class today?
2. What are you confused about?
3. Related to today's subject, what would you like to know more about?
4. Any helpful comments.

Put your name in upper right-corner.

Then tear off your name before turning in.
(That way you can be brutally honest!)

Answer, and turn in at the end of class.

(I'll give you ~5 minutes.)