

# Biomolecular structure (including protein structure)

CS/CME/BioE/Biophys/BMI 279

Sept. 23 and 28, 2021

Ron Dror

# Outline

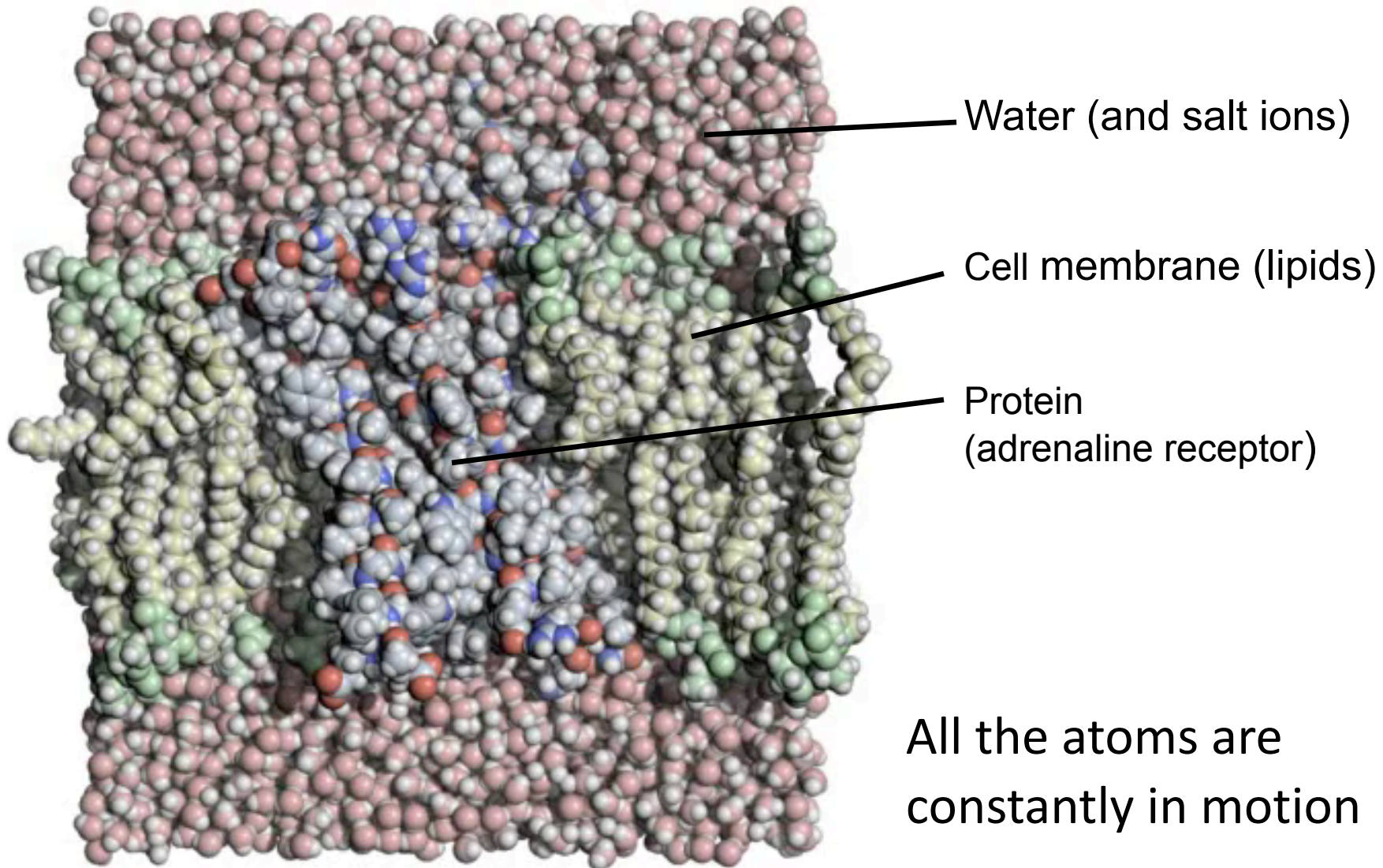
Note: I'll discuss proteins first, as an example.

These concepts apply to other biomolecules as well.

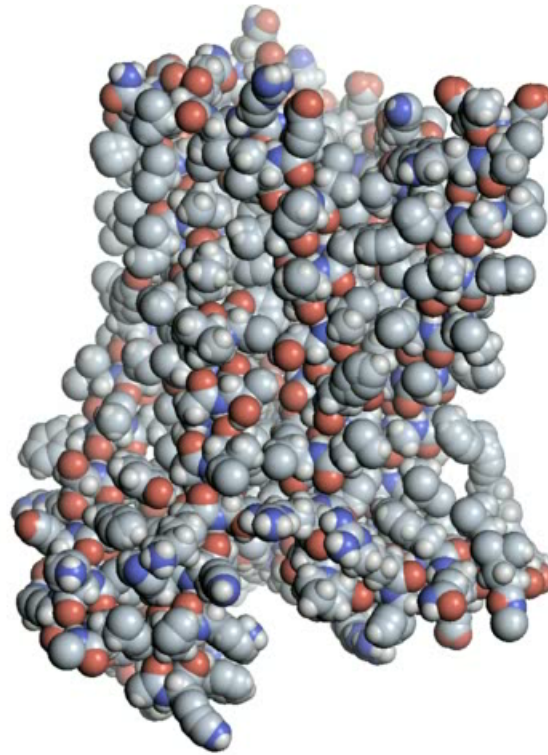
- Visualizing biomolecules (e.g, proteins)
- The Protein Data Bank (PDB)
- Chemical (2D) structure of proteins
- What determines the 3D structure of a protein?  
Physics underlying biomolecular structure
  - Basic interactions
  - Complex interactions
- Protein structure: a more detailed view
  - Properties of amino acids
  - Secondary structure
  - Tertiary structure, quaternary structure, and domains
- Structures of other biomolecules

Visualizing biomolecules (e.g., proteins)

# Protein surrounded by other molecules



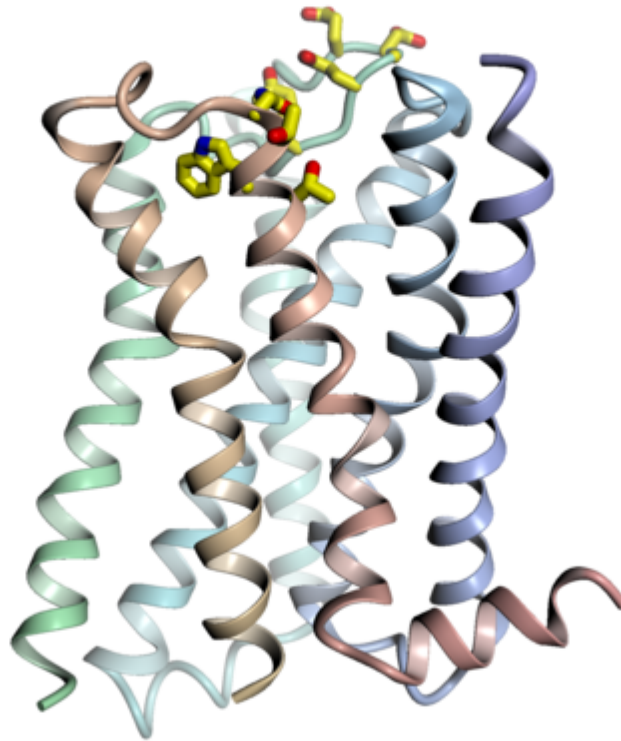
# Protein only, static structure



Adrenaline receptor

# Further simplified representation

- A cartoon representation of the backbone
- Gives overall architecture of protein



Adrenaline receptor

# Key take-aways from these visualizations

- Protein and surrounding atoms fill space (close-packed).
- All of these atoms are constantly moving around, and the protein's shape keeps changing.
- Simplified visual representations help you figure out what's going on.

Simplified visual presentation is called a “cartoon”

# The Protein Data Bank (PDB)

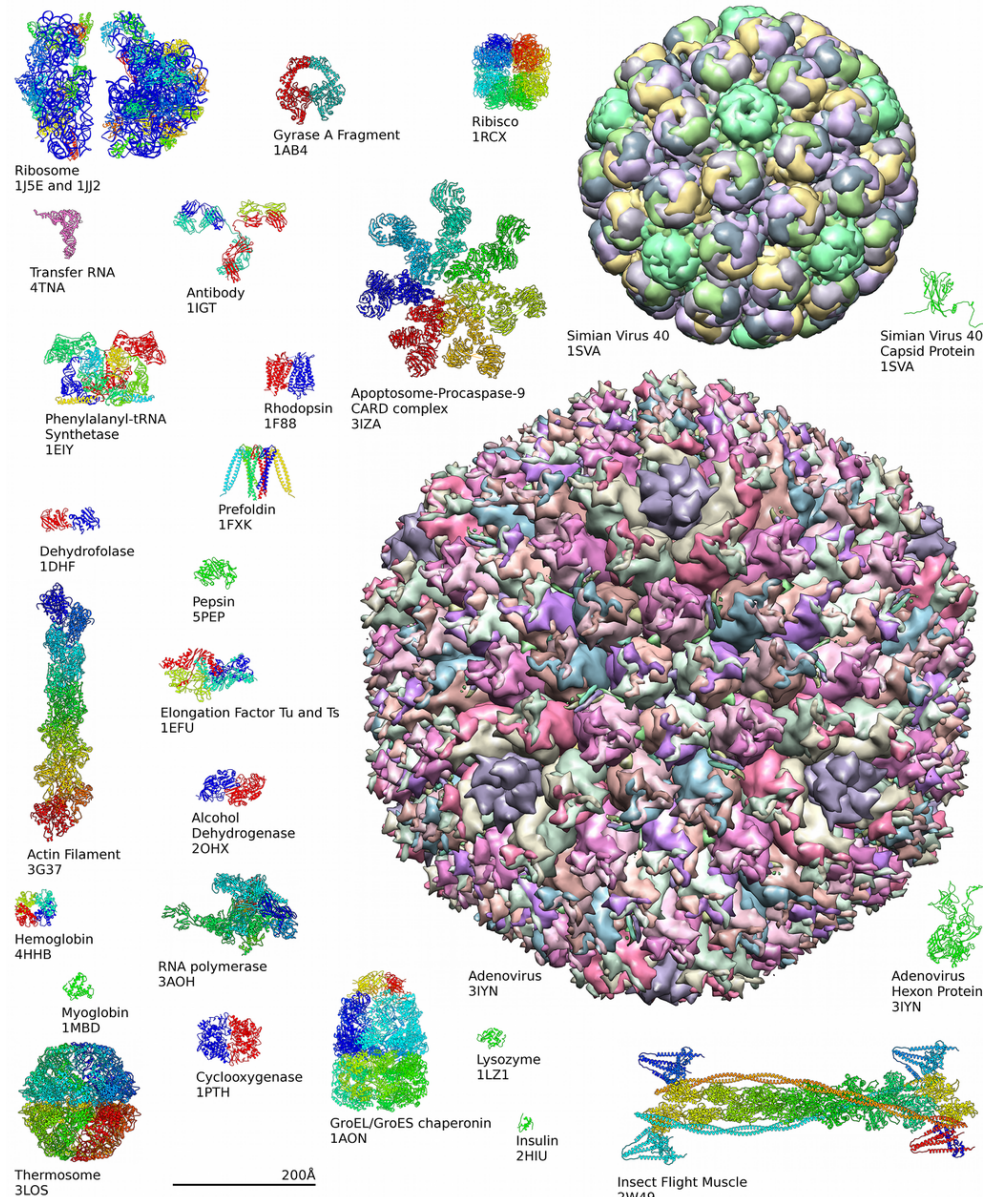
# The Protein Data Bank (PDB)

- Examples of structures from PDB

It is named PDB since proteins were the first structures in the database. The PDB today contains the 3D structures of many biomolecules, including proteins, DNA, RNA.

