Large Organic "Macro"molecules

Proteins; DNA; RNA

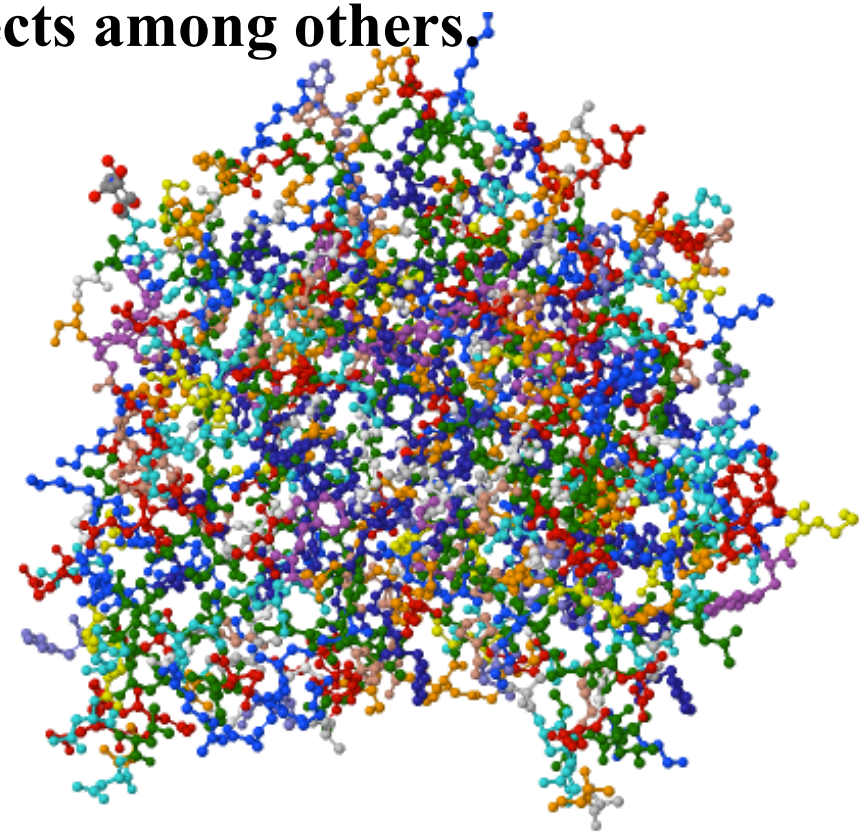
Biological Polymers

https://www.youtube.com/watch?v=JQZQiEdOPJY

Proteins: Macromolecular Biopolymers

Acetylcholinesterase (ACE)

***ACE*, an enzyme, which catalyzes a key reaction in a repetitive biochemical cycle that is crucial to neurological and physiological functions in humans…. and insects among others.**



4,496 atoms;
4,404 bonds
574 amino acid residues

Proteins & Small Molecules

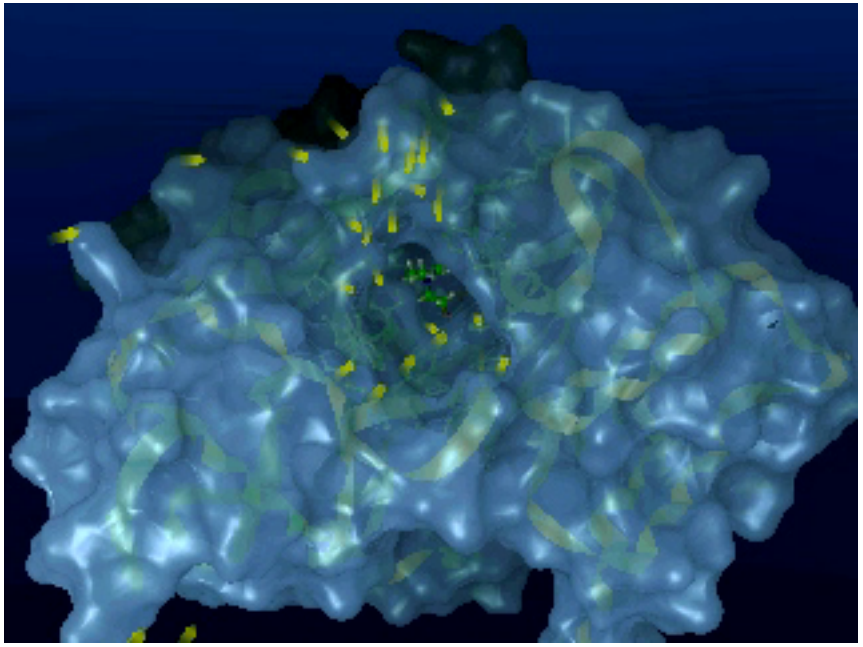
Acetylcholinesterase

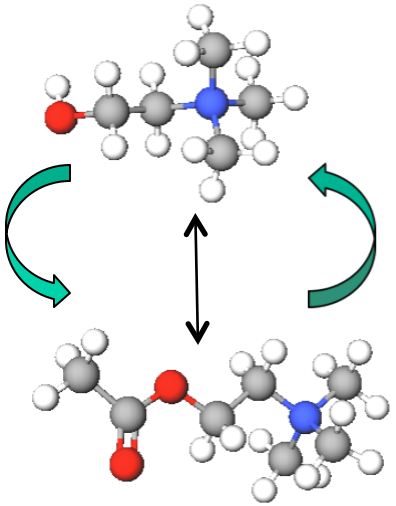
The normal interaction of acetylcholinesterase with the neurotransmitter choline is a general, reversible process that is similar to the way we smell. It relates to many physiological and pharmacological processes, which can be enhanced or inhibited chemically .

Japan
(1995)

Syria
(2013-2018)

Great Britain
(2018)

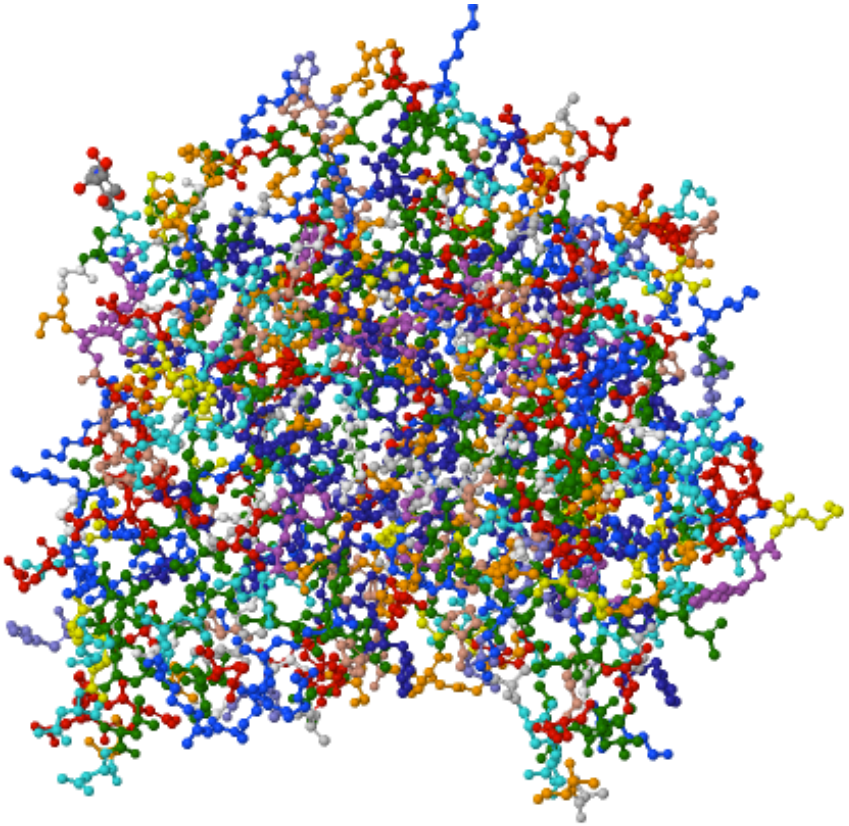


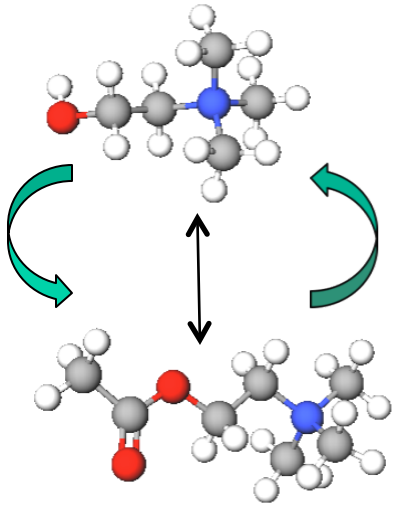


http://chemconnections.org/general/movies/richard.mpg

Chemical Weapons of Mass Destruction

Target: Acetylcholinesterase





Attacks:

Japan
(1995)

Syria
(2013-2018)

Great Britain
(2018)

http://chemconnections.org/general/movies/richard.mpg

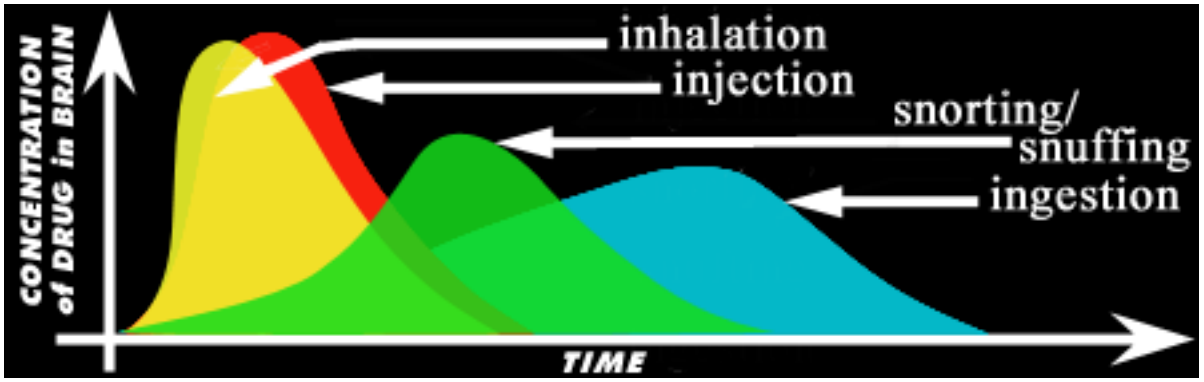
Chemical Weapons of Mass Destruction

Target: Acetylcholinesterase

Chemical Uptake:

,Rank the following 4 possible routes of entry into the bloodstream from slowest to fastest.

a) injection; b) ingestion; c) inhalation; d) nasal "snorting"



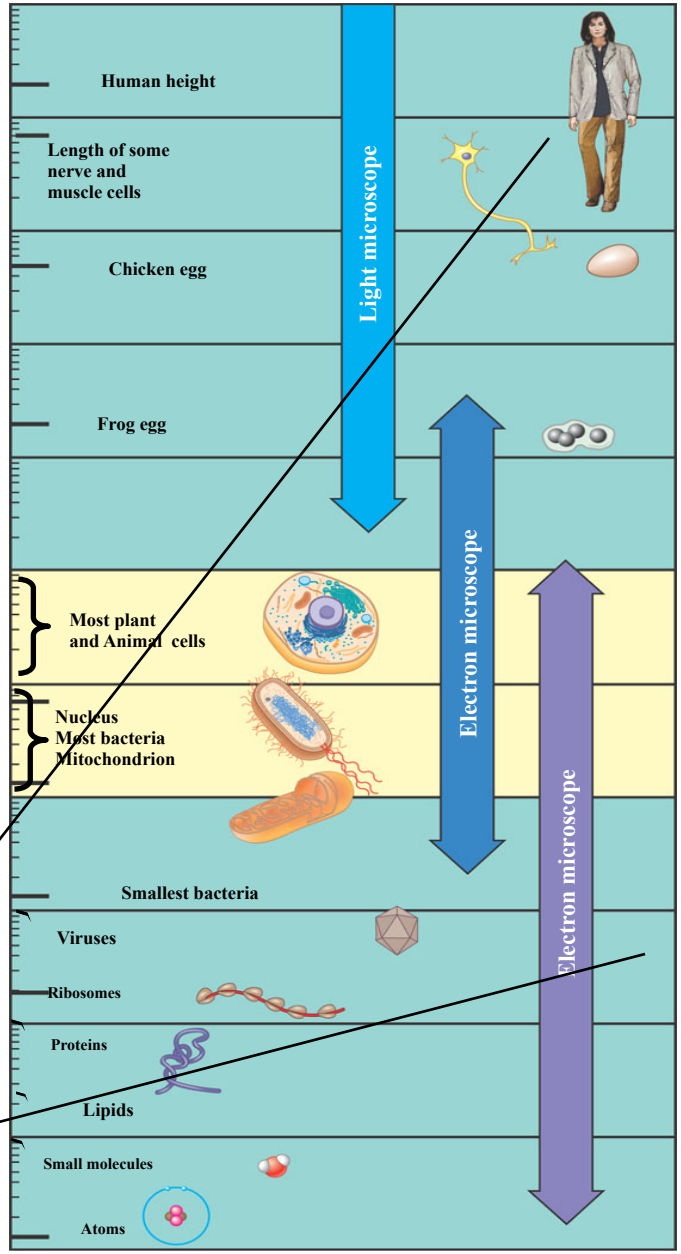
A) a<b<c<d **B) c<a<d<b**

C) b<d<a<c **D) d<b<c<a**

Connections

10^{+18}	exa
10^{+15}	peta
10^{+12}	tera
10^{+9}	giga
10^{+6}	mega
10^{+3}	kilo
10^{0}	
10^{-3}	milli
10^{-6}	micro
10^{-9}	nano
10^{-12}	pico
10^{-15}	femto
10^{-18}	atto

Powers of Ten



Organic Molecules

millions

← **You**

Bones? **206 bones**

Organs? **78 organs**

↓

Cells

# of cells? **~5 x 10^{13} cells**

↓ *moles of cells?*

~22,000

Proteins / DNA

3 x 10^{9} bases

(Genome)

Measurements

1 centimeter (cm) = 10^{-2} meter (m) = 0.4 inch

1 millimeter (mm) = 10^{-3} m

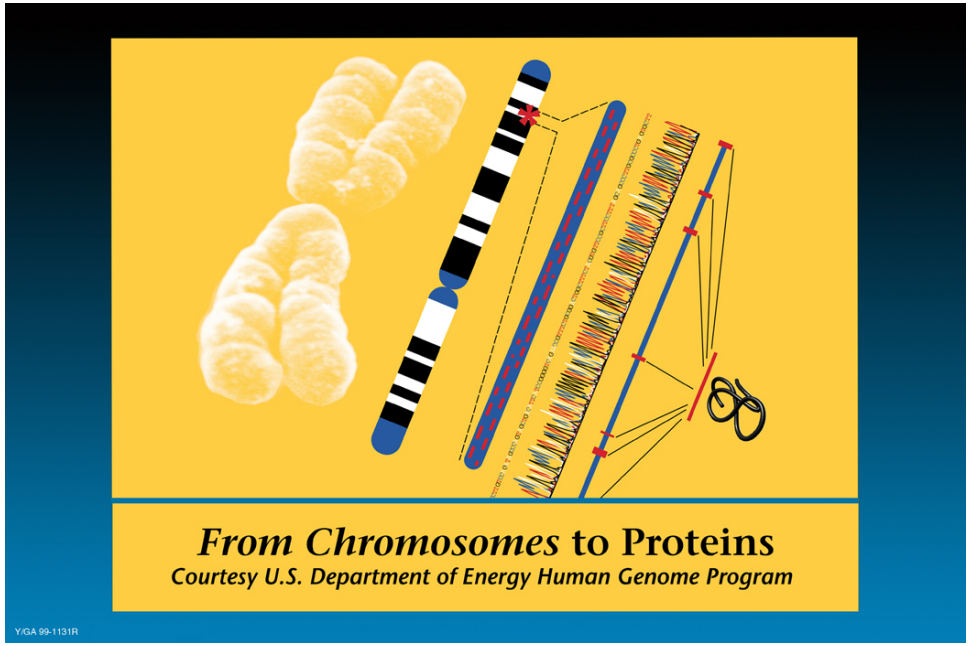
1 micrometer (µm) = 10^{-3} mm = 10^{-6} m