[https://upload.wikimedia.org/wikipedia/commons/thumb/2/24/Protein\\_structure\\_examples.png/1024px-Protein\\_structure\\_examples.png](https://upload.wikimedia.org/wikipedia/commons/thumb/2/24/Protein_structure_examples.png/1024px-Protein_structure_examples.png)

(Axel Griewel)



# The Protein Data Bank (PDB)

← → ↻ rcsb.org ☆ 🔍 ⚙️ 📄 🌐

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**RCSB PDB** PROTEIN DATA BANK **168889** Biological Macromolecular Structures Enabling Breakthroughs in Research and Education

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PDB-101 WORLDWIDE PDB PROTEIN DATA BANK EMDatabank EMDataResource Official Data Resource for IUCr NDB NUCLEIC ACID DATABASE Worldwide Protein Data Bank Foundation

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## A Structural View of Biology

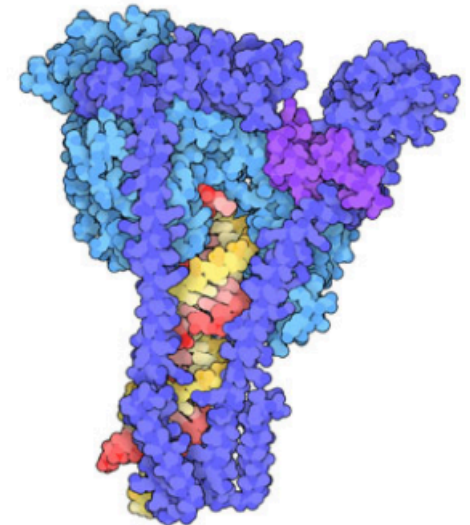
This resource is powered by the Protein Data Bank archive—information about the 3D shapes of proteins, nucleic acids, and complex assemblies that helps students and researchers understand all aspects of biomedicine and agriculture, from protein synthesis to health and disease.

As a member of the wwPDB, the RCSB PDB curates and annotates PDB data.

The RCSB PDB builds upon the data by creating tools and resources for research and education in molecular biology, structural biology, computational biology, and beyond.



## September Molecule of the Month



SARS-CoV-2 RNA-dependent RNA Polymerase

# 6YYT

## Structure of replicating SARS-CoV-2 polymerase

Display Files Download Files

Help

Sequence of 6YYT | Struct... 1: nsp12 A

```
SNASADAQSF LNRVCGVSAARLTPCGTGTSTDVVYRAFDIYNDKVAGFAKFLKTNCCRFQEKDEDDNLIDSYFVVKRHTFSNYQHEETIYNLLKDCPAVAKHDFKFRIDGD
118 128 138 148 158 168 178 188 198 208 218
MVPHISRQRLTKYTMADLVYALRHFDEGNCIDLKEILVTYNCCDDYFNKKDWYDFVENPDILRVYANLGERVRQALLKTVQFC DAMRNAGIVGVLTLDNQDLNGNWDYDFGD
228 238 248 258 268 278 288 298 308 318 328
FIQTTPGSGVPVDSYYSLMLPILTLRALTAESHVDTDLTKPYIKWDLKDYDFTEERLKLFDYFKYWDQTYHPNCVNLDDRCILHCANFNVLFSVTFPPTSFGLVVRKI
338 348 358 368 378 388 398 408 418 428 438
```

Structure

Type	Assembly
Asm Id	1: Author And Softwar...

Nothing Focused

Measurements

Components 6YYT

Preset	+ Add	⌵	⌚
Polymer	Cartoon	👁	🗑
Ion	Ball & Stick	👁	🗑

Density

Assembly Symmetry



Roger Kornberg first solved the structure of human RNA polymerase

Human RNA polymerase translates DNA to RNA

Coronavirus RNA polymerase → genetic code is encoded in RNA



# The Protein Data Bank (PDB)

Biomolecules are not static, so the structures in the database are the average or most common

- <https://www.rcsb.org/>
- A collection of essentially all published, experimentally determined structures of biomacromolecules (e.g., proteins, DNA, RNA)
- Each identified by 4-character code (e.g., 6YYT)
- Currently ~182,000 structures. ~80% of those are determined by x-ray crystallography.
- Browse it and look at some structures. Options:
  - 3D view in applet on PDB web pages
  - PyMol: fetch 6YYT

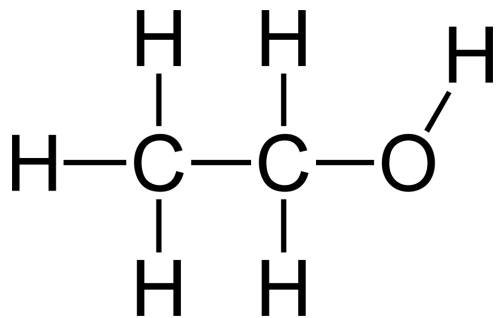
# Chemical (two-dimensional) structure of proteins

# Chemical (two-dimensional) structure vs. three-dimensional structure

- Chemical (two-dimensional) structure shows *covalent bonds* between atoms. Essentially a graph.
- Three-dimensional structure shows relative positions of atoms.

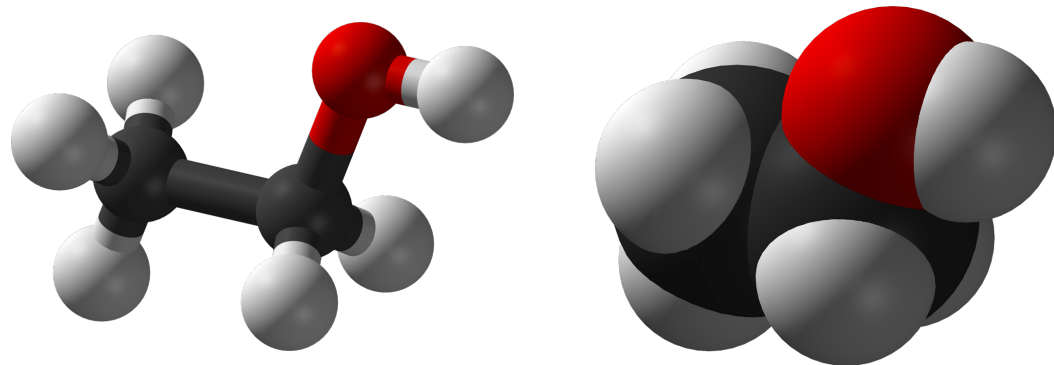
2D structure

Ethanol



3D structure

Ethanol

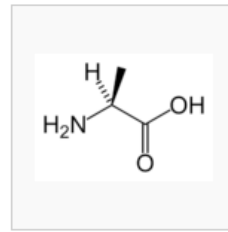


# Proteins are built from amino acids

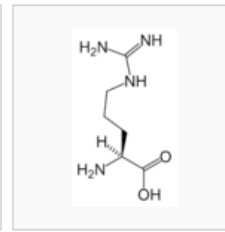
- 20 “standard” amino acids
- Each has three-letter and one-letter abbreviations (e.g., Threonine = Thr = T; Tryptophan = Trp = W)

The “side chain” is different in each amino acid.

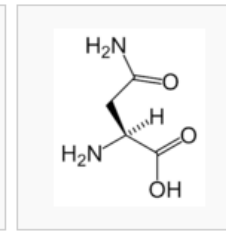
All amino acids have this part in common.



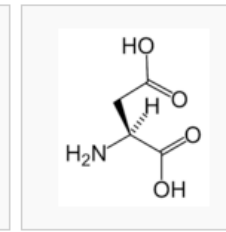
L-Alanine  
(Ala / A)



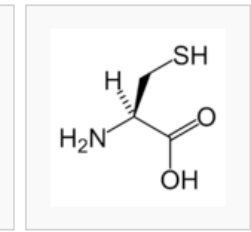
L-Arginine  
(Arg / R)



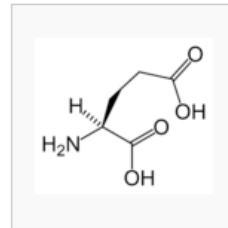
L-Asparagine  
(Asn / N)



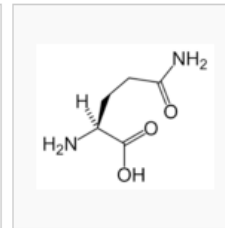
L-Aspartic acid  
(Asp / D)



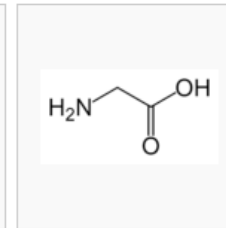
L-Cysteine  
(Cys / C)



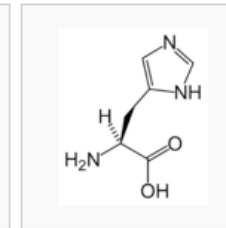
L-Glutamic acid  
(Glu / E)



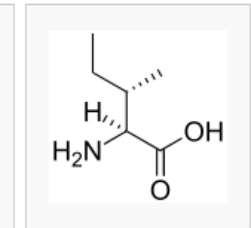
L-Glutamine  
(Gln / Q)



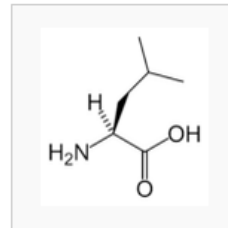
Glycine  
(Gly / G)



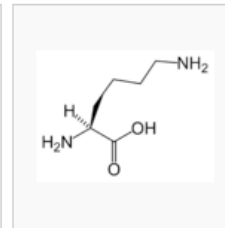
L-Histidine  
(His / H)



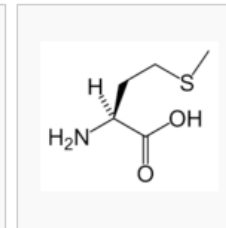
L-Isoleucine  
(Ile / I)



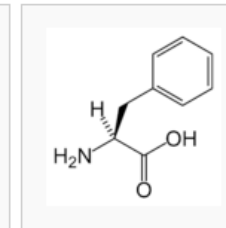
L-Leucine  
(Leu / L)



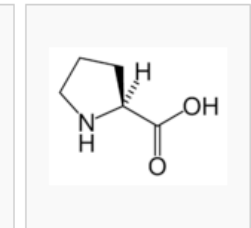
L-Lysine  
(Lys / K)



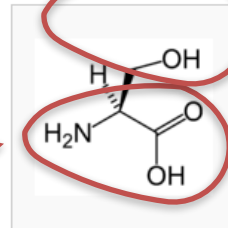
L-Methionine  
(Met / M)



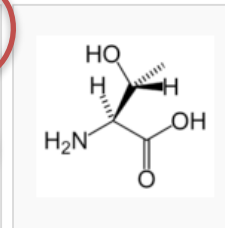
L-Phenylalanine  
(Phe / F)



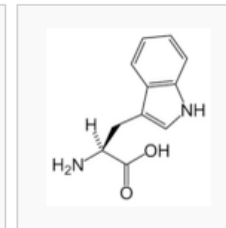
L-Proline  
(Pro / P)



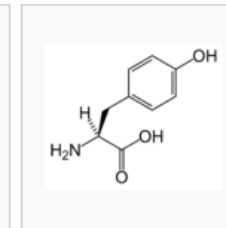
L-Serine  
(Ser / S)



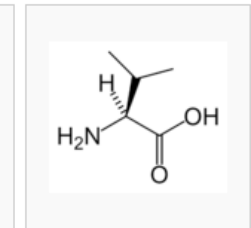
L-Threonine  
(Thr / T)



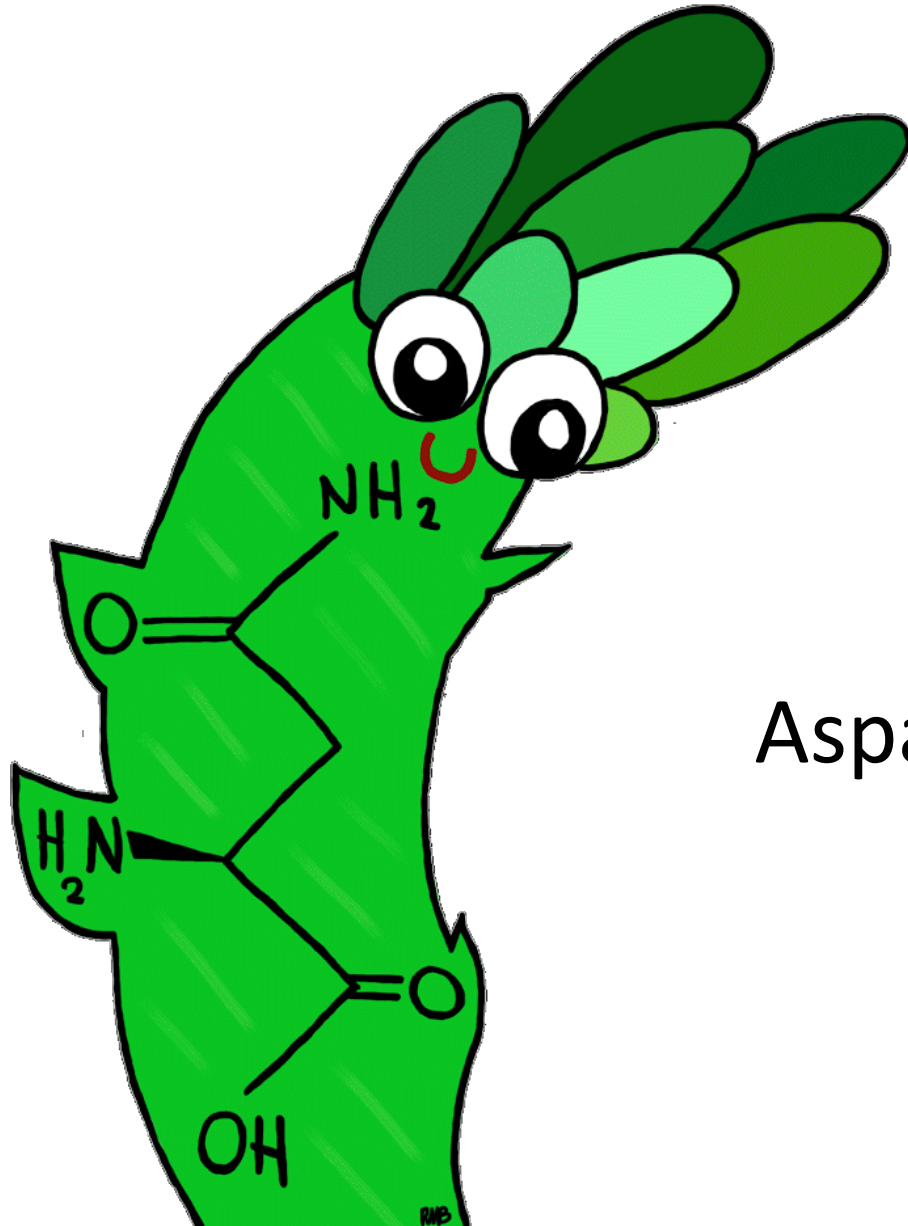
L-Tryptophan  
(Trp / W)