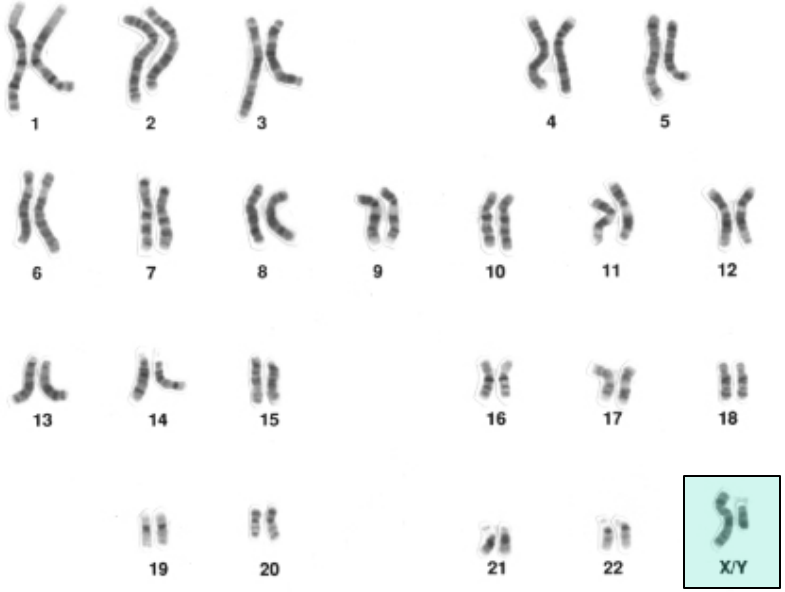
1 nanometer (nm) = 10^{-3} mm = 10^{-9} m

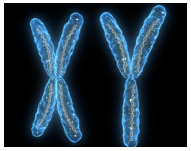
Genetic Controls

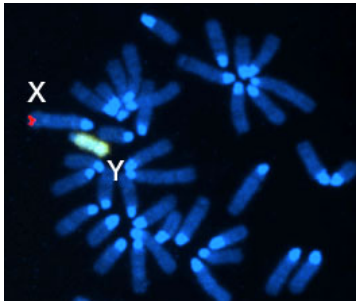
Chromosomes (DNA/RNA)

https://ghr.nlm.nih.gov/primer/basics/howmanychromosomes





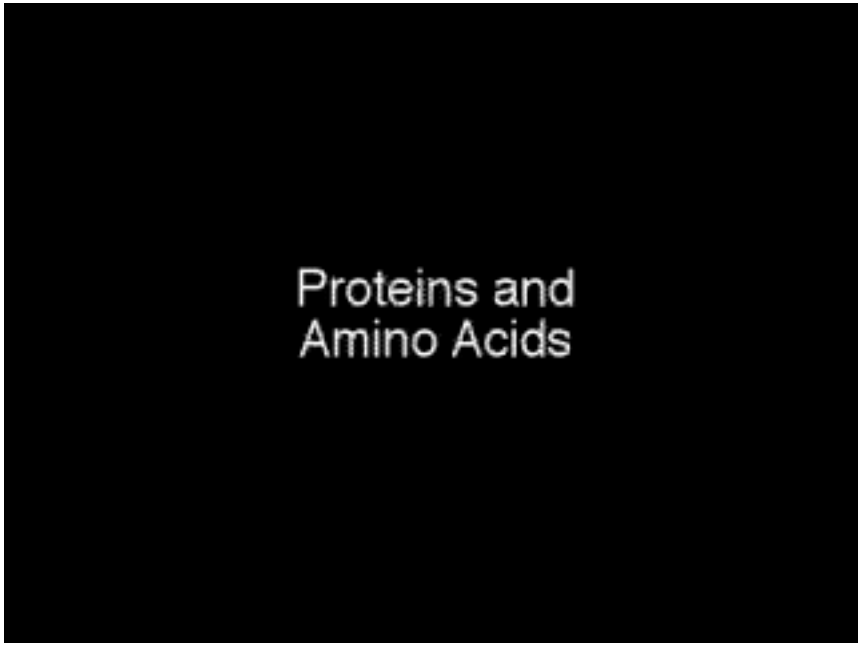


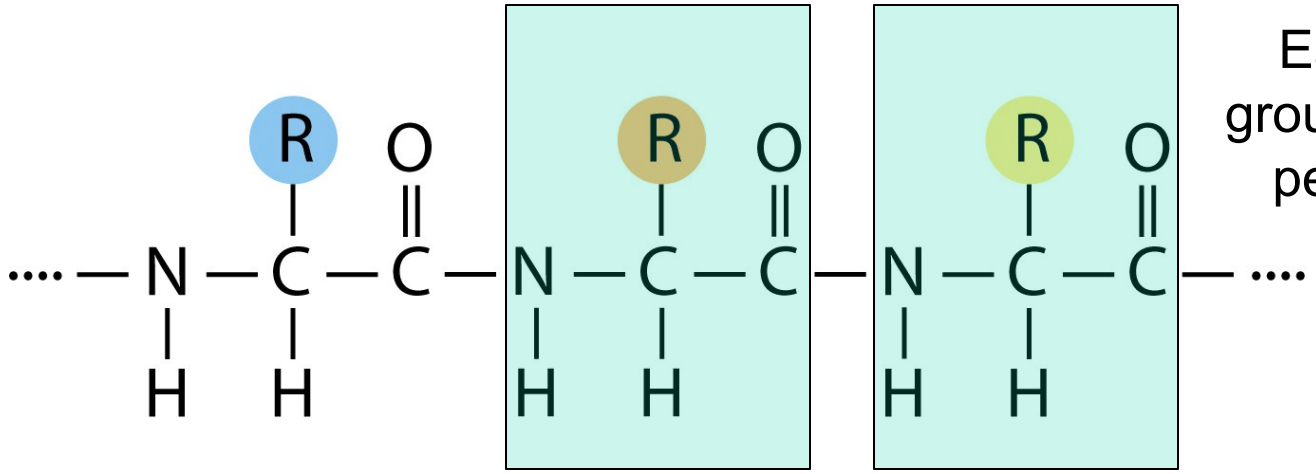


Male or female?

Amino Acids & Proteins

http://chemconnections.org/general/movies/Proteins-amino-acids.mov



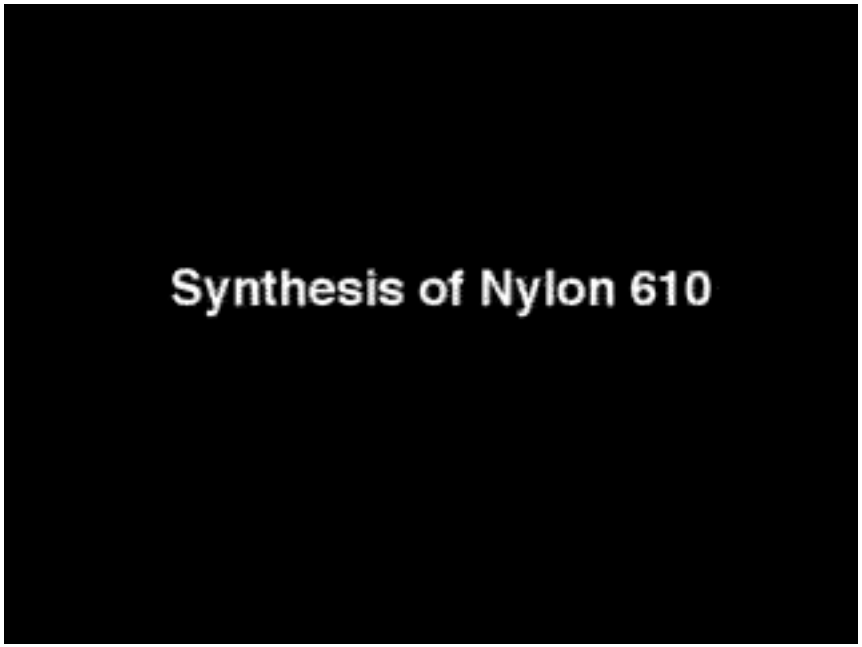


Each amide group is called a peptide bond

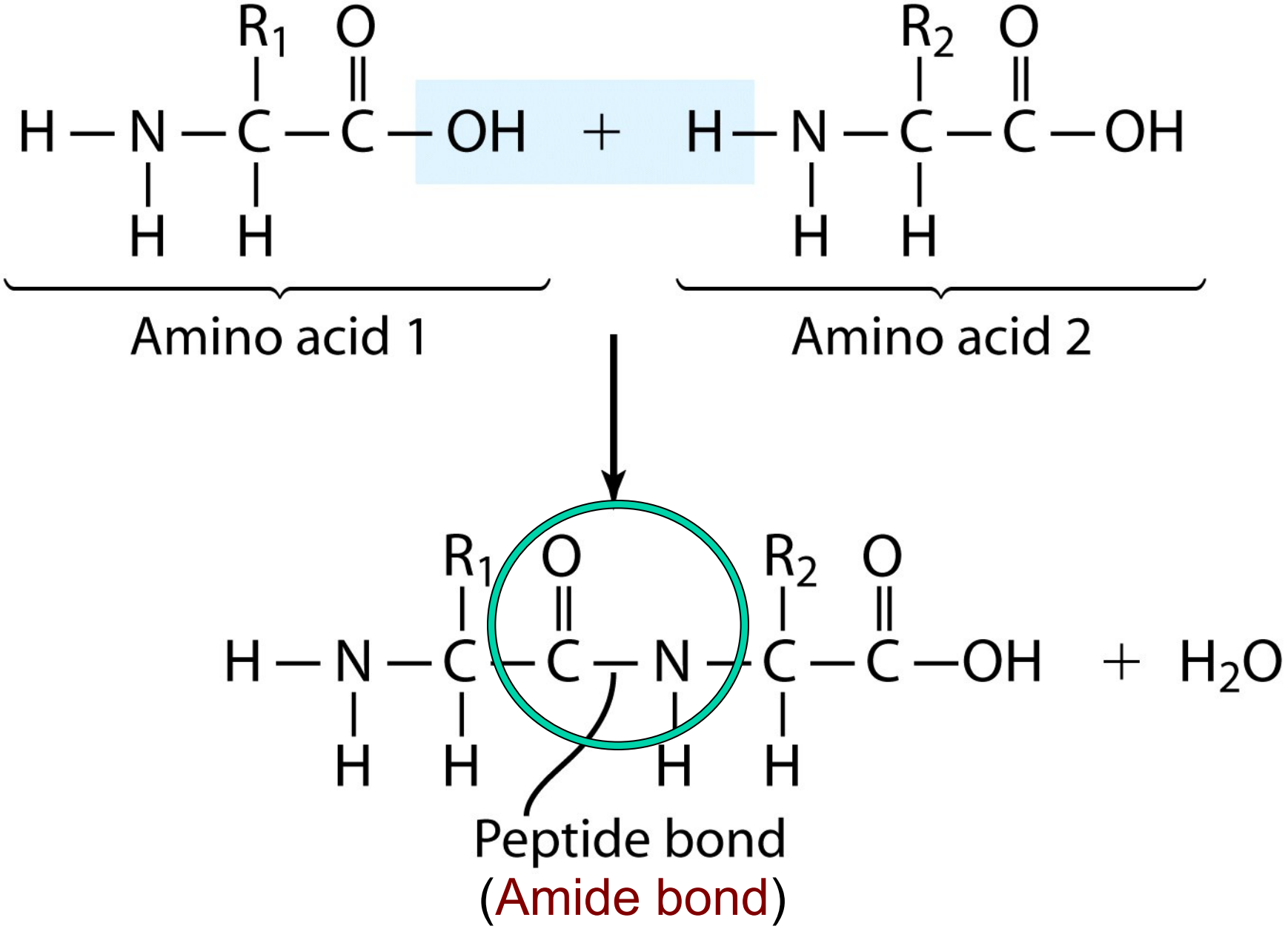
Proteins (bio-polymers):

Polypeptides, Amides and Proteins

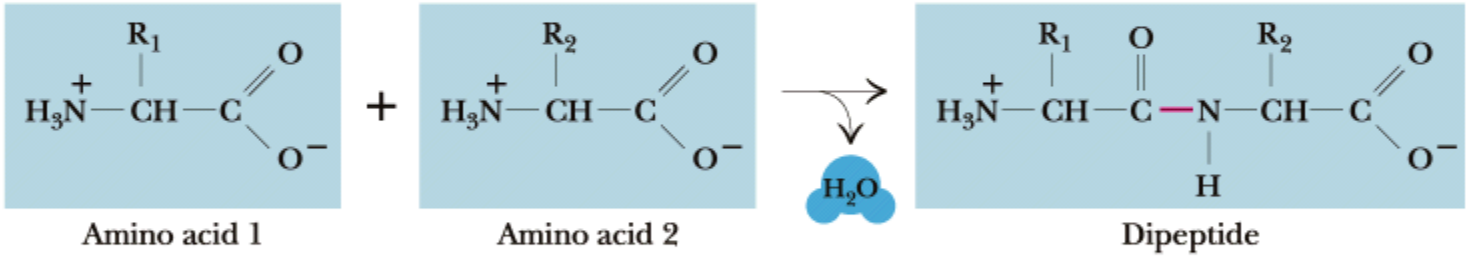
- **Proteins are polyamides, each amide group is called a peptide bond. (Nylon is a synthetic poly-amide)**



- **Peptides are formed by condensation of the -COOH group of one amino acid and the $-NH_2$ group of another amino acid.**


R1
O
H — N — C — C — OH
H
H
+
R2
O
H — N — C — C — OH
H
H
Amino acid 1
Amino acid 2
R1
O
R2
O
H — N — C — C — N — C — C — OH
H
H
H
H
+ H2O
Peptide bond
(Amide bond)

Proteins are Polymers of Amino Acids

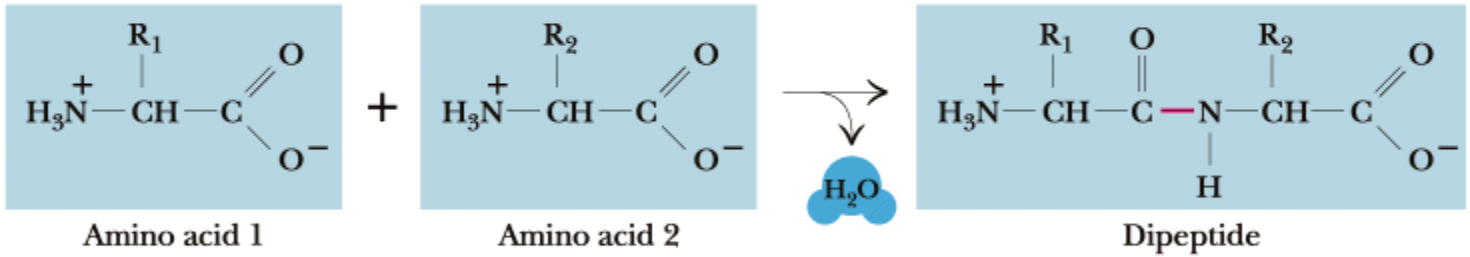


- **Peptides have various numbers of amino acids.**
- **Peptides are always written with the -NH_2 terminus on the left, -CO_2H on the right.**
- **Each amino acid unit is called a residue.**
- **2 residues = dipeptide,**
- **3 residues = tripeptide,**
- **12-20 residues = oligopeptide,**
- **Many residues = polypeptide.**

QUESTION

Proteins are made when amino acids form peptide bonds to link together. Which of the following contains the correct number and type of atoms that are necessary to define a peptide bond?