L-Tyrosine  
(Tyr / Y)



L-Valine  
(Val / V)



# Asparagine

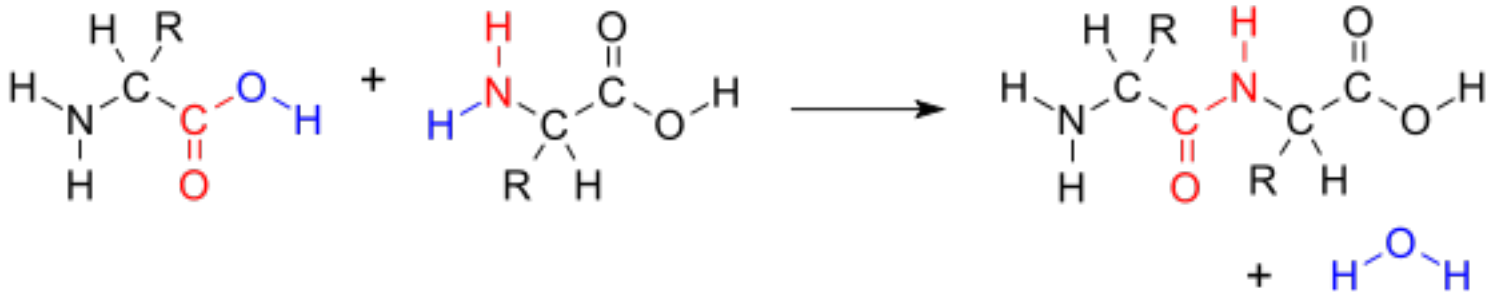


THAT'S RIGHT, FOU'REYES!  
YOU'RE **NOTHING**  
WITHOUT ME! WHILE  
I'M AN ESSENTIAL PART  
OF ANY PROTEIN, EVEN  
**YOURS**, YOU'RE STILL  
A SO-SO PROFESSOR  
WITH **NO CHANCE**  
OF TENURE! **HAHAHA**

a mean o' acid

# Proteins are chains of amino acids

- Amino acids link together through a chemical reaction (“condensation”)

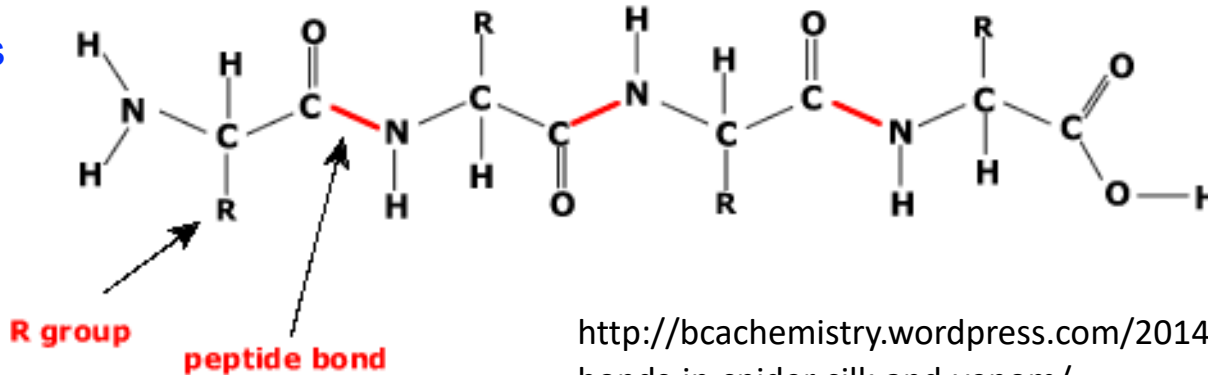


[http://en.wikipedia.org/wiki/Condensation\\_reaction](http://en.wikipedia.org/wiki/Condensation_reaction)

- Strictly speaking, elements of the chain are amino acid *residues*. They are usually called “**residues**” (important term!)
- The bonds linking these residues are “peptide bonds.” The chains are also called “polypeptides”

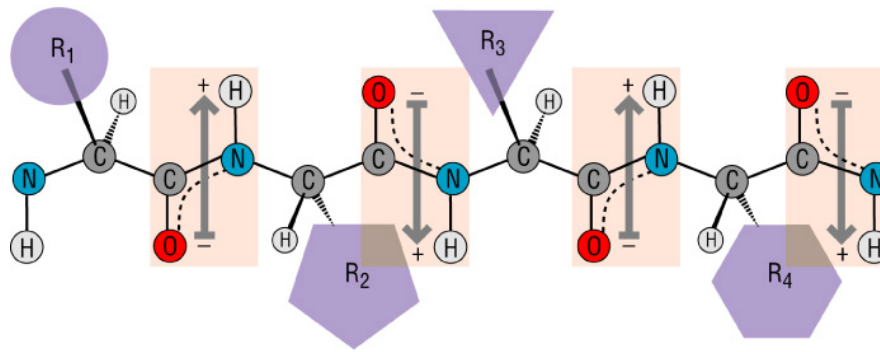
# Proteins have uniform backbones with differing side chains

“Backbones” are the atoms going along the center of the chain



<http://bcachemistry.wordpress.com/2014/05/28/chemical-bonds-in-spider-silk-and-venom/>

From **Protein Structure and Function** by Gregory A Petsko and Dagmar Ringe



“Side chains” are the R groups and are different for each amino acid

What determines the 3D structure of a protein?  
Physics underlying biomolecular structure

# Why do proteins have well-defined structure?

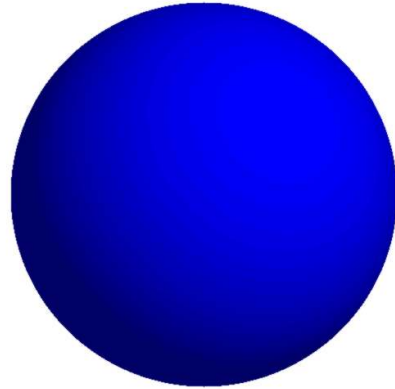
- The sequence of amino acids in a protein (usually) suffices to determine its structure.
- A chain of amino acids (usually) “folds” spontaneously into the protein’s preferred structure, known as the “native structure”
- Why?
  - Intuitively: some amino acids prefer to be inside, some prefer to be outside, some pairs prefer to be near one another, etc.
  - To understand this better, examine forces acting between atoms

Exception: Prions (associated with mad cow disease) are proteins that occur naturally in the brain. The default configuration is not its preferred structure. Over time, they adopt their preferred structure

What determines the 3D structure of a protein?  
Physics underlying biomolecular structure

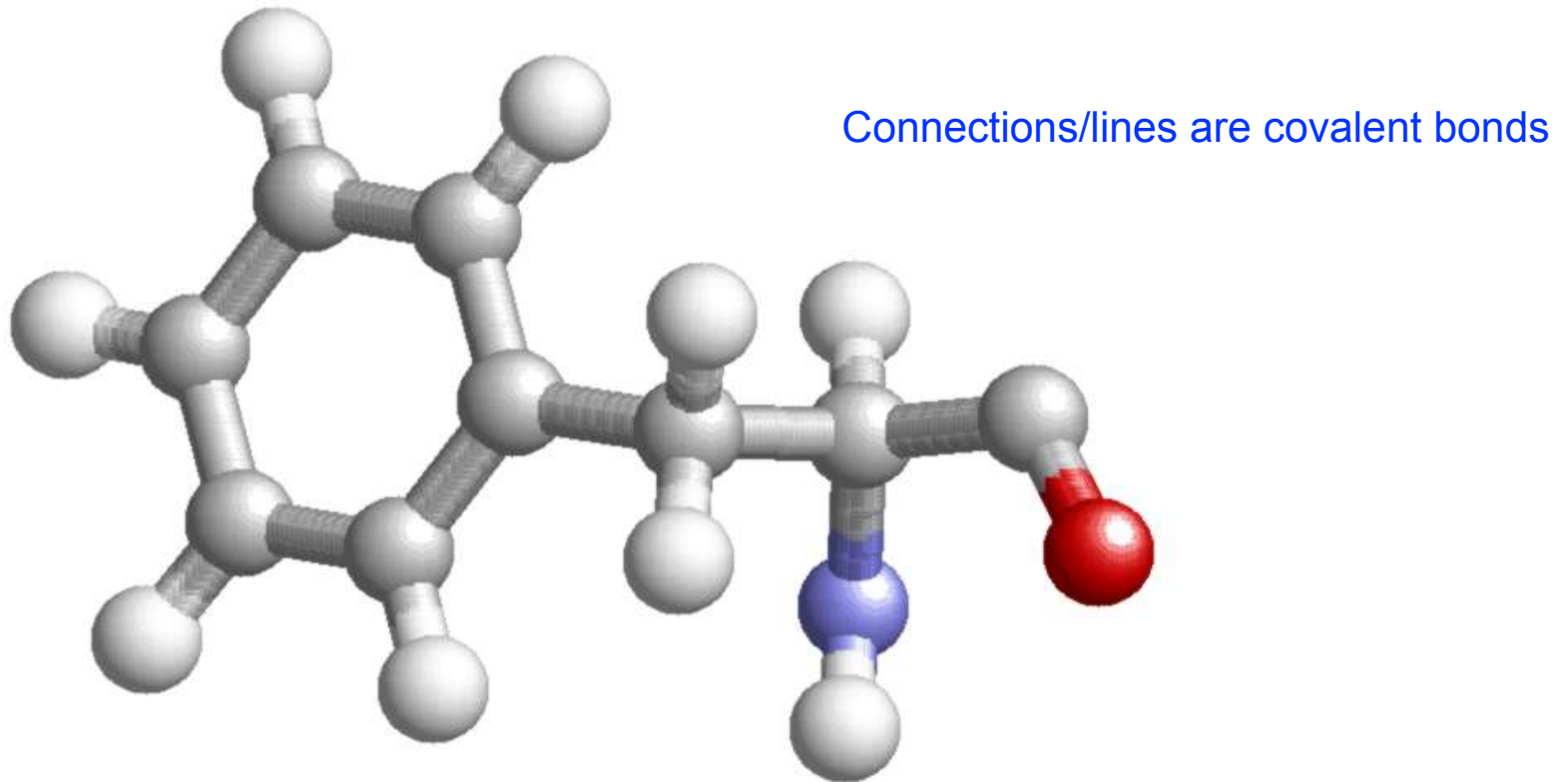
**Basic interactions**

# Geometry of an atom



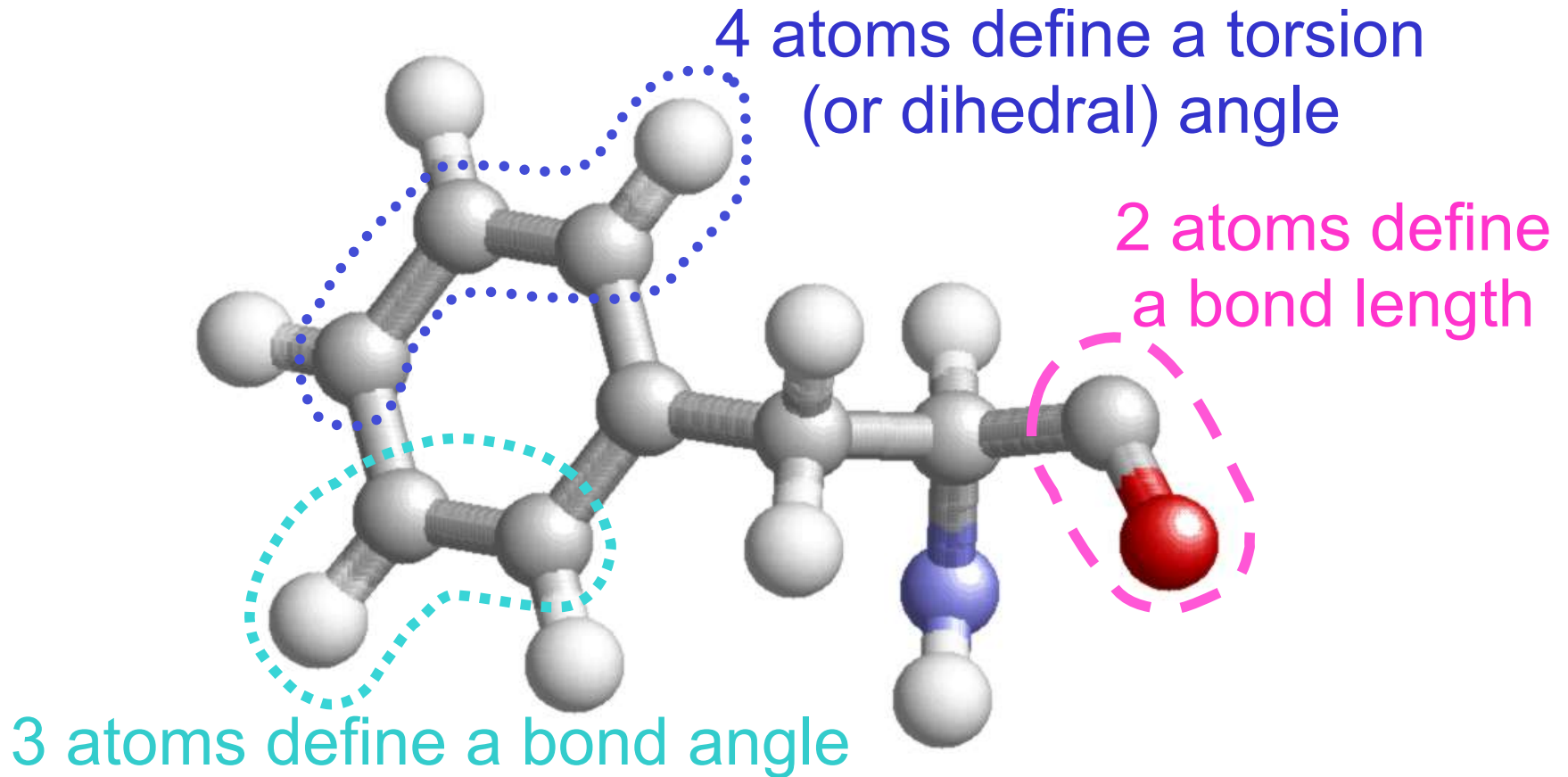
- To a first approximation (which suffices for the purposes of this course), we can think of an atom simply as a sphere.
- It occupies a position in space, specified by the  $(x, y, z)$  coordinates of its center, at a given point in time

# Geometry of a molecule



- A molecule is a set of atoms connected in a graph
- $(x, y, z)$  coordinates of every atom specify the molecule's geometry

# Geometry of a molecule



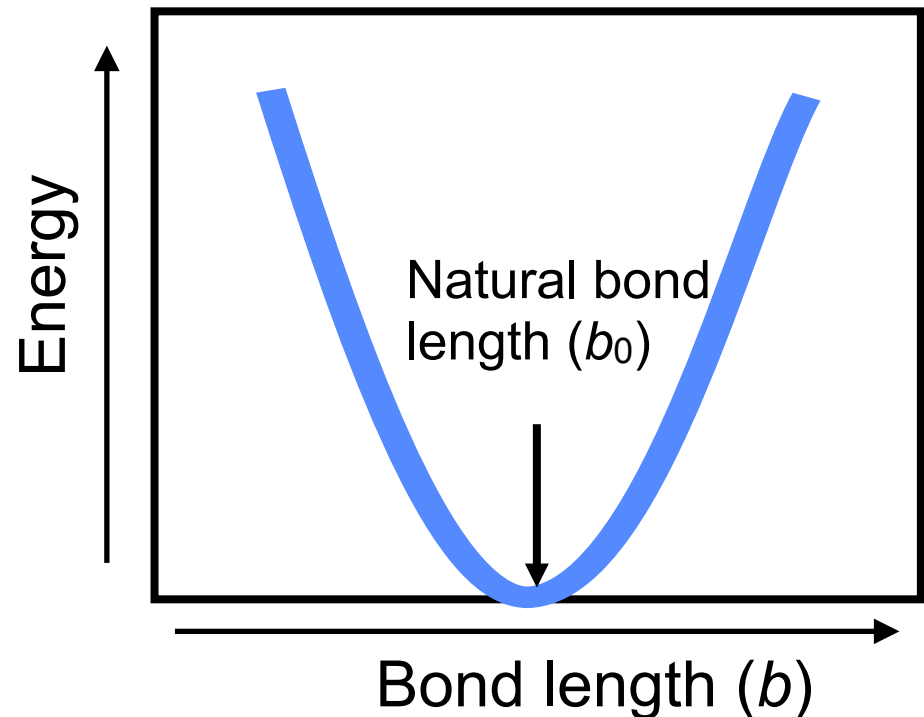
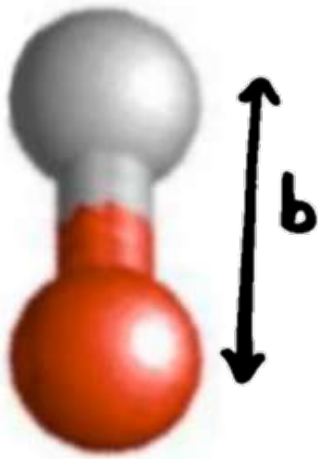
- Alternatively, we can specify the geometry of a molecule using bond lengths, bond angles, and torsion angles

# Forces between atoms

- We can approximate the total potential energy of a molecular system as a sum of individual contributions. Terms are additive.
  - Thus force on each atom is also a sum of individual contributions. Remember: force is the derivative of energy.
  - We will ignore quantum effects. Think of atoms as balls and forces as springs.
- Two types of forces:
  - Bonded forces: act between closely connected sets of atoms in the graph of covalent bonds
  - Non-bonded forces: act between all pairs of atoms

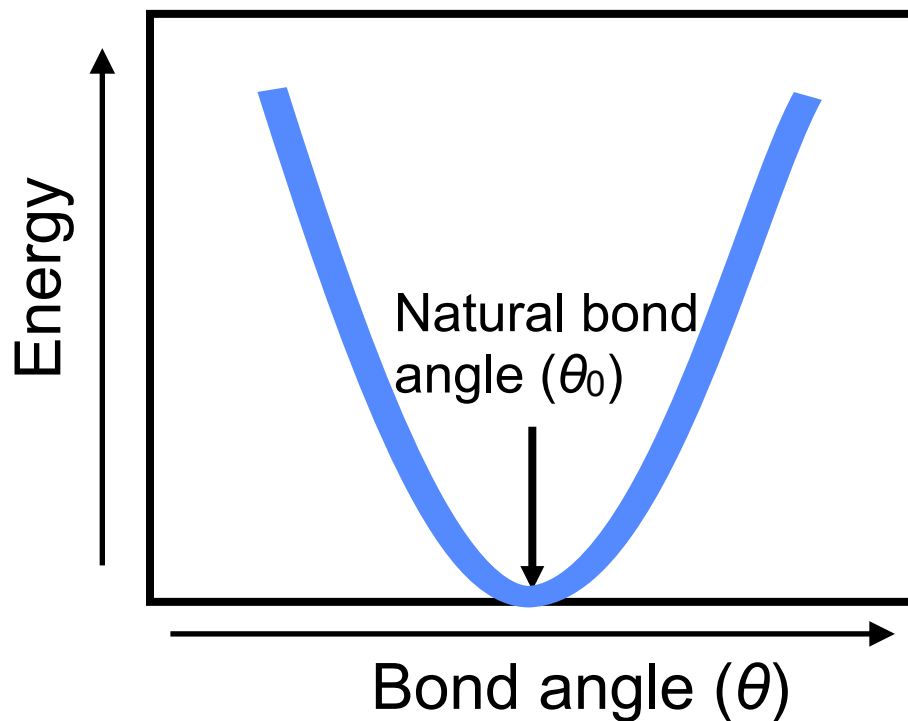
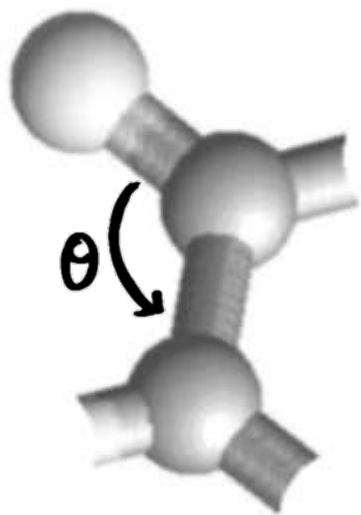
# Bond length stretching

- A covalently bonded pair of atoms is effectively connected by a “spring” with some preferred (natural) length. Stretching or compressing this spring requires energy.



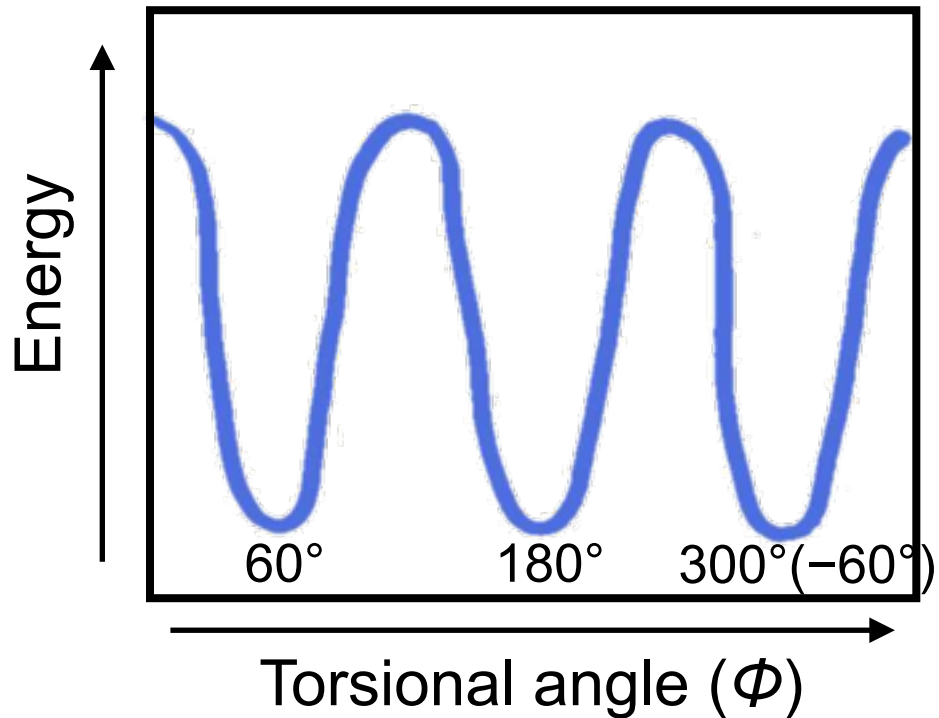
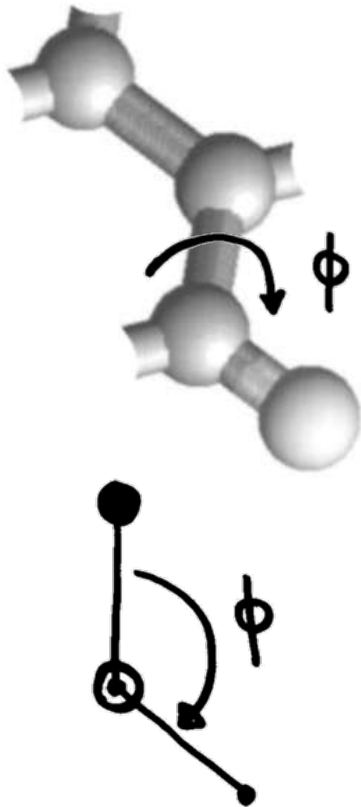
# Bond angle bending

- Likewise, each bond angle has some natural value. Increasing or decreasing this angle requires energy.