A. One carbon, two oxygen, one nitrogen
B. Two carbons, one oxygen, one nitrogen, one hydrogen
C. One carbon, two oxygen, one nitrogen, two hydrogen
D. One carbon, one oxygen, one nitrogen, one hydrogen



Proteins (Polypeptides)

Polypeptides

- **Polypeptides are formed with a large number of amino acids (usually resulting in proteins with molecular weights between 6000 and 50 million amu).**

Protein Structure

- **Primary structure is the sequence of the amino acids in the protein.**
- **A change in one amino acid can alter the biochemical behavior of the protein. *Eg. Sickle Cell Anemia***

Four Levels of Protein Structure

- **1º : (Primary) The linear sequence of amino acids and disulfide bonds. eg. ARDV:Ala·Arg·Asp·Val.**
- **2º : (Secondary) Local structures which include, folds, turns, ∝-helices and β -sheets held in place by hydrogen bonds. eg. hair curls, silk, denaturing egg albumin**
- **3º : (Tertiary) *3-D* arrangement of all atoms in a single polypeptide chain. eg. collagen**
- **4º : (Quaternary) Arrangement of polypeptide chains into a functional protein, eg. hemoglobin.**

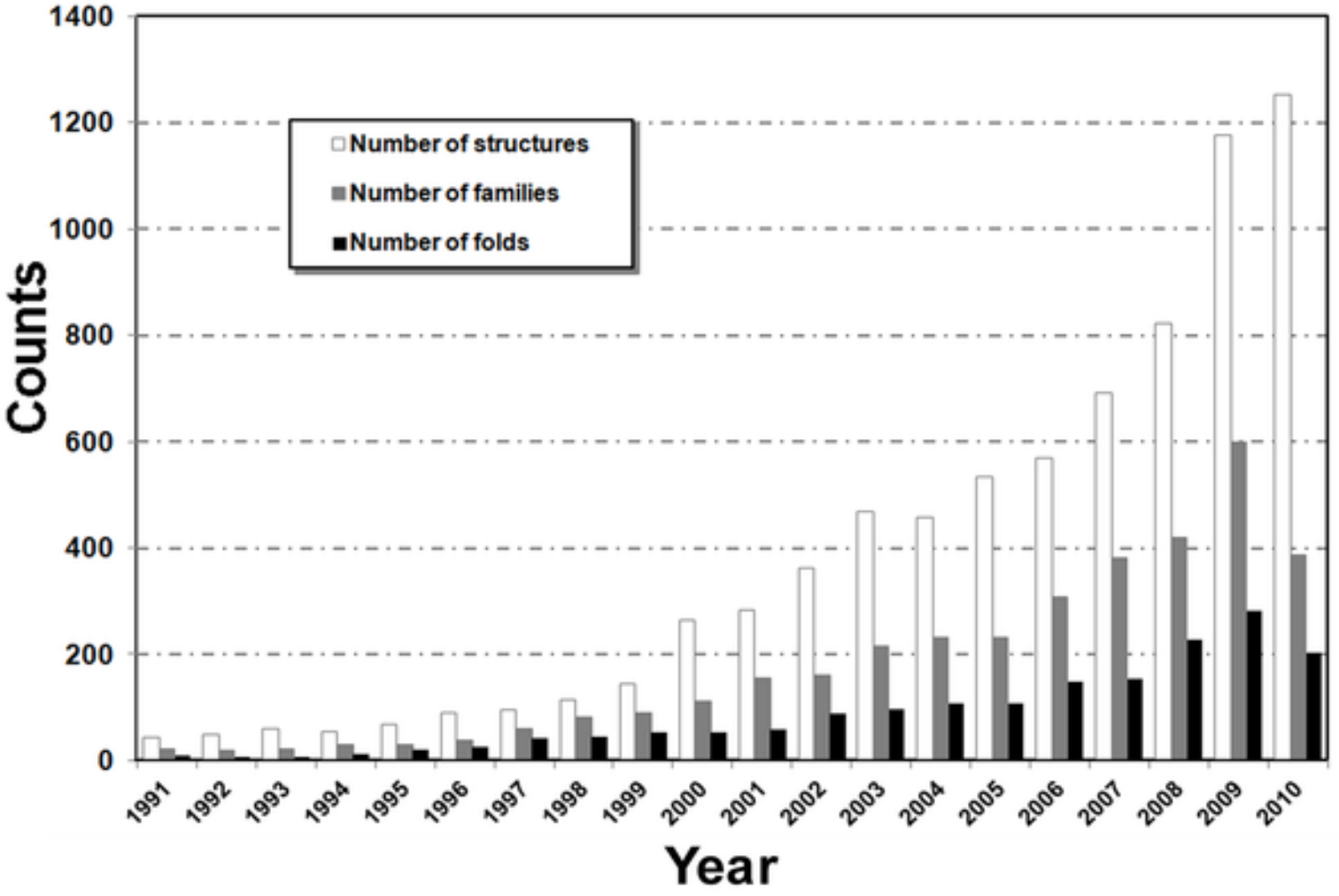
Different Protein Types -

- **Enzymes**: ***Glutamine synthetase*** **- 12 subunits of 468 residues each; total mol. wt. = 600,000 daltons**
- **Regulatory proteins**: ***Insulin*** **- α -alpha chain of 21 residues, β - beta chain of 30 residues; total mol. wt. of 5,733 amu**
- **Structural proteins**: ***Collagen***

  Connectin proteins**, β - MW of 2.1 million g/mol; length = 1000 nm; can stretch to 3000 nm.**
- **Transport proteins**: ***Hemoglobin***
- **Contractile proteins**: ***Actin, Myosin***
- **Specialized proteins**: ***Antifreeze in fish***

A gene was first defined as: one piece of DNA that codes for one protein. (The definition is being expanded beyond proteins to include certain types of RNA.)

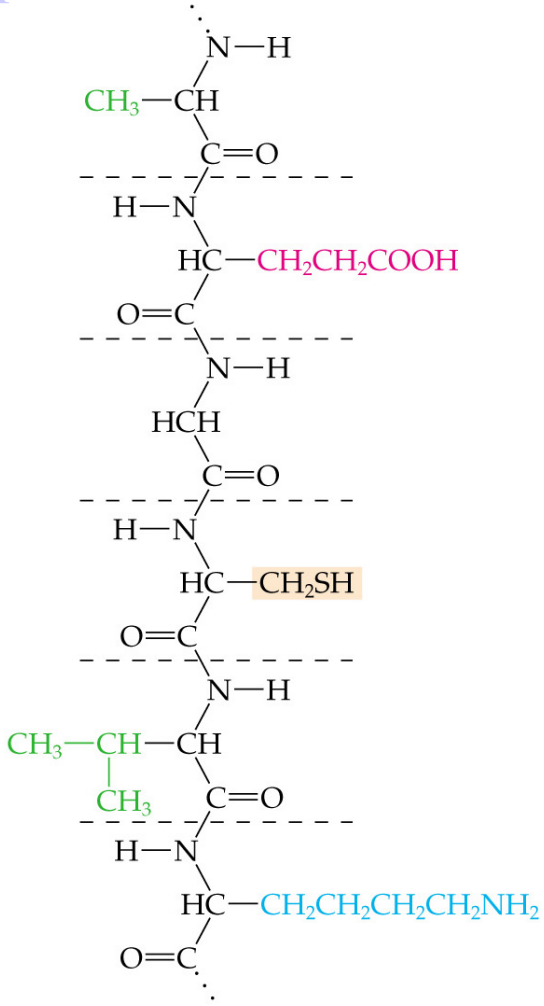
Figure 4. The number of new complex structure entries deposited per year in the PDB.



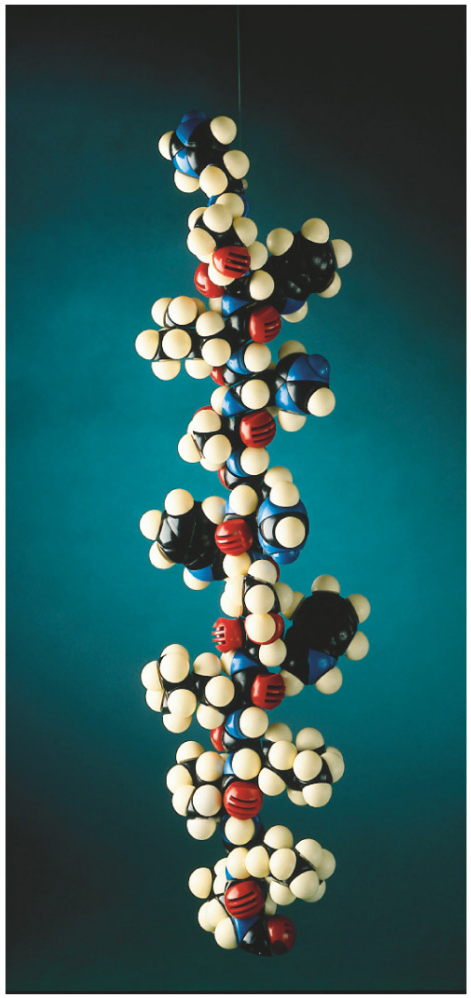
Garma L, Mukherjee S, Mitra P, Zhang Y (2012) How Many Protein-Protein Interactions Types Exist in Nature?. PLOS ONE 7(6): e38913. https://doi.org/10.1371/journal.pone.0038913
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0038913

Proteins: Size, Shape & Self Assembly

http://www.stark.kent.edu/~cearley/PChem/protein/protein.htm



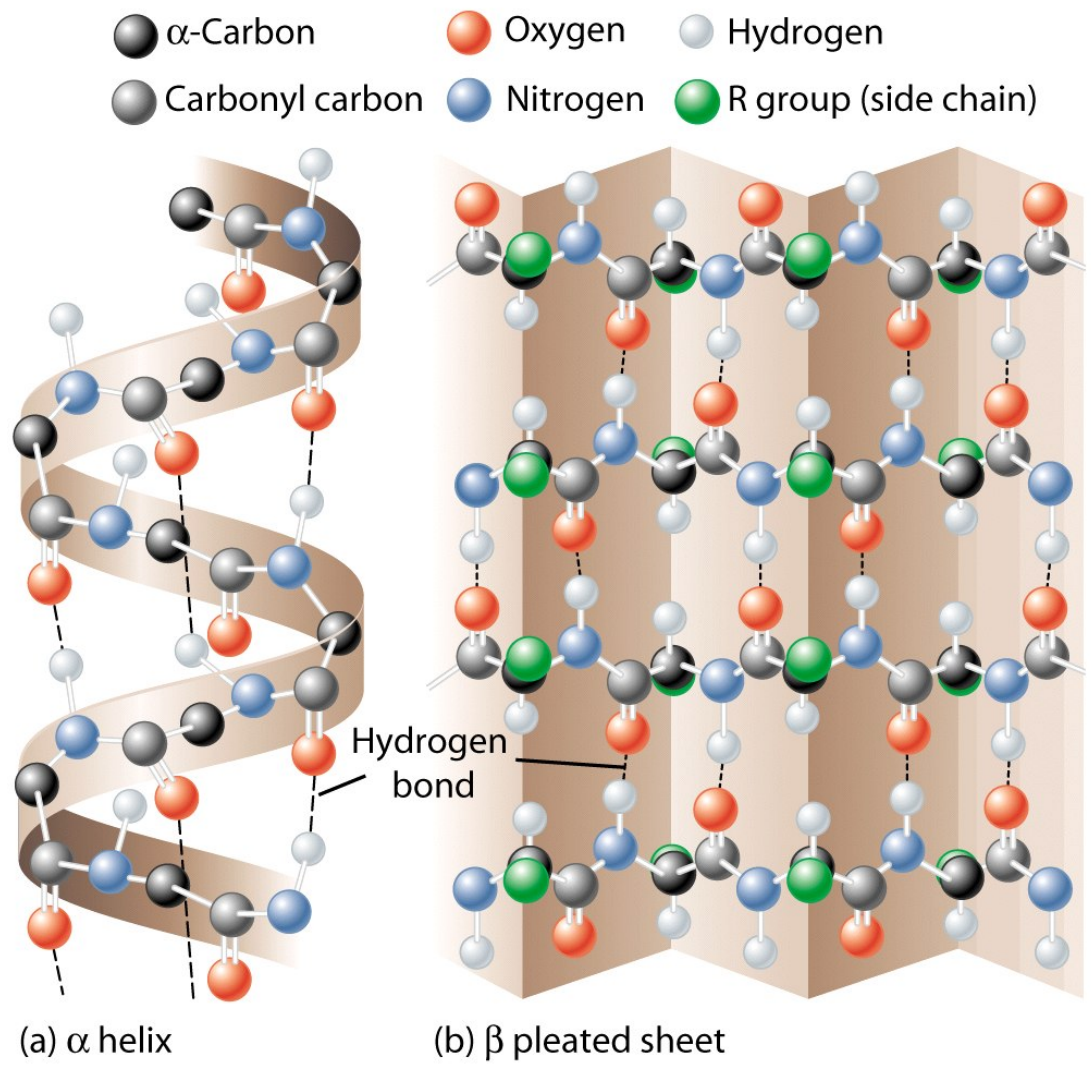
(a)