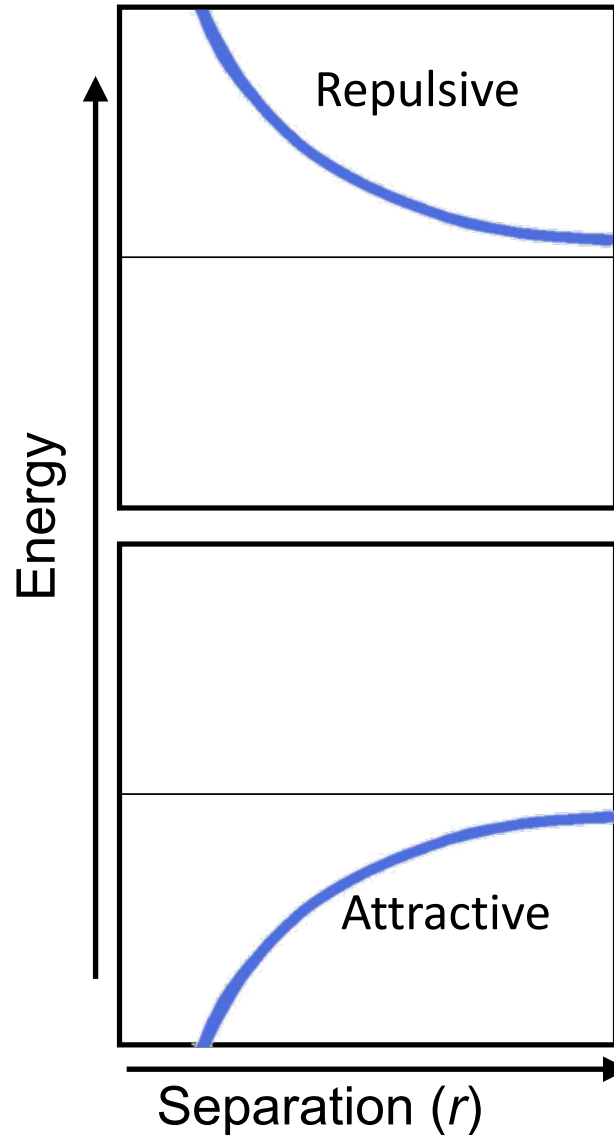
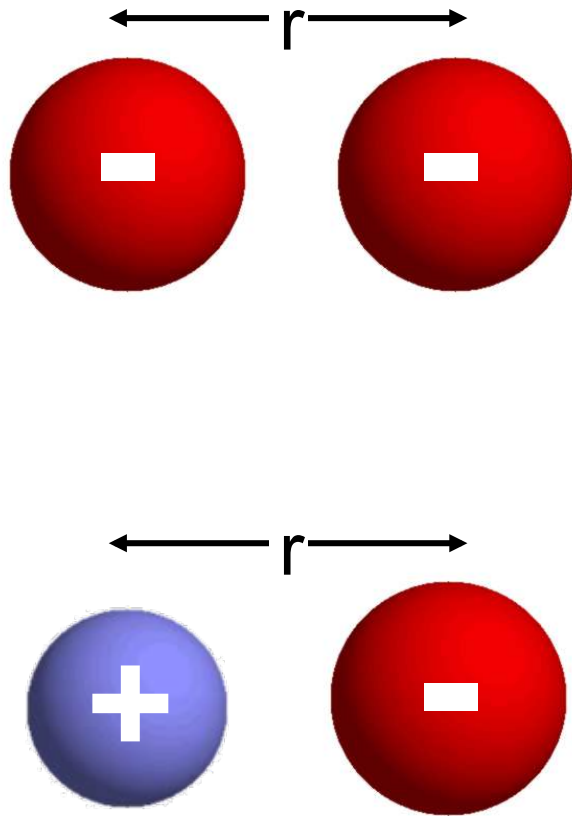


# Torsional angle twisting

- Certain values of each torsional angle are preferred over others.

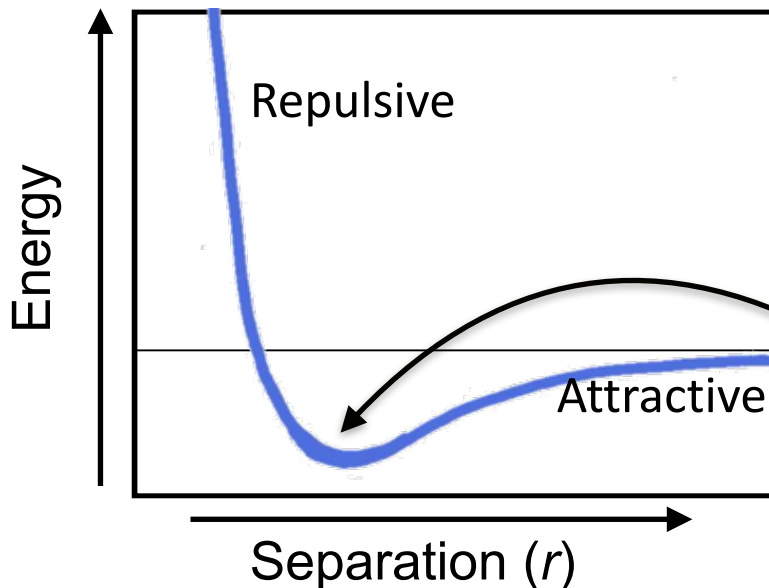
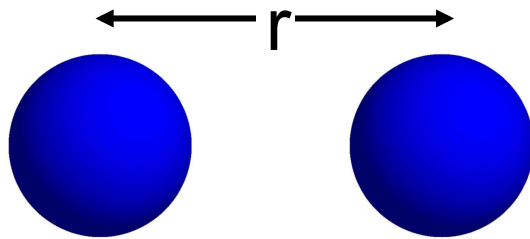


# Electrostatic interaction



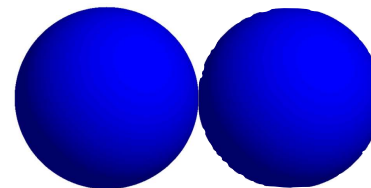
- Like charges repel. Opposite charges attract.
- Electrostatic forces act between all pairs of atoms, including those in different molecules.
- Each atom carries some “partial charge” (may be a fraction of an elementary charge), which depends on which other atoms it’s connected to.

# van der Waals interaction



- van der Waals forces act between all pairs of atoms and do not depend on charge.
- When two atoms are too close together, they repel strongly.
- When two atoms are a bit further apart, they attract one another weakly.

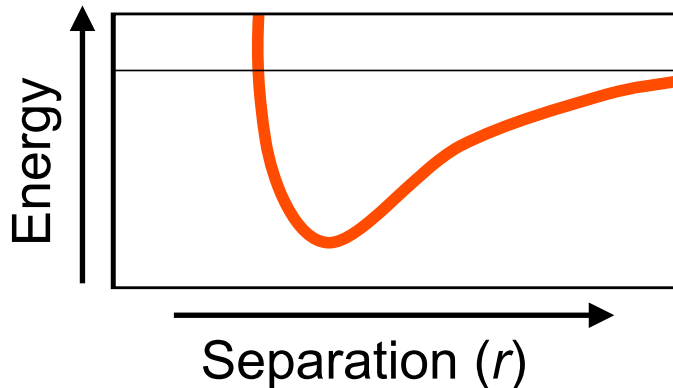
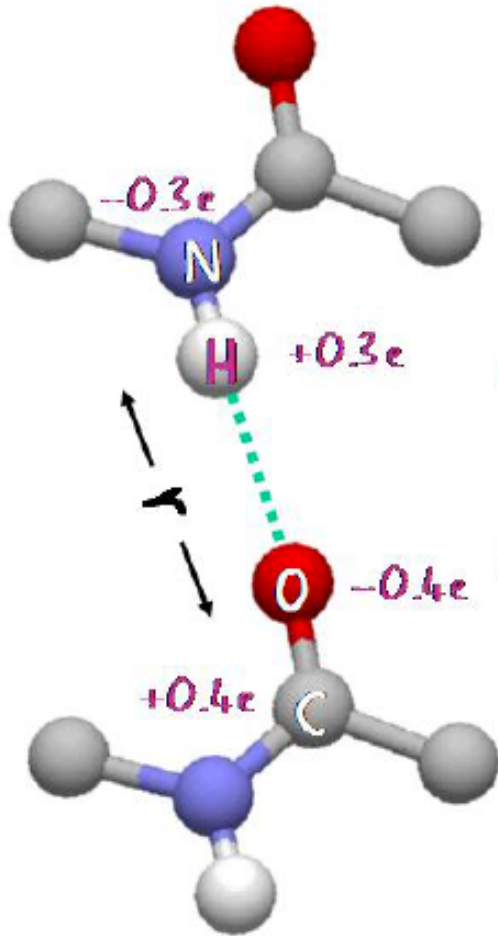
Energy is minimal when atoms are "just touching" one another



What determines the 3D structure of a protein?  
Physics underlying biomolecular structure

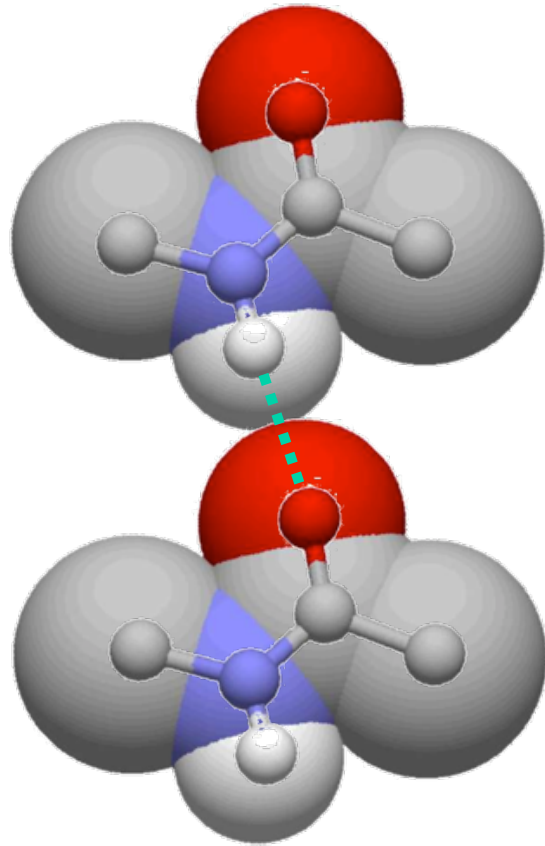
**Complex interactions**

# Hydrogen bonds

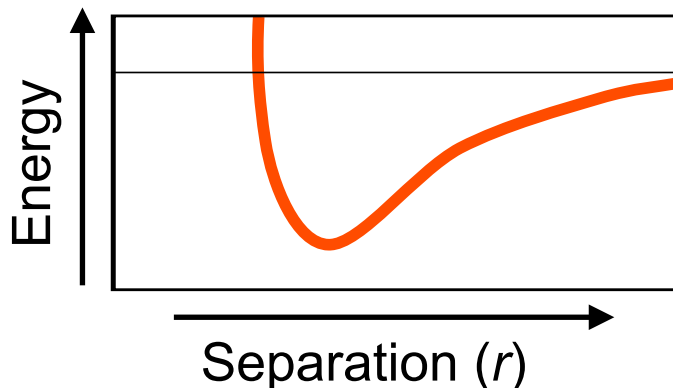


- Favorable interaction between an electronegative atom (e.g., N or O) and a hydrogen bound to another electronegative atom
- Result of multiple electrostatic and van der Waals interactions
- Very sensitive to geometry of the atoms (distance and alignment)
- Strong relative to typical van der Waals or electrostatic forces
- Critical to protein structure