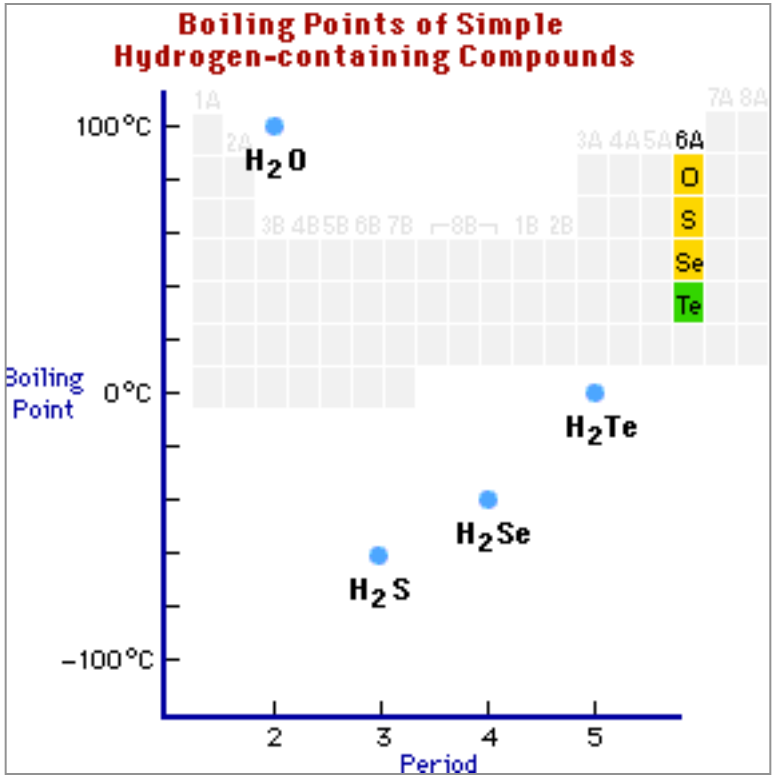
(b)

Protein Structure

- **1^o : The linear sequence of amino acids and disulfide bonds eg. ARDV:Ala·Arg·Asp·Val.**
- **2^o : Local structures which include, folds, turns, $\propto$-helices and β -sheets held in place by hydrogen bonds.**
- **3^o : *3-D* arrangement of all atoms in a single polypeptide chain.**
- **4^o : Arrangement of polypeptide chains into a functional protein, eg. hemoglobin.**

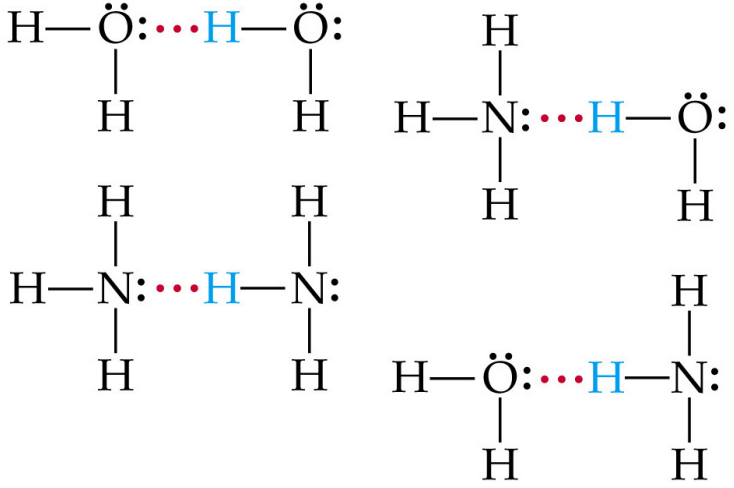

α-Carbon
Carbonyl carbon
Oxygen
Nitrogen
Hydrogen
R group (side chain)
Hydrogen bond
(a) α helix
(b) β pleated sheet

Boiling Points & Hydrogen Bonding



Hydrogen Bonding

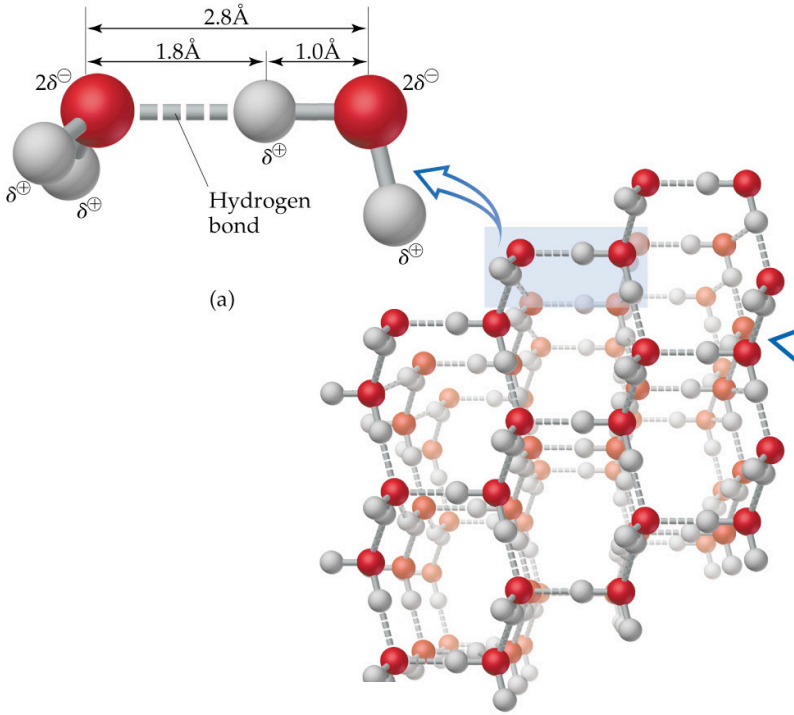
- **Hydrogen bonds, a unique dipole-dipole attraction (10-40 kJ/mol).**



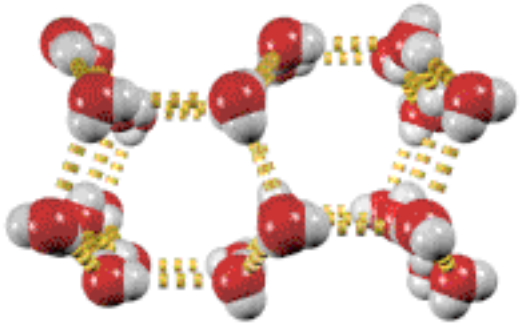
http://chemconnections.org/general/movies/HydrogenBonding.MOV

Intermolecular Forces

Hydrogen Bonding




(c)



http://chemconnections.org/general/movies/ice-structure.MOV

QUESTION

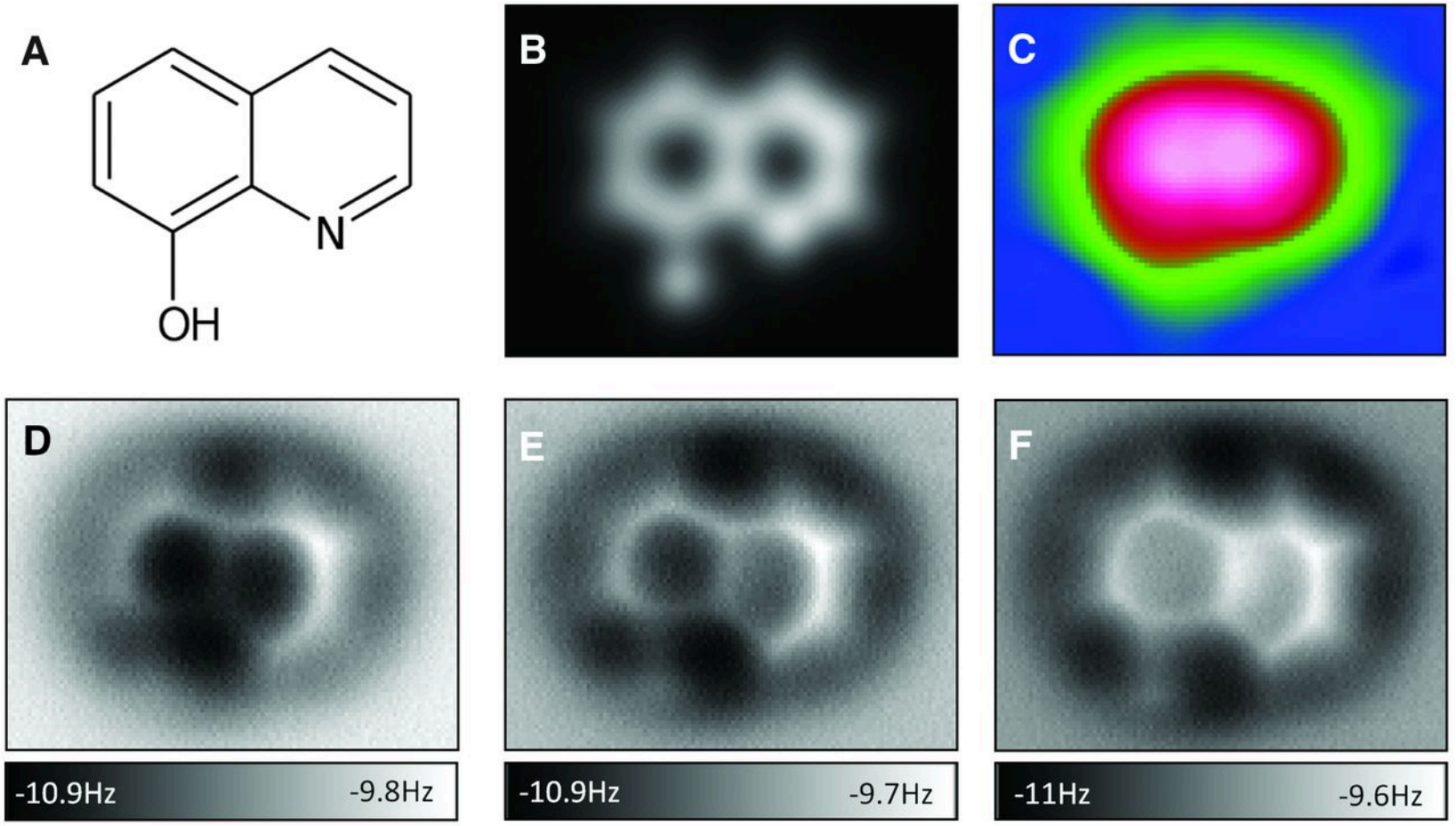
Which pure substances will not form hydrogen bonds?