# Hydrogen bonds

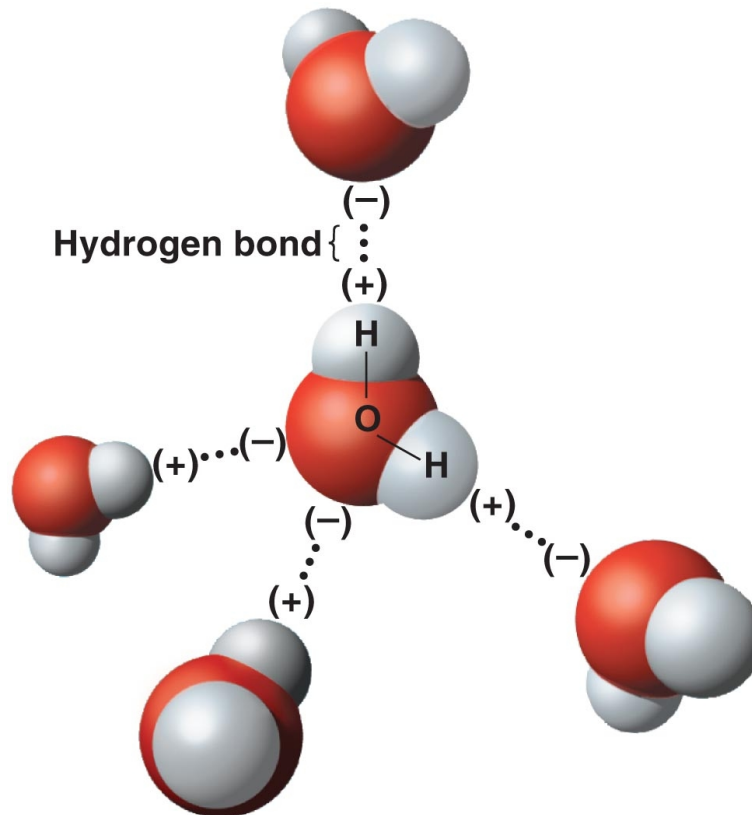


- Favorable interaction between an electronegative atom (e.g., N or O) and a hydrogen bound to another electronegative atom
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# Water molecules form hydrogen bonds

- Water molecules form extensive hydrogen bonds with one another and with protein atoms
- The structure of most proteins depends on the fact that it is surrounded by water



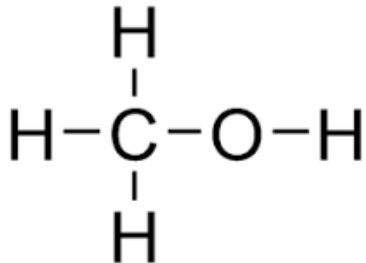
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<http://like-img.com/show/hydrogen-bond-water-molecule.html>

# Hydrophilic vs. hydrophobic

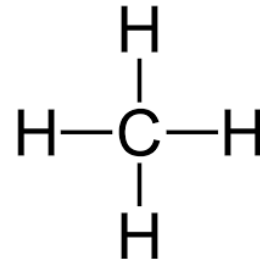
- Hydrophilic molecules are polar and thus form hydrogen bonds with water
  - Polar = contains charged atoms. Molecules containing oxygen or nitrogen are usually polar.
- Hydrophobic molecules are apolar and don't form hydrogen bonds with water “hydrophobic”: afraid of water

Hydrophilic (polar)



Methanol (the “bad” alcohol)

Hydrophobic (apolar)



Methane (natural gas)

# Hydrophobic effect

- Hydrophobic molecules cluster in water
  - “Oil and water don’t mix”

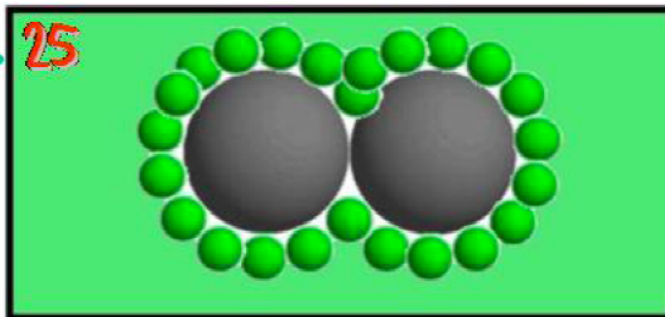
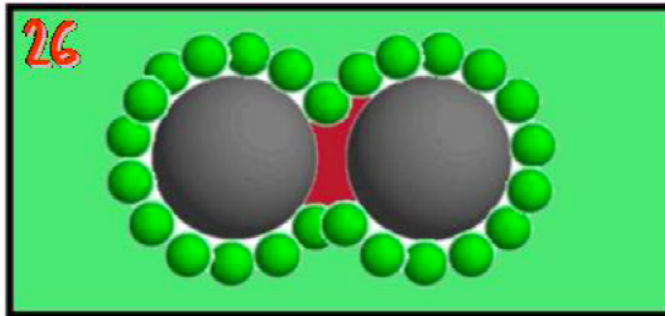
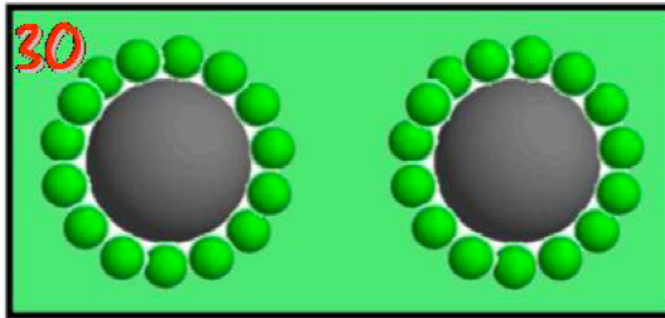


<http://science.taskermilward.org.uk/mod1/KS4Chemistry/AQA/Module2/Mod%20%20img/Oil-in-Water18.jpg>

- This is critical to protein structure
  - And other biomolecular structures!

# EXPLAINING HYDROPHOBICITY

Number of unhappy water molecules



- Water molecules next to solute cannot move freely.

- They are ordered and have less entropy. They are unhappy.

- The system changes so that fewer water molecules are in the surface layer.

- The hydrophobic solutes aggregate.

©Michael Levitt 04

Slide from Michael Levitt

- We will discuss entropy next week. If this isn't clear now, don't worry.

Protein structure: a more detailed view

# “Levels” of protein structure

- Primary structure: sequence of amino acids
- Secondary structure: local structural elements
- Tertiary structure: overall structure of the polypeptide chain
- Quaternary structure: how multiple polypeptide chains come together

Protein structure: a more detailed view

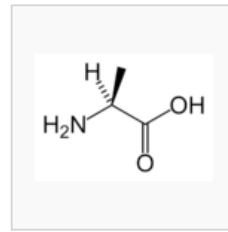
**Properties of amino acids**

# Proteins are built from amino acids

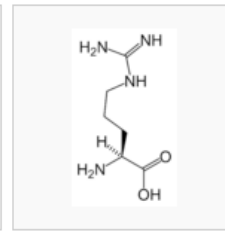
- 20 “standard” amino acids
- Each has three-letter and one-letter abbreviations (e.g., Threonine = Thr = T; Tryptophan = Trp = W)

The “side chain” is different in each amino acid

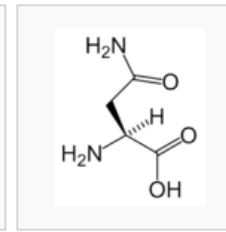
All amino acids have this part in common.



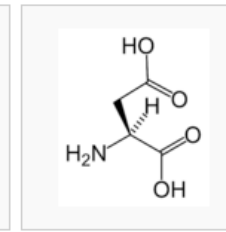
L-Alanine  
(Ala / A)



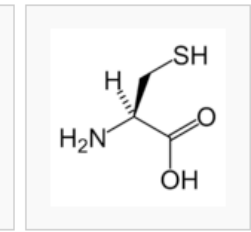
L-Arginine  
(Arg / R)



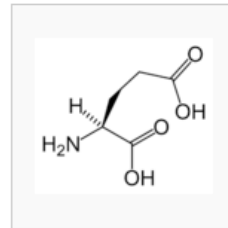
L-Asparagine  
(Asn / N)



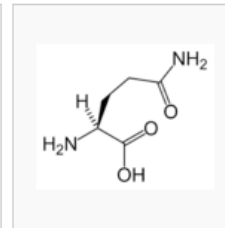
L-Aspartic acid  
(Asp / D)



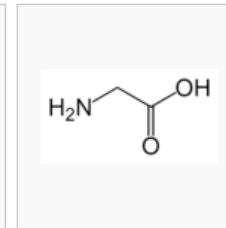
L-Cysteine  
(Cys / C)



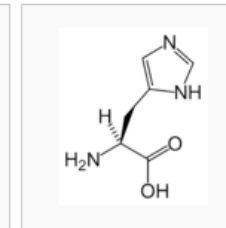
L-Glutamic acid  
(Glu / E)



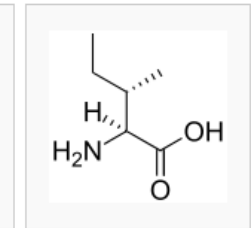
L-Glutamine  
(Gln / Q)



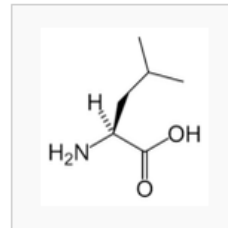
Glycine  
(Gly / G)



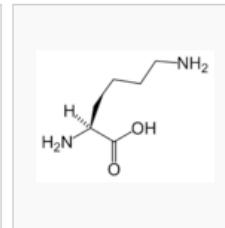
L-Histidine  
(His / H)



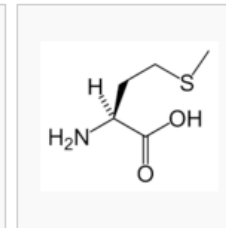
L-Isoleucine  
(Ile / I)



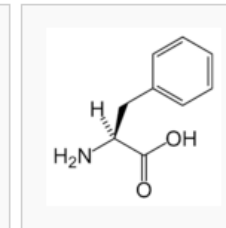
L-Leucine  
(Leu / L)



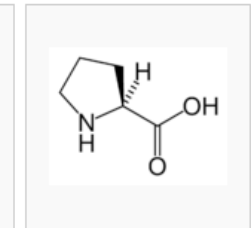
L-Lysine  
(Lys / K)



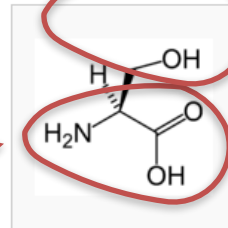
L-Methionine  
(Met / M)



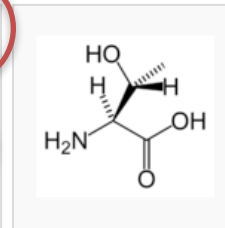
L-Phenylalanine  
(Phe / F)



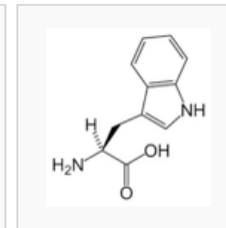
L-Proline  
(Pro / P)



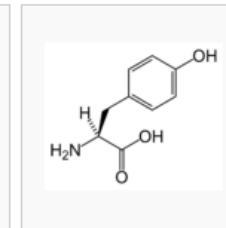
L-Serine  
(Ser / S)



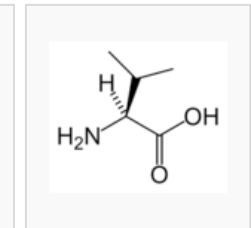
L-Threonine  
(Thr / T)



L-Tryptophan  
(Trp / W)



L-Tyrosine  
(Tyr / Y)



L-Valine  
(Val / V)