I) CH_3CH_2OH **II) CH_3OCH_3**

III) $H_3C{-}NH{-}CH_3$ **IV) CH_3F**

A) I and II **B) I and III** **C) II and III** **D) II and IV**

Visualizing Intermolecular Hydrogen Bonds

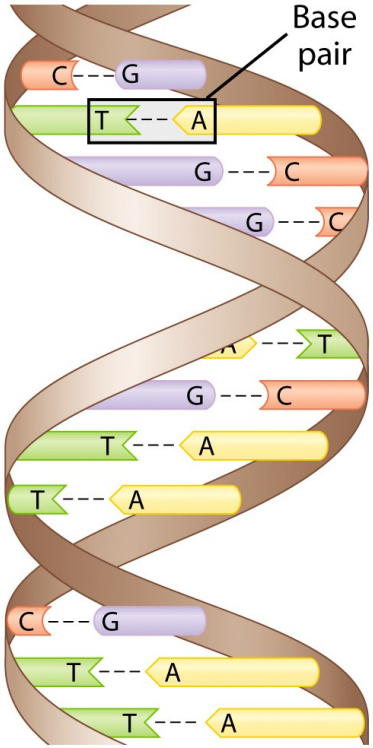


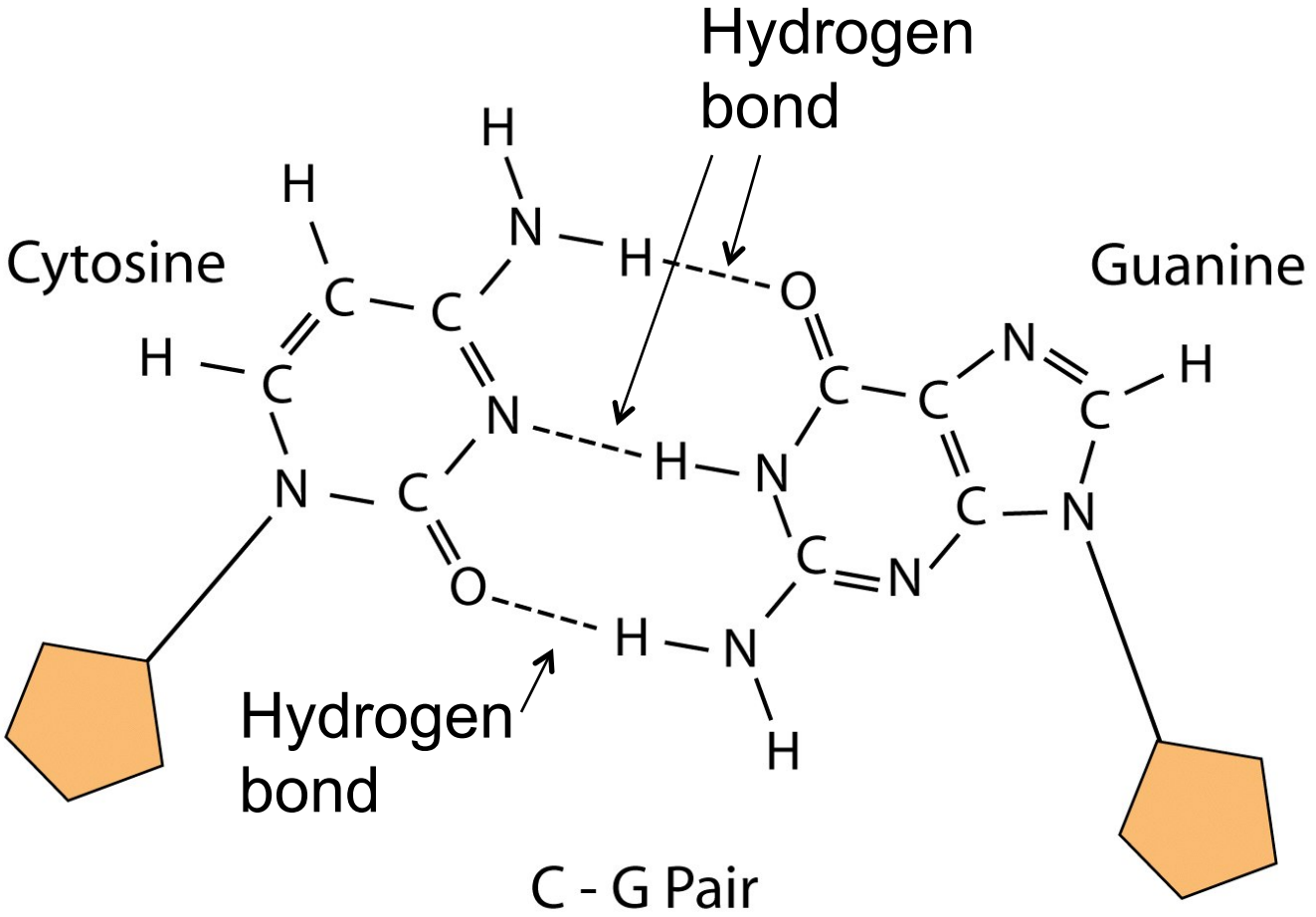
J Zhang et al. Science 2013;342:611-614

Fig. 1 STM and AFM measurements

Published by AAAS

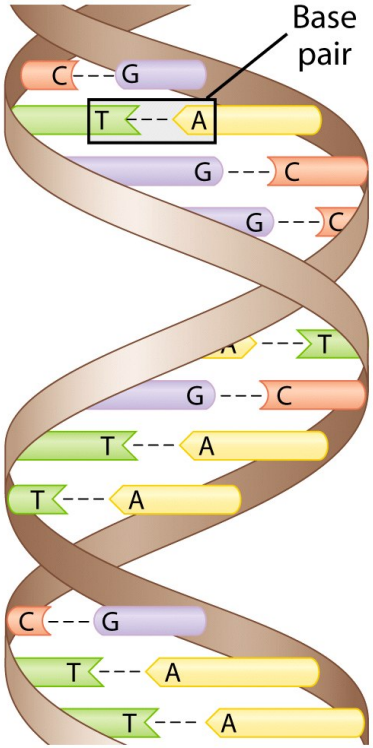
DNA Nucleotides

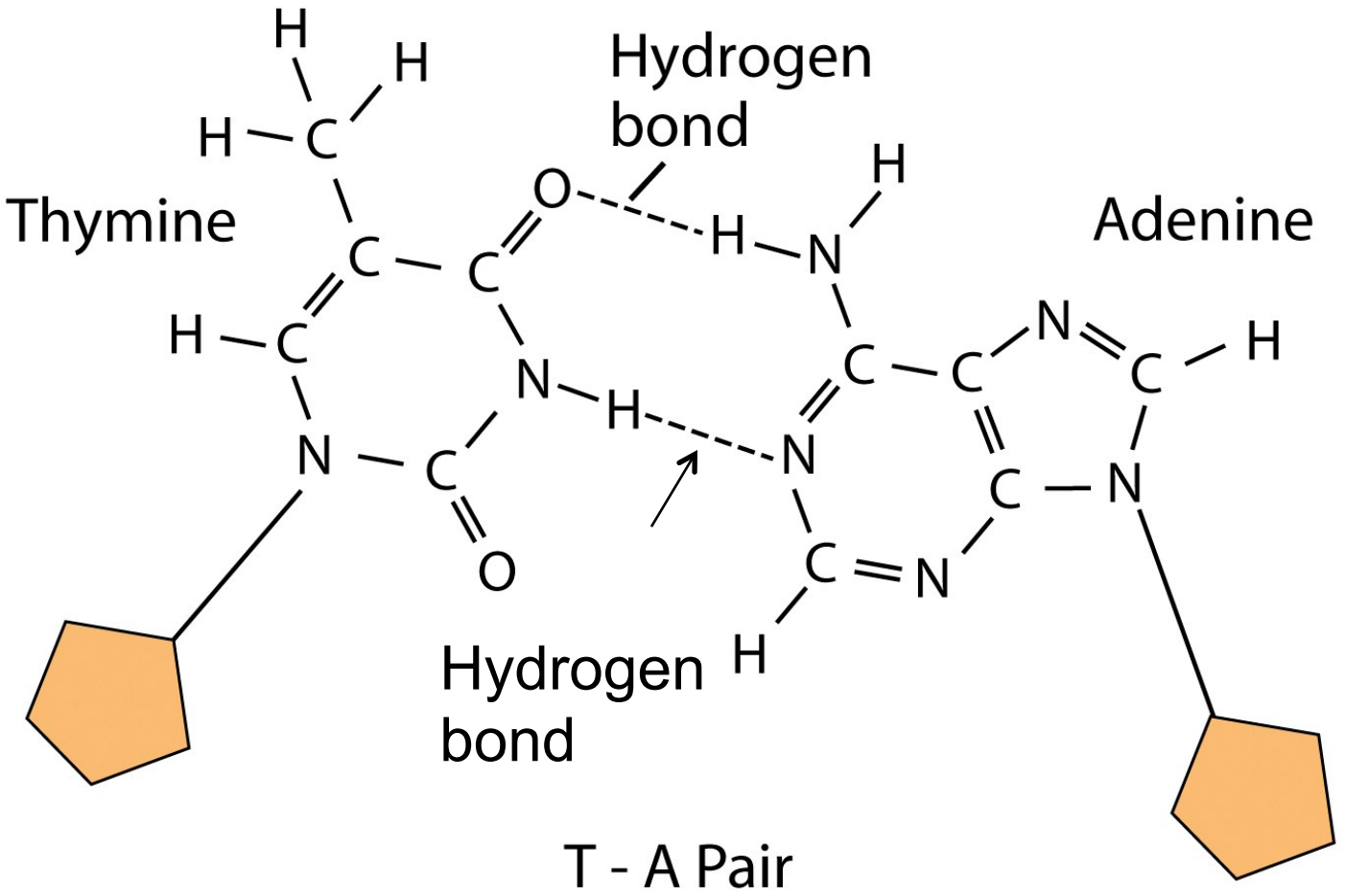




3 Hydrogen Bonds /
C – G Pair

DNA Nucleotides





RNA has Uracil (U) in place of Thymine (T)

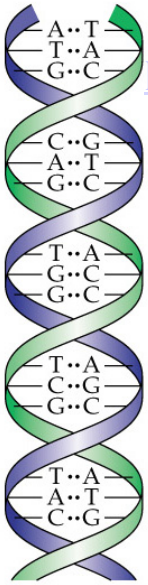
2 Hydrogen Bonds / T (U) – A Pair

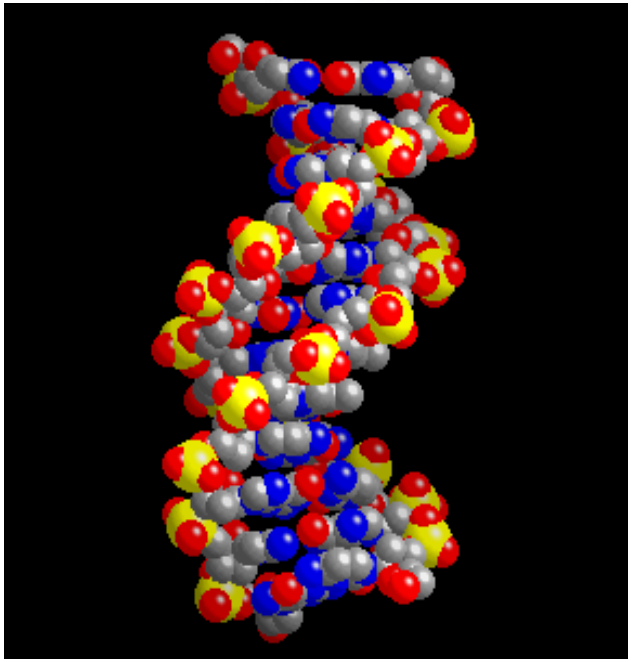
T – U Pair

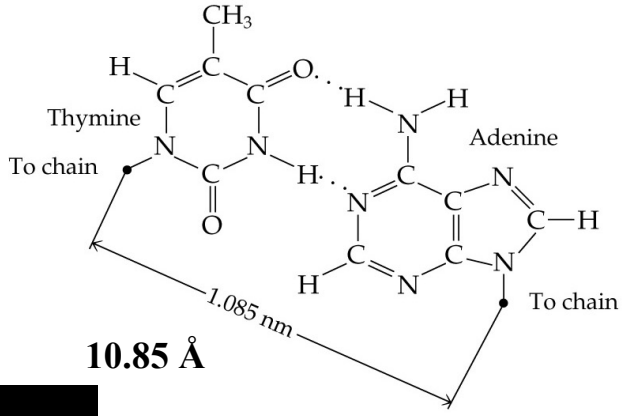
DNA: Size, Shape & Self Assembly

http://www.umass.edu/microbio/chime/beta/pe_alpha/atlas/atlas.htm

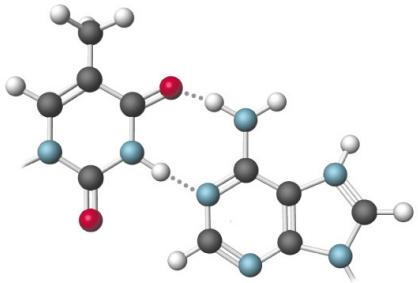
Views & Algorithms

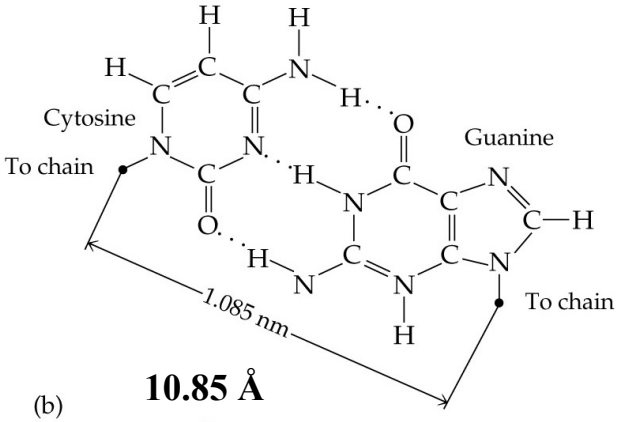






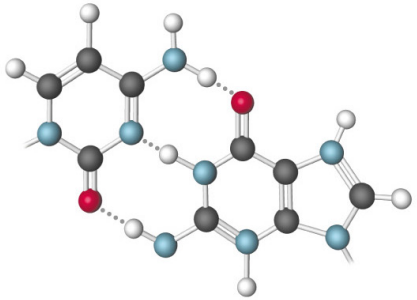
10.85 Å



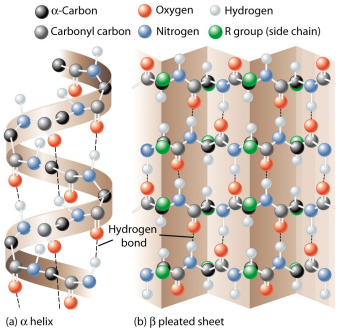


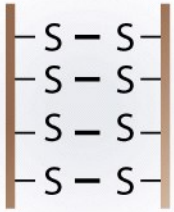
(b)

10.85 Å

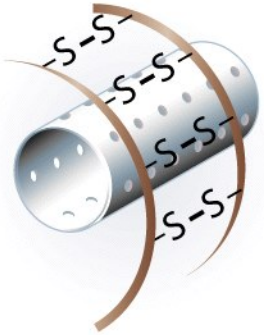


Hair: α-Helix

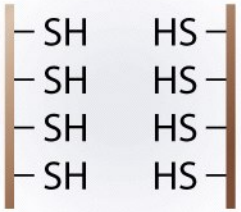




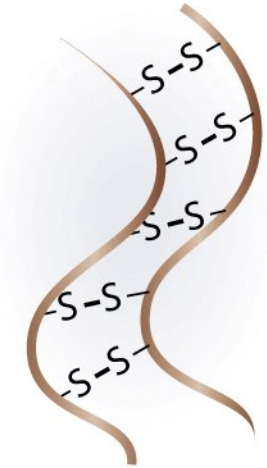
1. Straight hair with disulfide links



3. Hair is rolled around a curler, and new disulfide links form



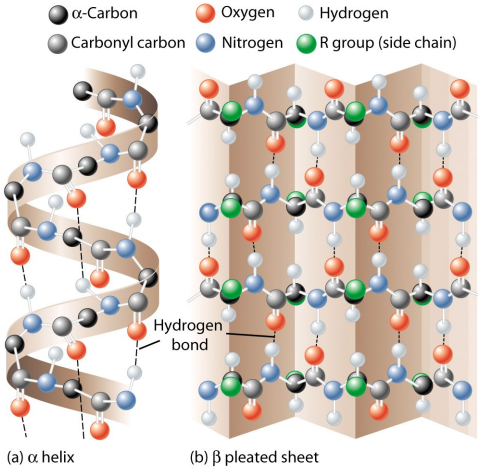
2. Chemicals are added to break disulfide links

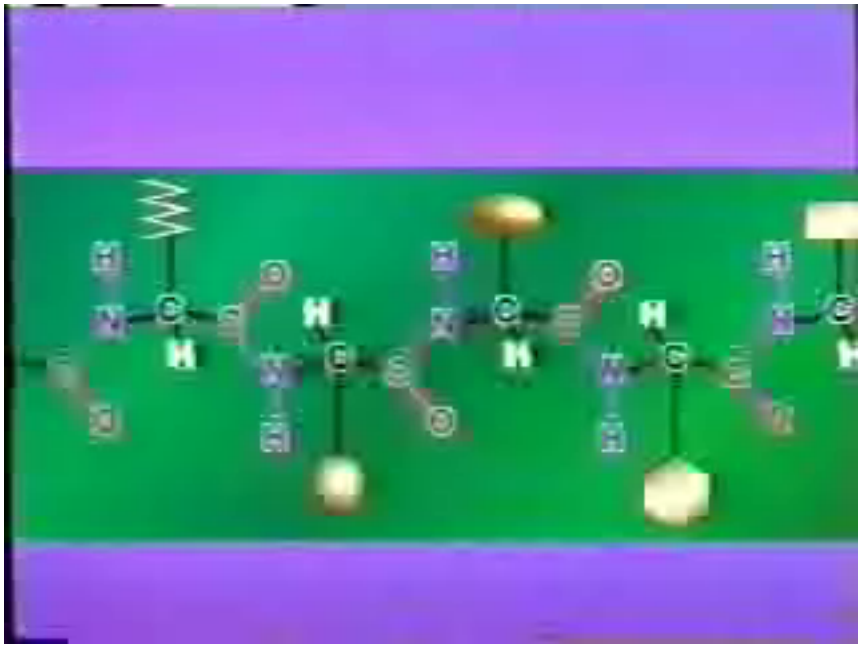


4. New disulfide links create curls

http://chemconnections.org/general/movies/protein-hair-2.mov

Hair: α-Helix Protein



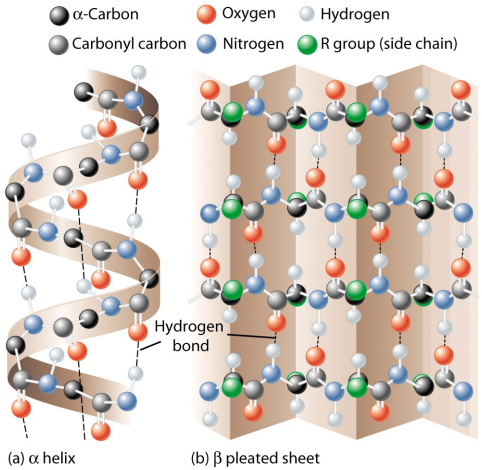


http://chemconnections.org/general/movies/protein-hair-2.mov

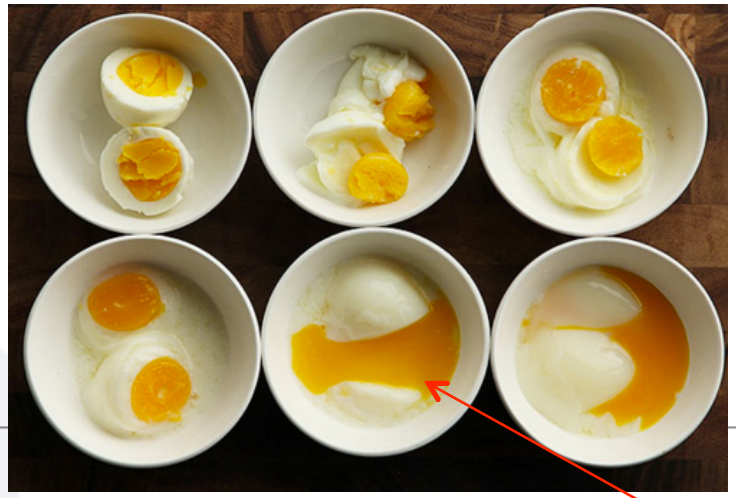
Annenberg World of Chemistry

#23 Proteins *:* http://www.learner.org/resources/series61.html

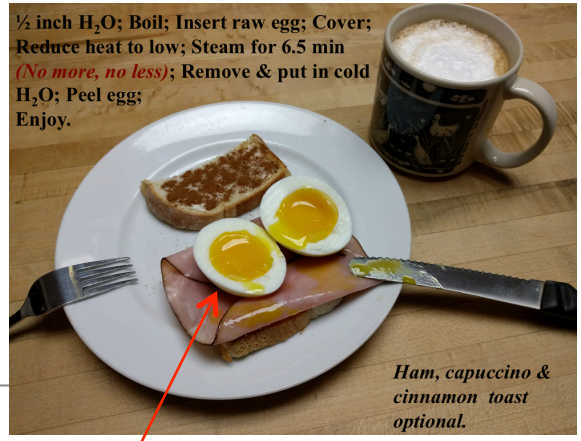
Silk: β-Sheets

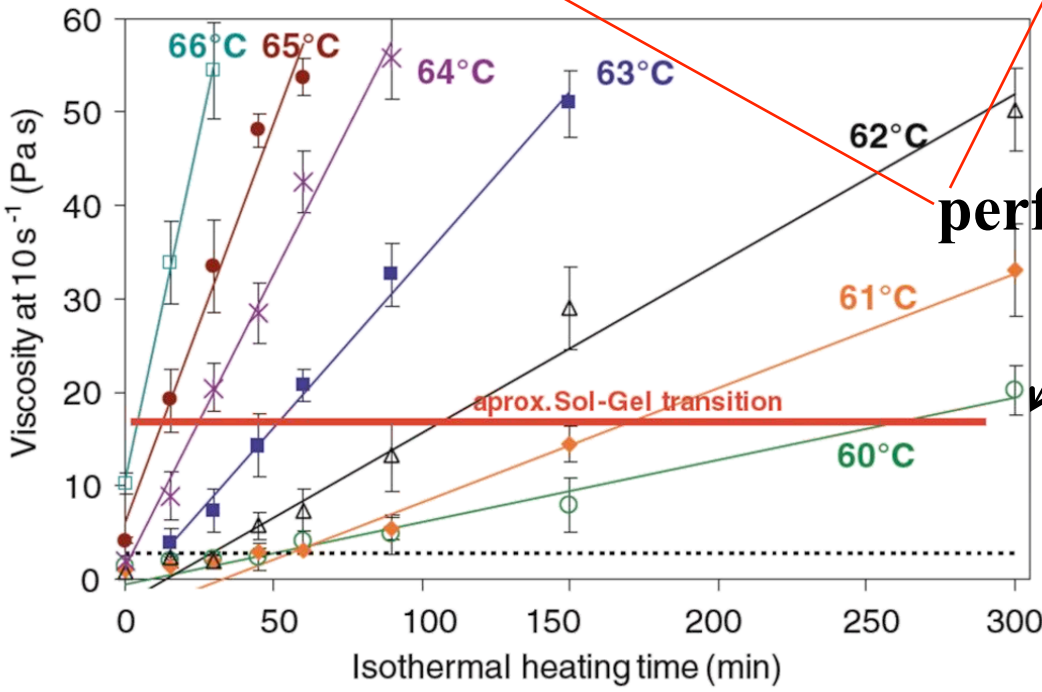


http://chemconnections.org/general/movies/proteins-silk-2.mov

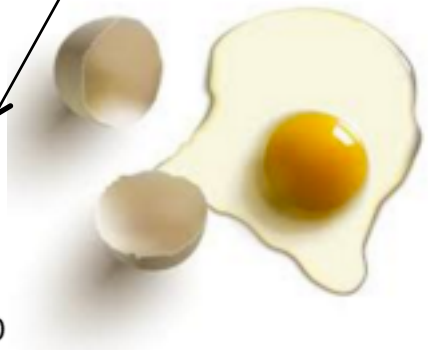


$T_{denaturation}$





perfectly softboiled



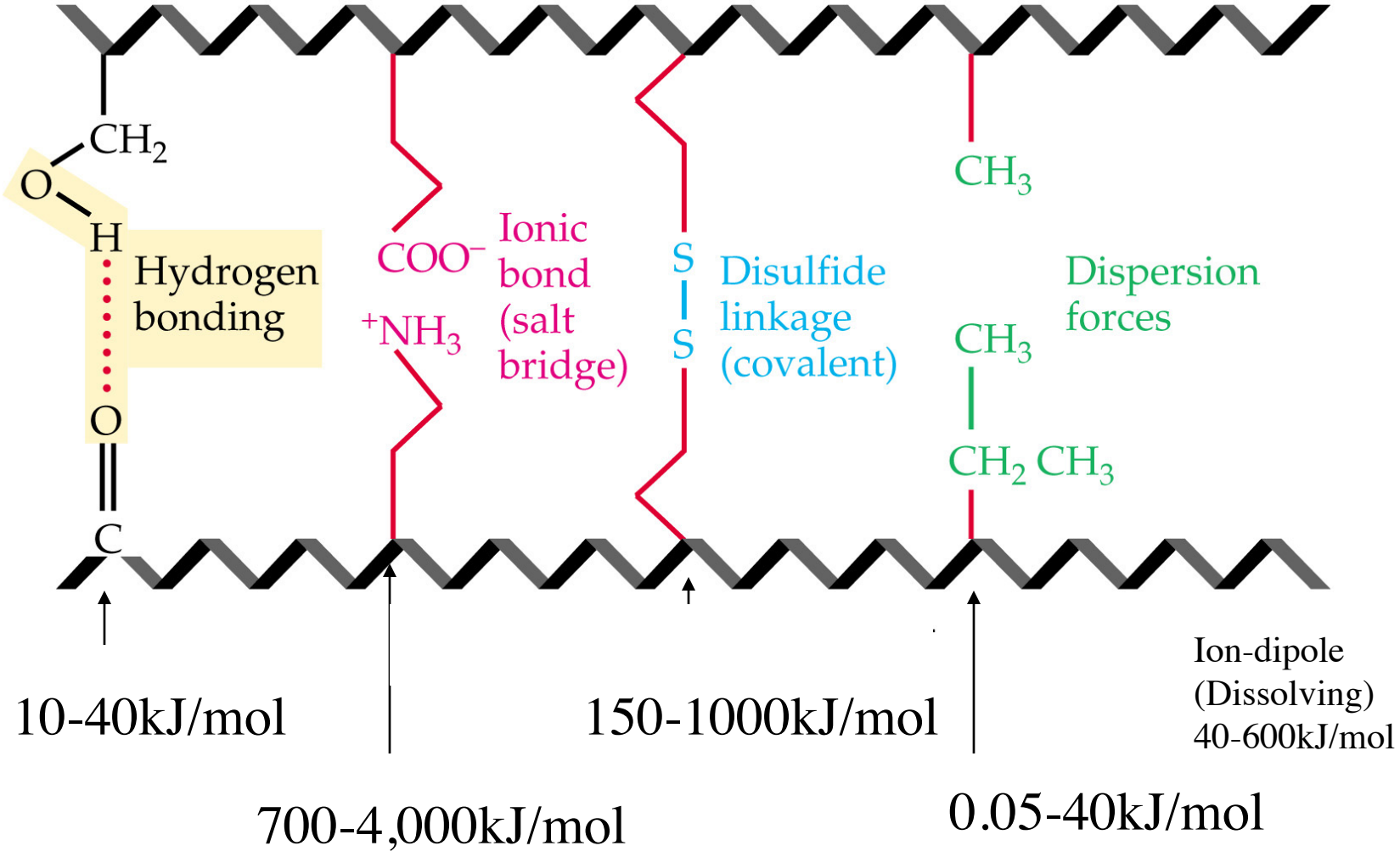
Cooking the perfect egg: **denaturing albumin protein**

http://chemconnections.org/general/chem106/Tech%20Prep/Protein%20Activity%20I-2016.html

Protein Structure

- **1^{o} : The linear sequence of amino acids and disulfide bonds eg. ARDV:Ala·Arg·Asp·Val.**
- **2^{o} : Local structures which include, folds, turns, ∝-helices and β -sheets held in place by hydrogen bonds.**
- **3^{o} : *3-D* arrangement of all atoms in a single polypeptide chain.**
- **4^{o} : Arrangement of polypeptide chains into a functional protein, eg. hemoglobin.**

Protein Shape: Forces, Bonds, Self Assembly, Folding



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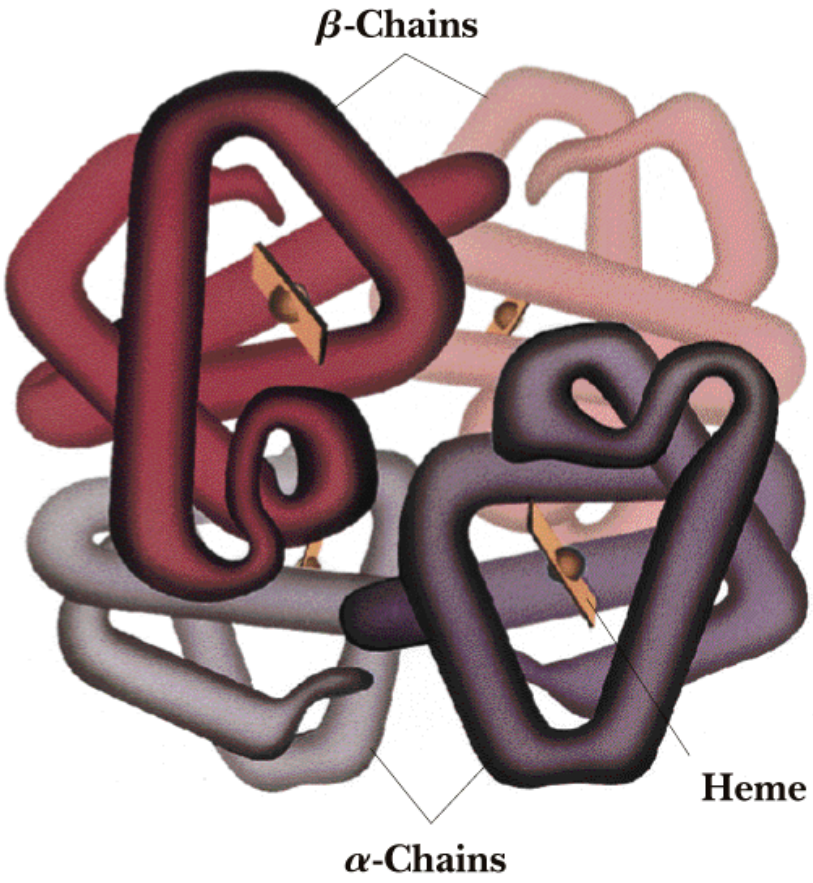
The quaternary structure of hemoglobin, Hb

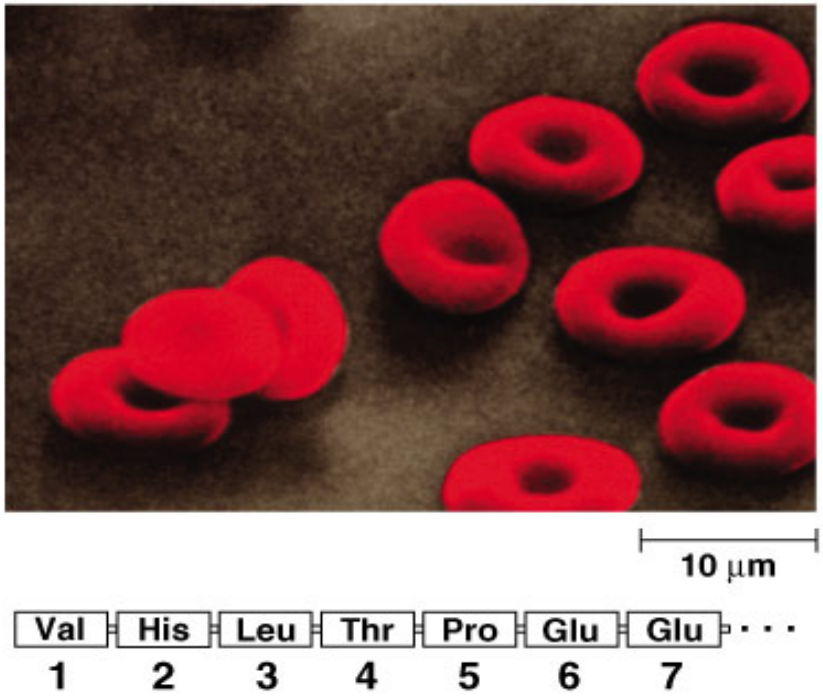
(A tetramer)



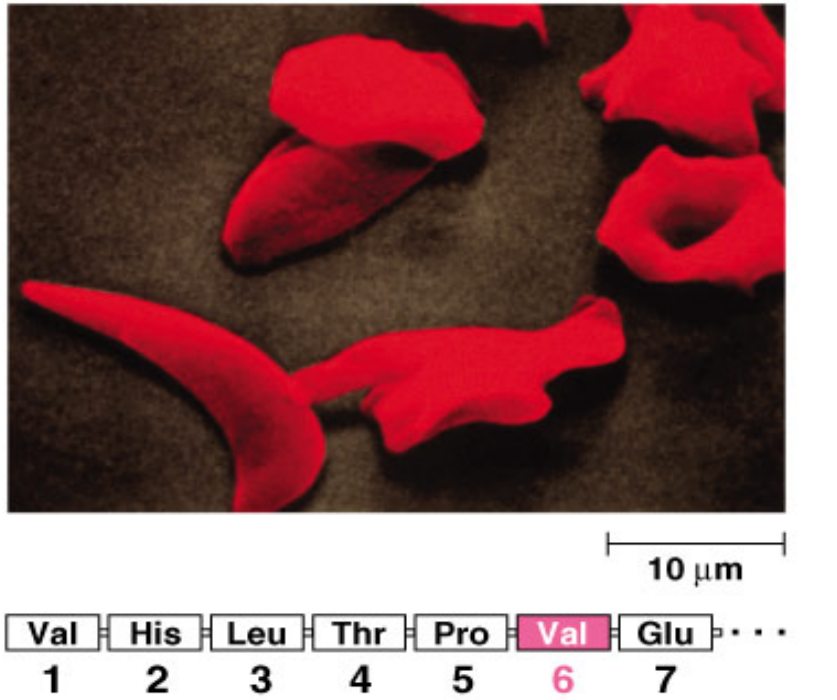
Hb: two alpha units of 141 residues, 2 beta units of 146

Sickle Cell Anemia

Hemoglobin / Valine (Glutamic Acid)