# Amino acid properties

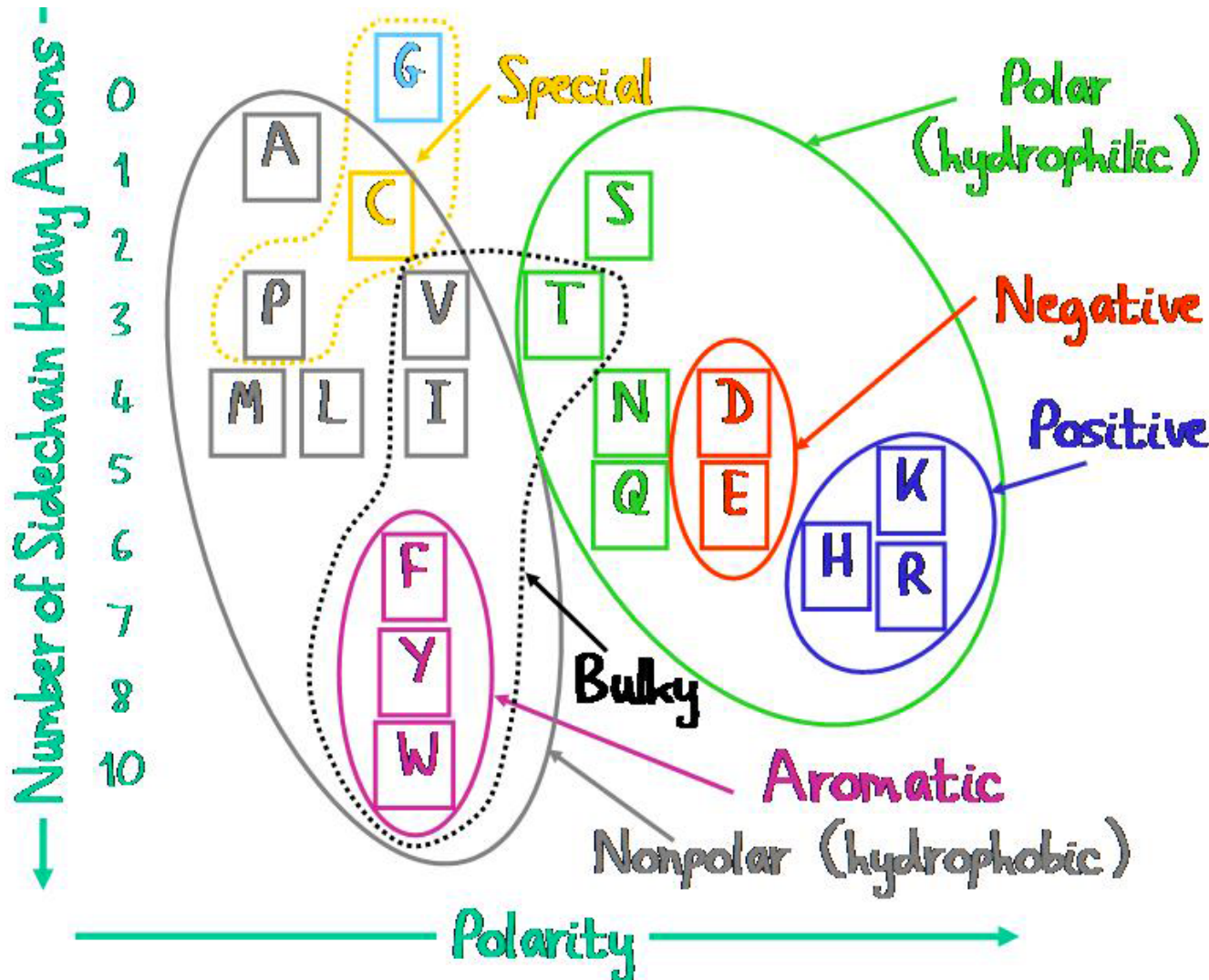
- Amino acid side chains have a wide range of properties. These differences bring about the 3D structures of proteins.
- Examples:
  - Large side chains take up more space than small ones
  - Negatively charged (acidic) side chains attract positively charged (basic) side chains
  - Hydrophilic side chains form hydrogen bonds to one another and to water molecules
  - Hydrophobic side chains “want” to be near one another

Hydrophilic = affinity for water

Hydrophobic = repels water

The hydrophobic effect occurs when hydrophobic substances aggregate together when in aqueous solutions, acting as if there was a force bringing them together. It is very important for determining protein structures.

# Amino acid properties



There are many properties.

They cluster logically.

Slide from Michael Levitt

44

You don't need to memorize which amino acids have which properties

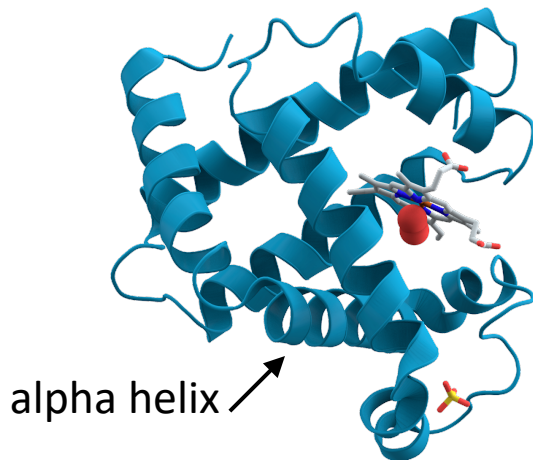
Protein structure: a more detailed view

**Secondary structure**

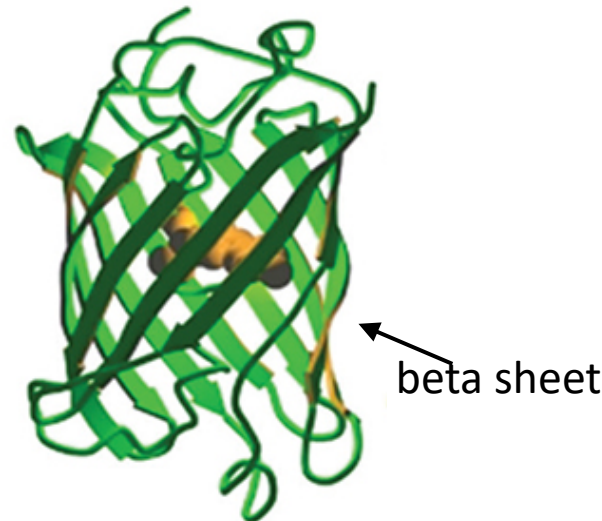
# Secondary structure

- “Secondary structure” refers to certain local structural elements found in many proteins
  - These are energetically favorable primarily because of hydrogen bonds between backbone atoms
- Most important secondary structure elements:
  - alpha helix
  - beta sheet

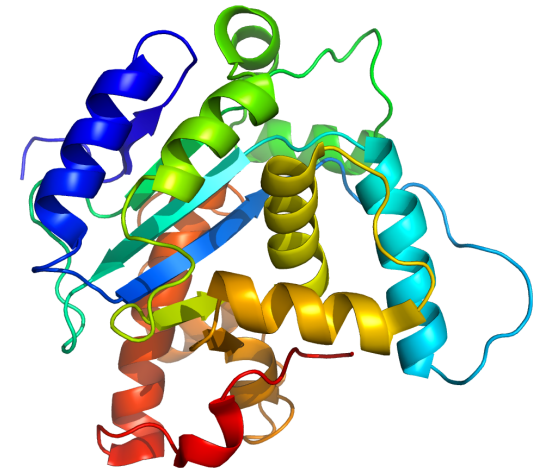
**Myoglobin**



**Green Fluorescent Protein**



**Pop2p**

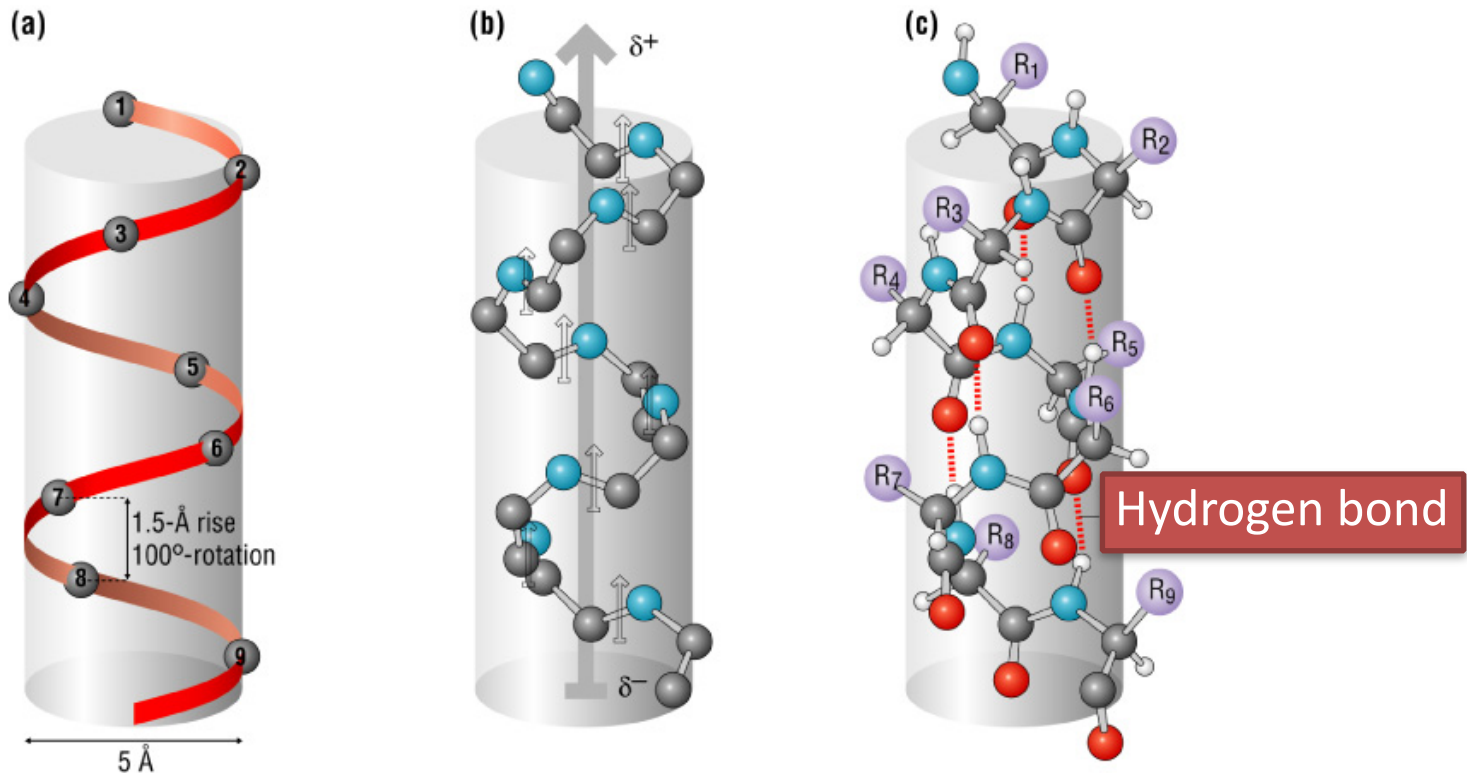


<https://upload.wikimedia.org/wikipedia/commons>,

[http://www.biotech.com/assets/tech\\_resources/11596/figure2.jpg](http://www.biotech.com/assets/tech_resources/11596/figure2.jpg)

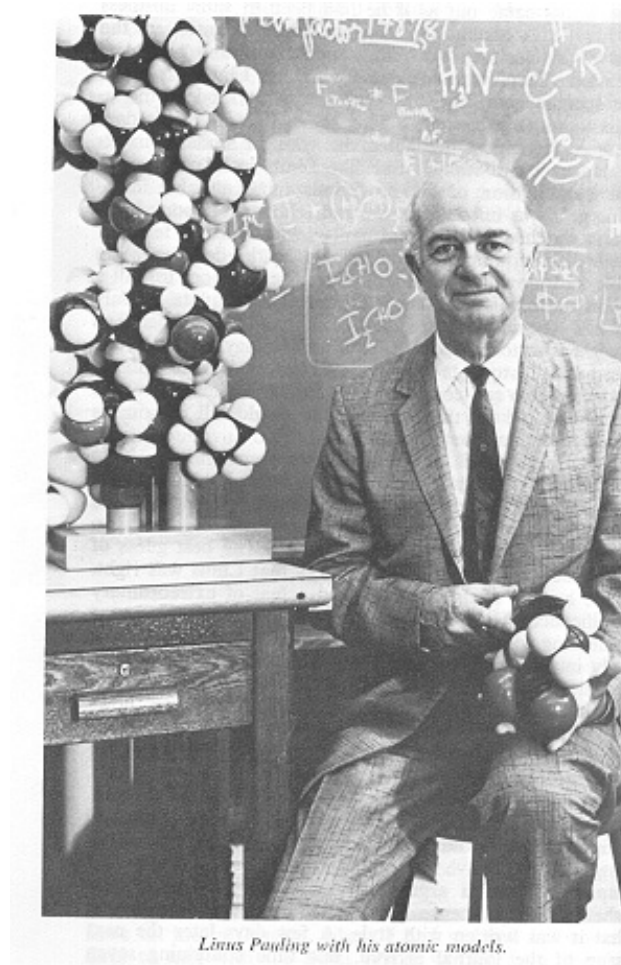
[http://upload.wikimedia.org/wikipedia/commons/e/e6/Spombe\\_Pop2p\\_protein\\_structure\\_rainbow.png](http://upload.wikimedia.org/wikipedia/commons/e/e6/Spombe_Pop2p_protein_structure_rainbow.png)

# The alpha helix



*Image from "Protein Structure and Function"  
by Gregory A Petsko and Dagmar Ringe*