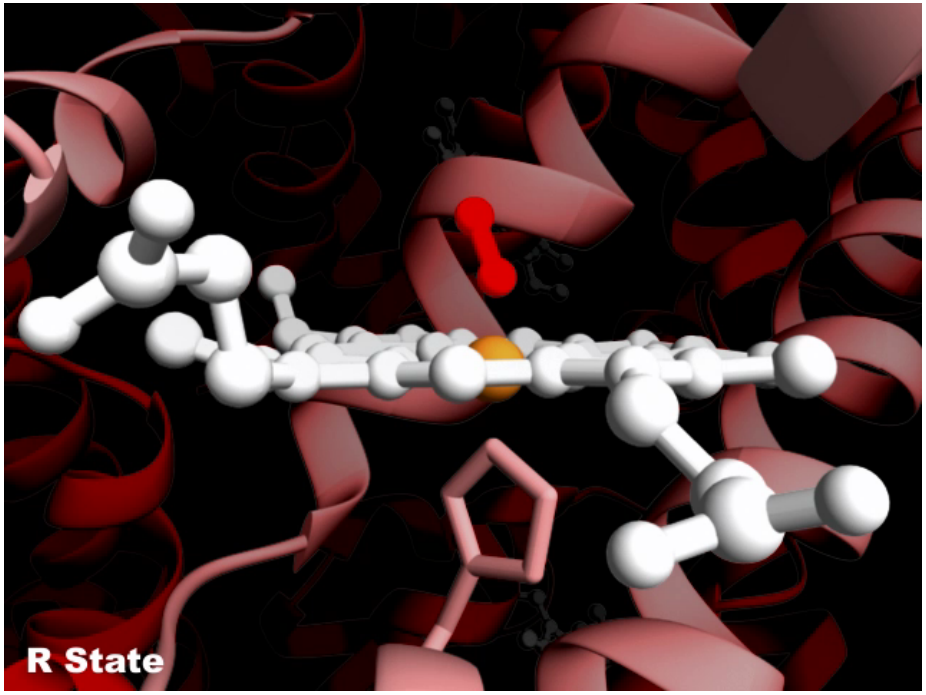


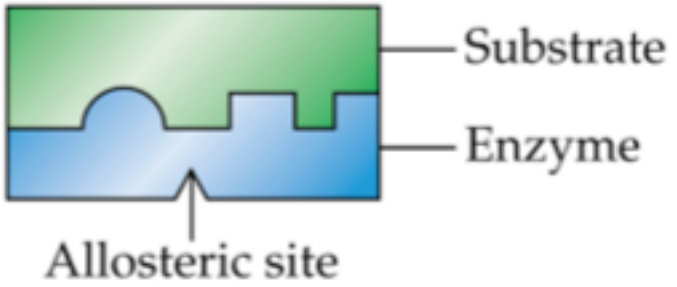
(a) Normal red blood cells and the primary structure of normal hemoglobin



(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

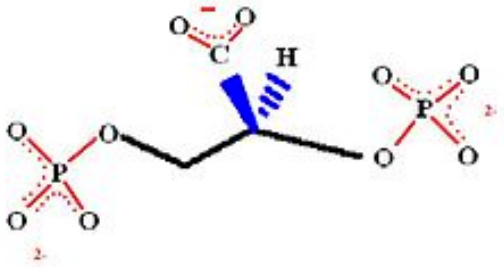
Hemoglobin and Oxygen Transport
An allosteric effect & sickle cell anemia

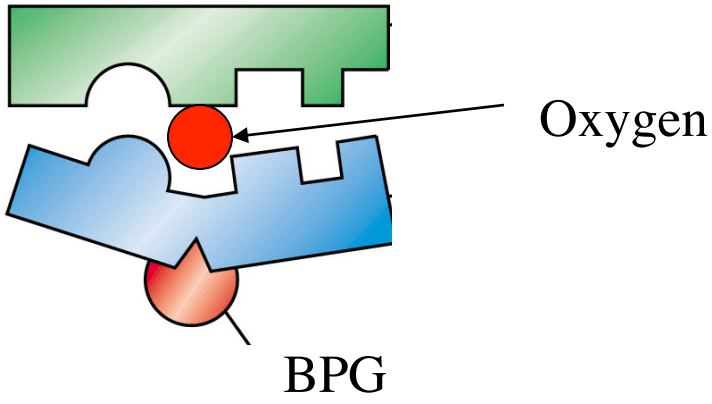




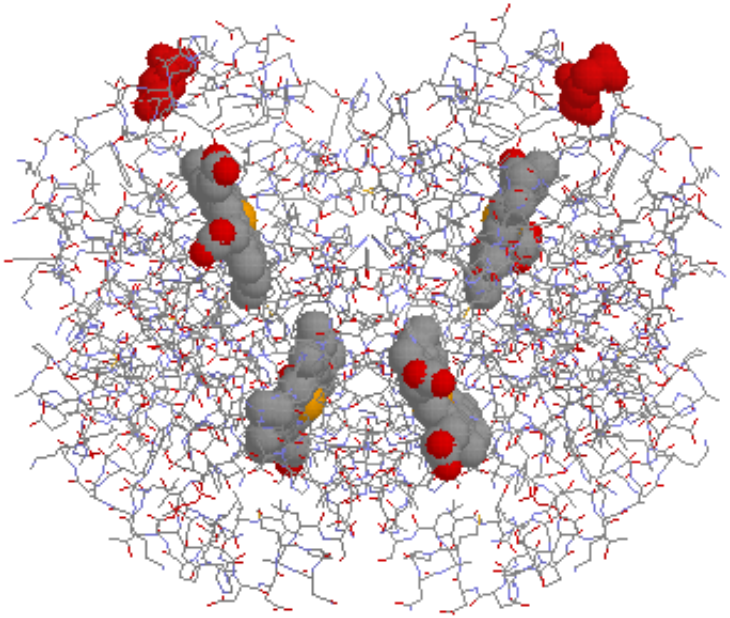
allosteric effector

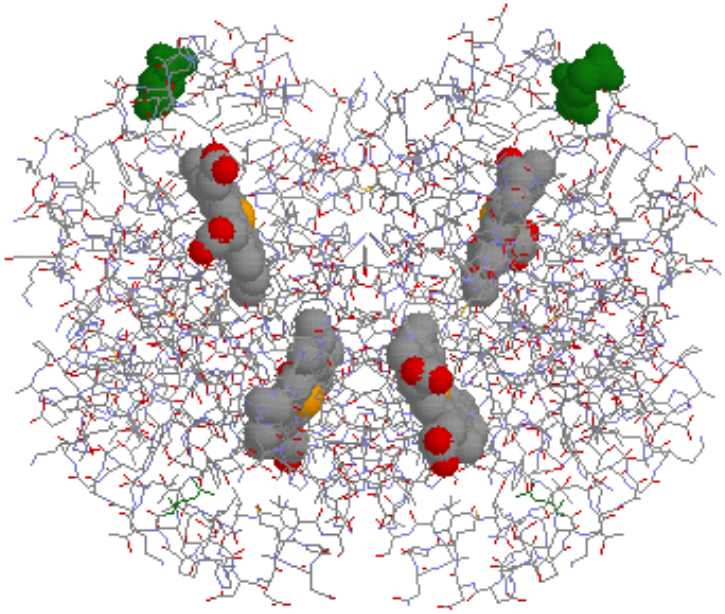
BPG: 2,3-Bisphosphoglycerate





Normal hemoglobin vs sickle cell hemoglobin



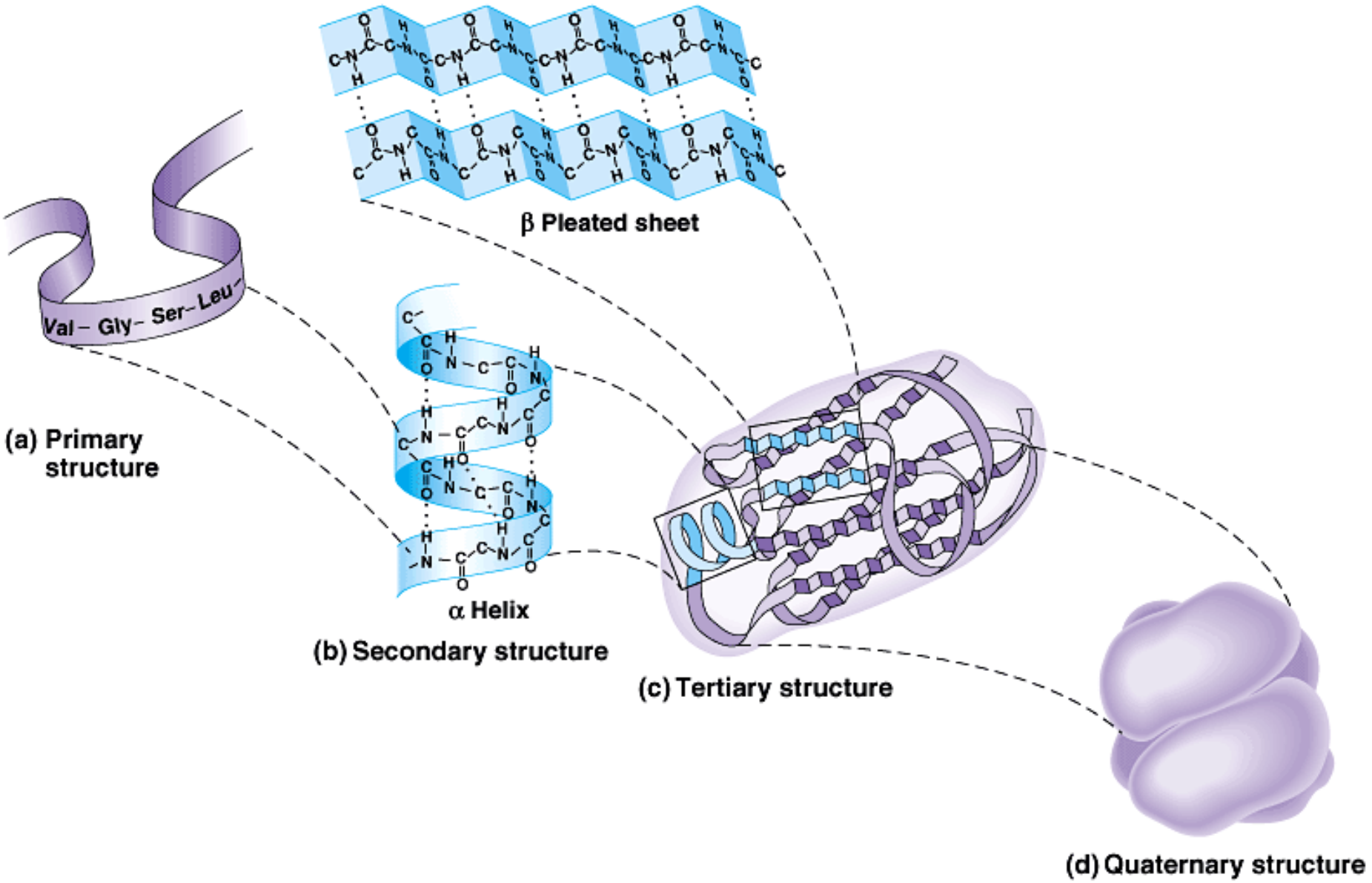


Valine replaces Glutamate

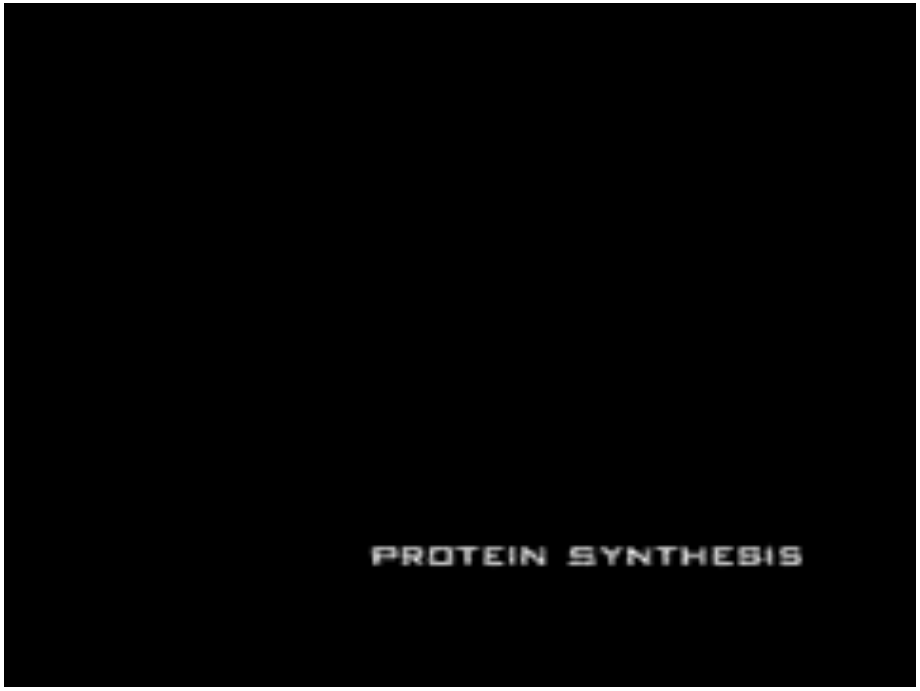
http://chemconnections.org/Presentations/Columbia/slide8-3.html

Firefox to listen

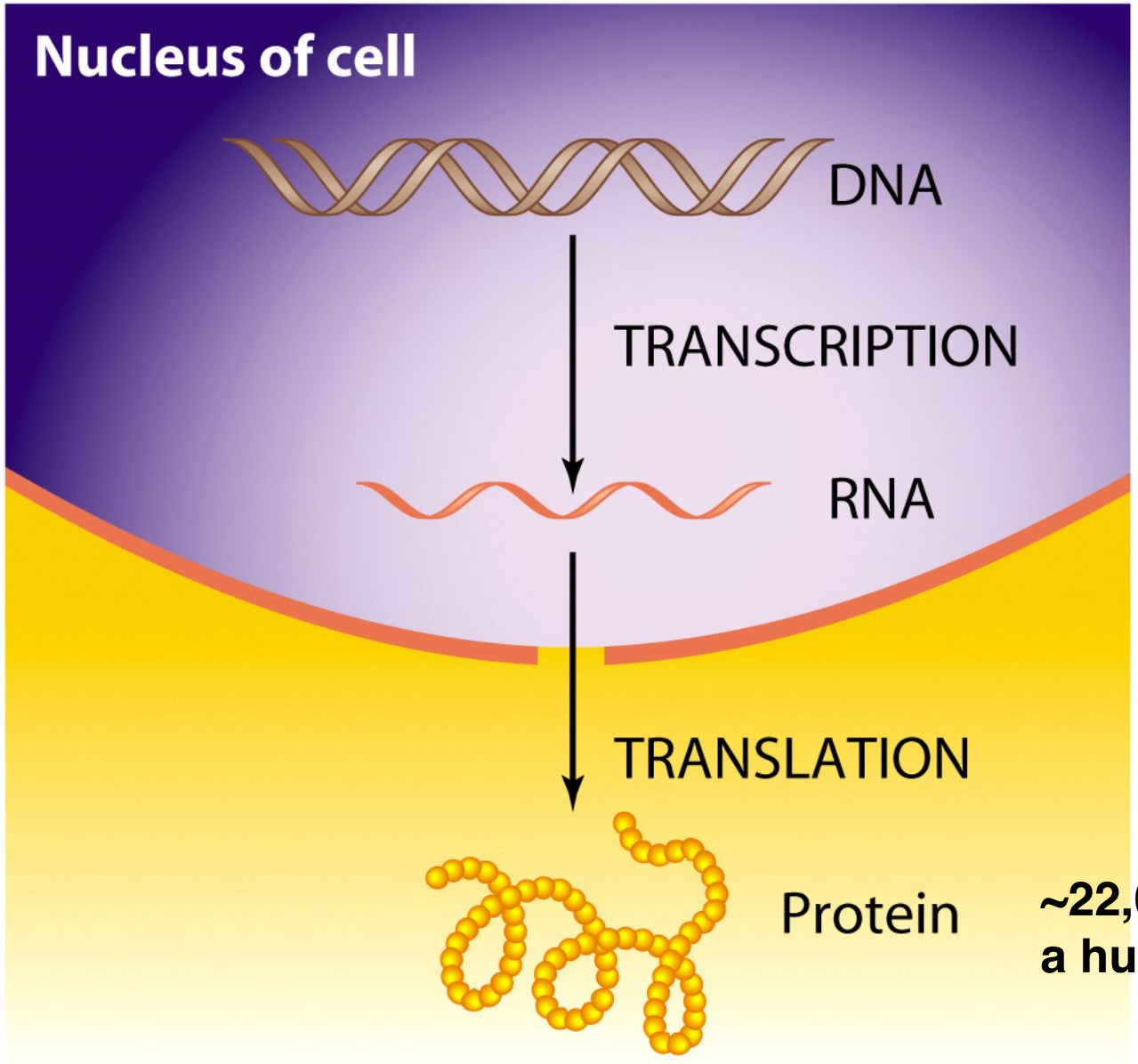
Summary


β Pleated sheet
Val – Gly – Ser – Leu
(a) Primary structure
α Helix
(b) Secondary structure
(c) Tertiary structure
(d) Quaternary structure

Protein Biosynthesis



https://www.dnalc.org/resources/3d/09-how-much-dna-codes-for-protein.html



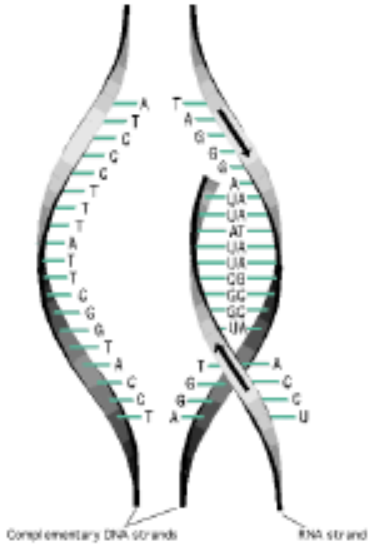
~22,000 define a human

Central Dogma

DNA

Transcription

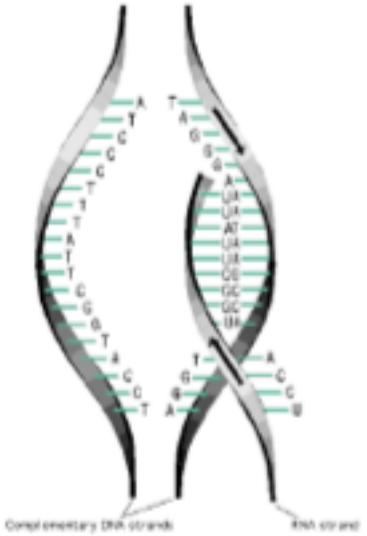
mRNA

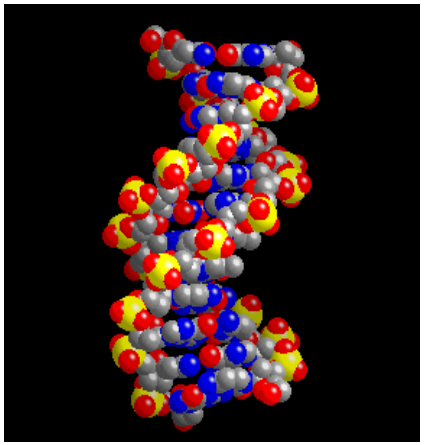


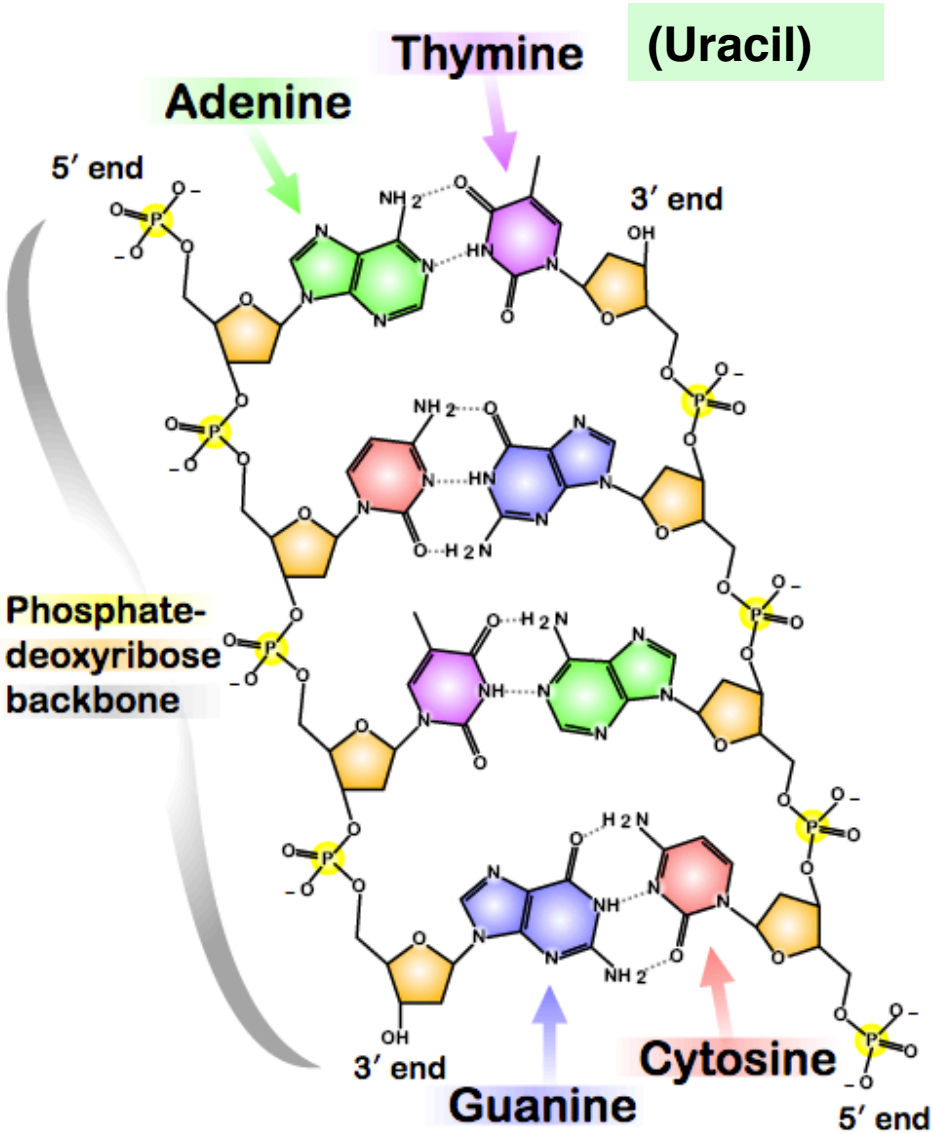
Translation

Protein

mRNA







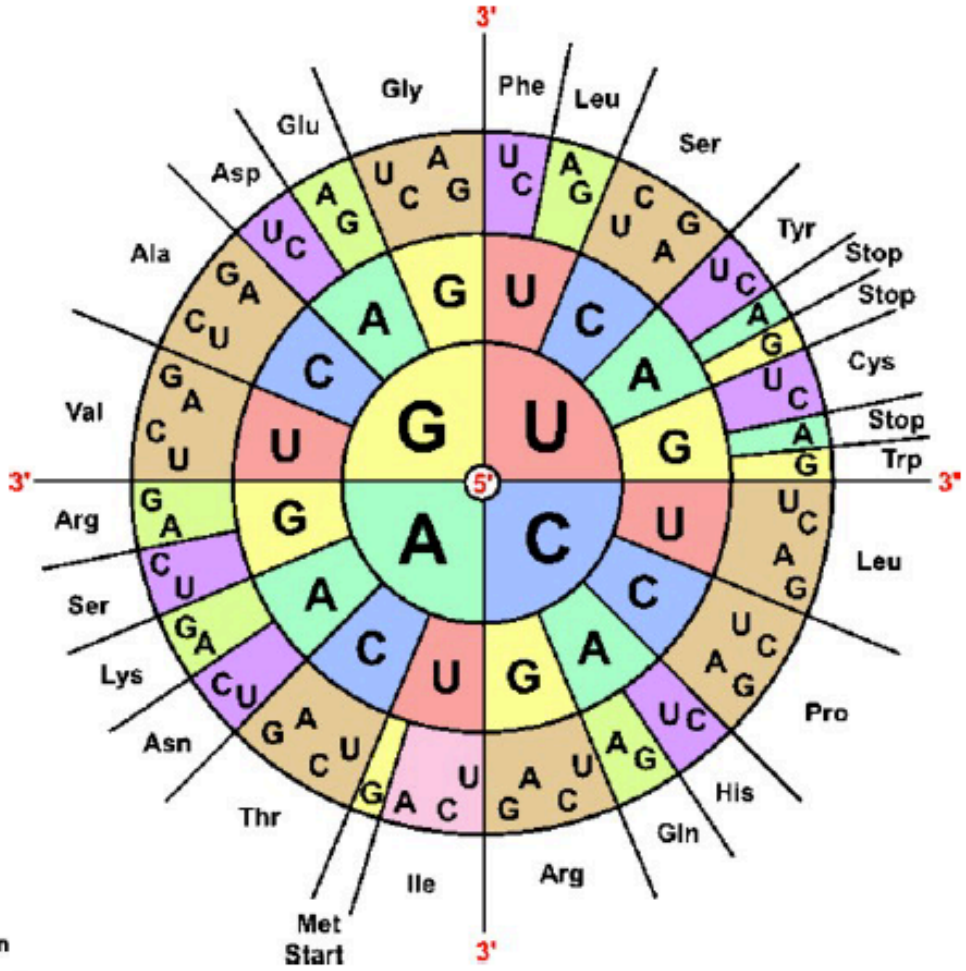
Backbone resembles a twisted ladder
with a sugar (ribose or deoxyribose) + phosphate ions forming the hand rails
and the nucleotide bases, A-T(U) and C-G, as the rungs

Protein Biosynthesis

Codons

- mRNA is translated in "chunks" of three, called **codons**
- The starting nucleotide is determined using bioinformatics to find the **reading frame**
- The genetic code is **degenerate**

(similar, but not identical)



5' AUG CAA CCC GAC UCC AGC 3' ← Codon
3' UAC GUU GGG CUG AGG UAG 5' ← AntiCodon
Met--Gln--Pro--Asp--Phe--Ser ← Amino Acids

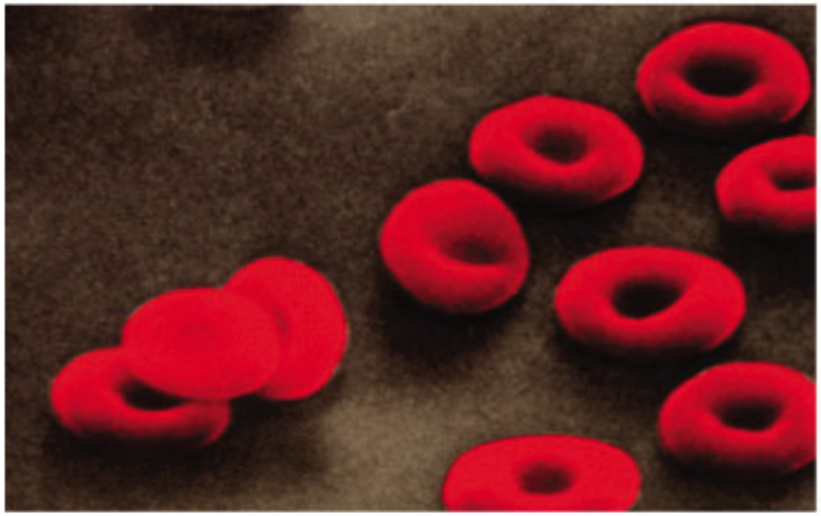
Protein Biosynthesis

Codon Chart

1st letter	Second Letter: U	Second Letter: C	Second Letter: A	Second Letter: G	3rd letter
U	UUU Phe UUC UUA Leu UUG	UCU UCC Ser UCA UCG	UAU Tyr UAC UAA Stop UAG Stop	UGU Cys UGC UGA Stop UGG Trp	U C A G
C	CUU CUC Leu CUA CUG	CCU CCC Pro CCA CCG	CAU His CAC CAA Gln CAG	CGU CGC Arg CGA CGG	U C A G
A	AUU AUC Ile AUA AUG Met	ACU ACC Thr ACA ACG	AAU Asn AAC AAA Lys AAG	AGU Ser AGC AGA Arg AGG	U C A G
G	GUU GUC Val GUA GUG	GCU GCC Ala GCA GCG	GAU Asp GAC GAA Glu GAG	GGU GGC Gly GGA GGG	U C A G

Curing Sickle Cell Anemia!

Target: Hemoglobin / Valine



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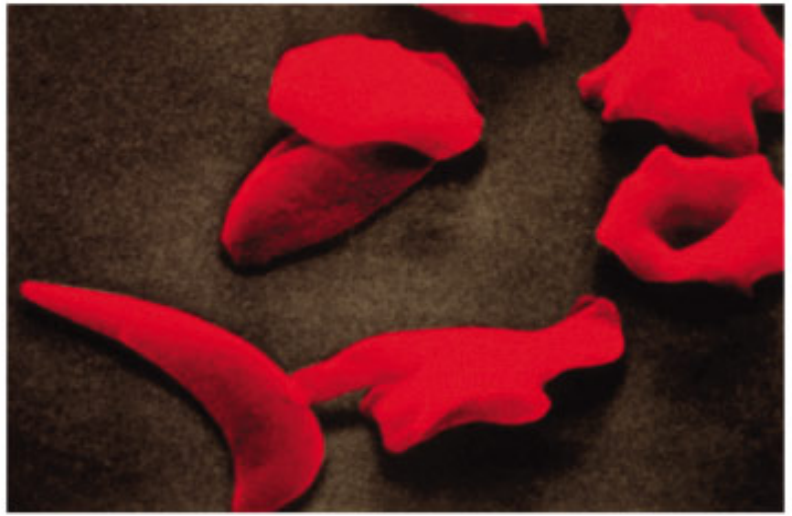

(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

GAA GAG	Glu	←	GUU GUC GUA GUG	Val

Biohacking:

- Biohackers may soon be able to afford an all-in-one desktop genome printer: a device much like an inkjet printer that employs the letters AGTC — genetic base pairs — instead of the color model CMYK.
- A similar device already exists for institutional labs, called BioXp 3200, which sells for about $65,000. But at-home biohackers can start with DNA Playground from Amino Labs, an Easy Bake genetic oven that costs less than an iPad, or The Odin's Crispr gene-editing kit for $159.

https://www.nytimes.com/2018/05/14/science/biohackers-gene-editing-virus.html?rref=collection%2Fsectioncollection%2Fscience&action=click&contentCollection=science&region=rank&module=package&version=highlights&contentPlacement=1&pgtype=sectionfront