# The alpha helix

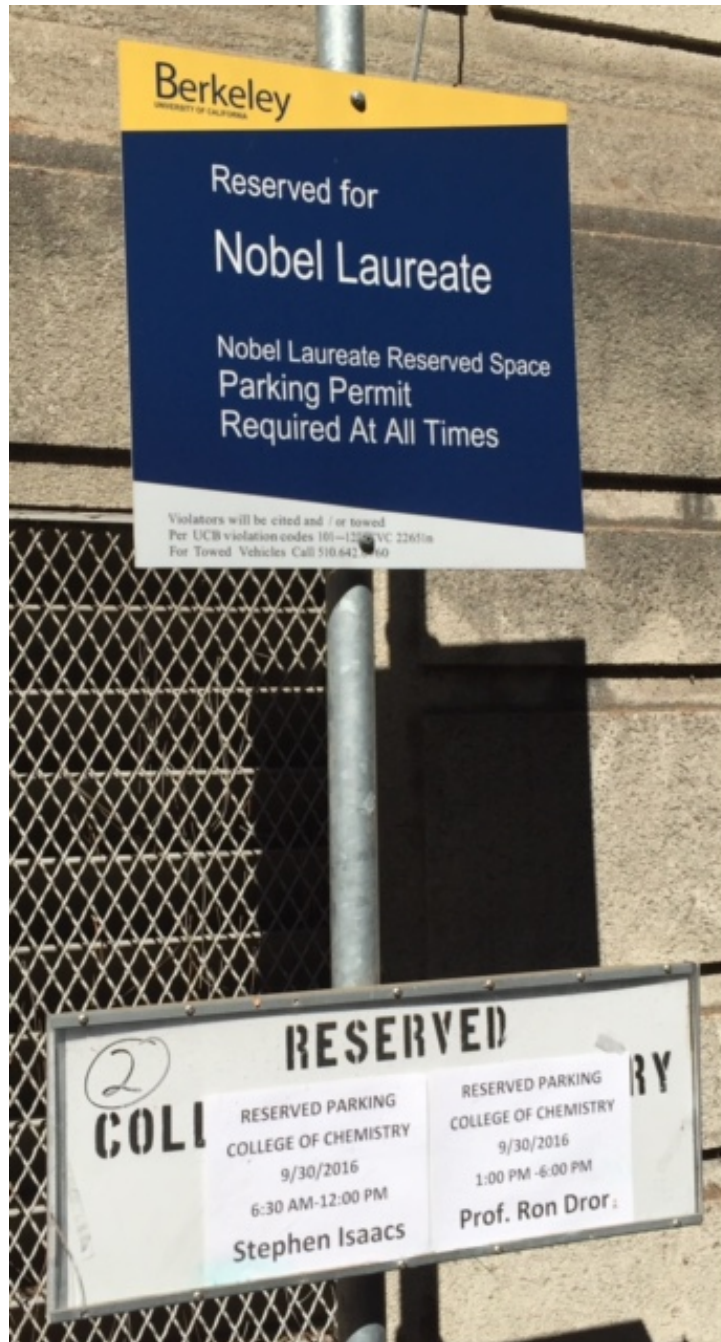


*Linus Pauling with his atomic models.*

Linus Pauling

The structure of the alpha helix was theoretically predicted in the 1950's, even before the actual structure was found.

<https://www.msu.edu/course/lbs/333/fall/images/PAULING.JPG>



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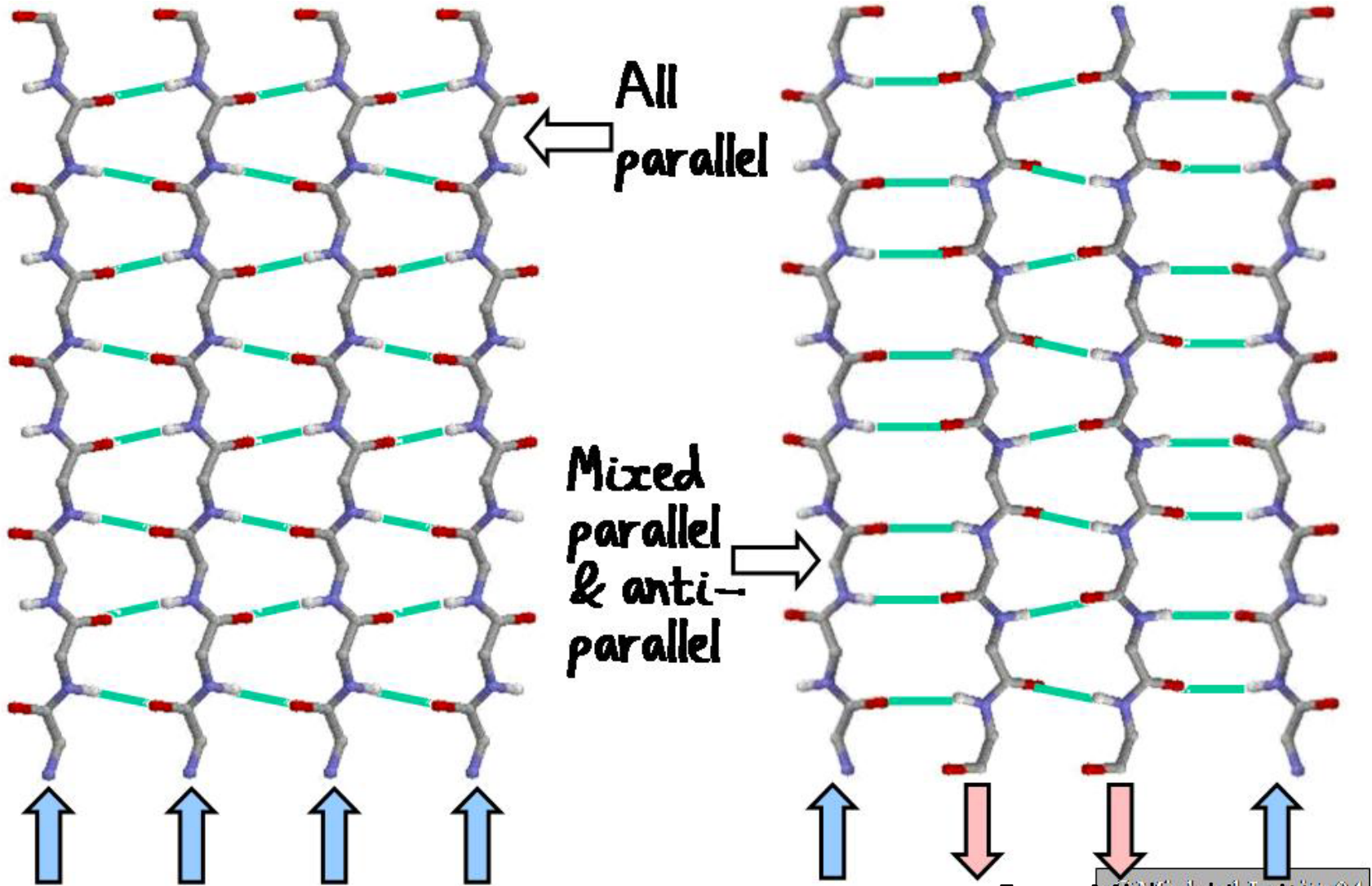
**RESERVED**

RESERVED PARKING  
COLLEGE OF CHEMISTRY  
9/30/2016  
6:30 AM-12:00 PM  
Stephen Isaacs

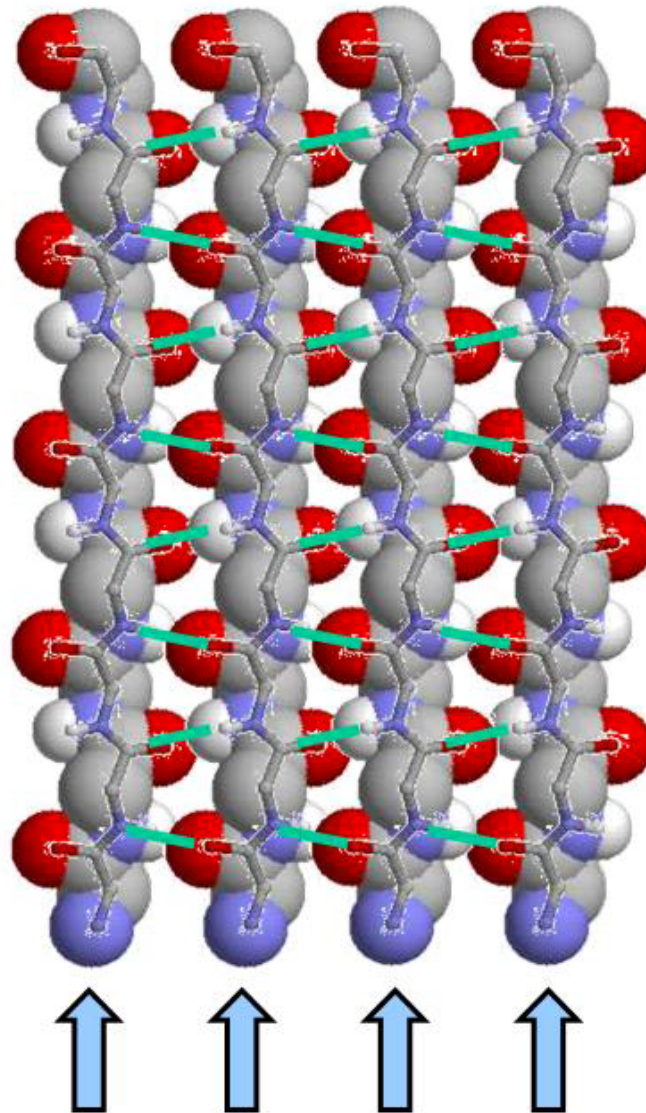
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COLLEGE OF CHEMISTRY  
9/30/2016  
1:00 PM-6:00 PM  
Prof. Ron Dror

RY

# The beta sheet



# The beta sheet



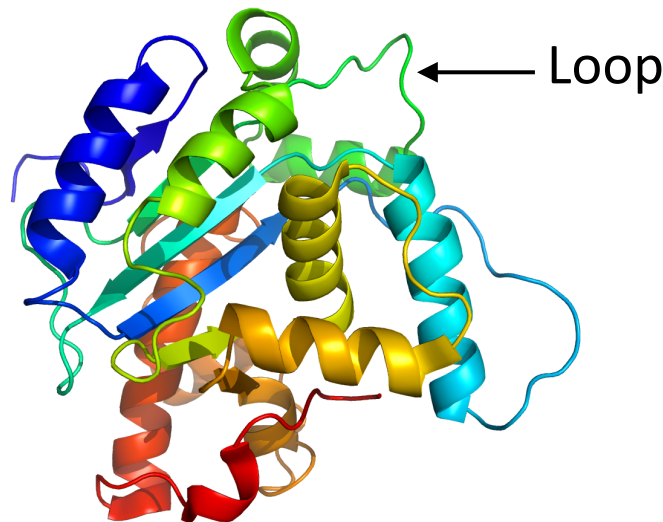
Green lines indicate hydrogen bonds between different strands

A *beta sheet* is made up of two or more *beta strands*, connected by hydrogen bonds

From Michael Levitt

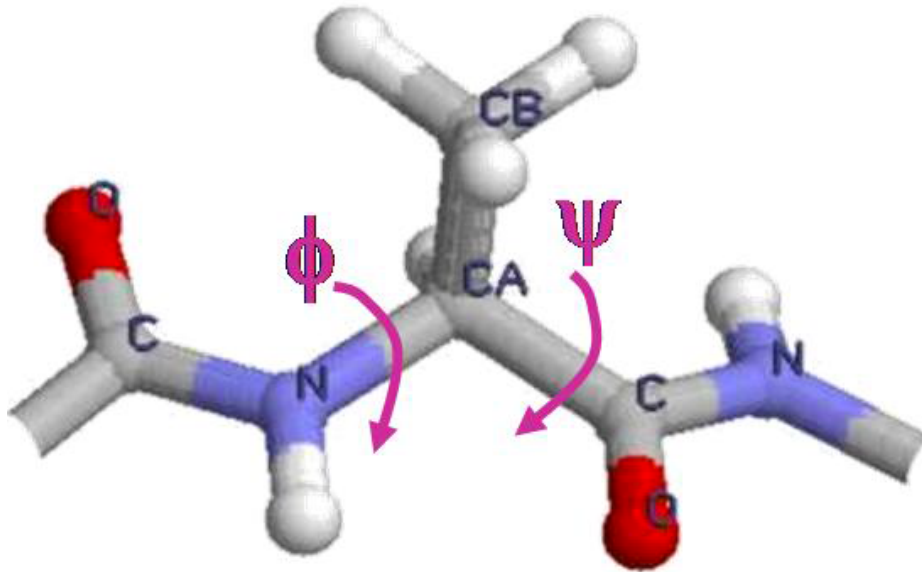
# Other secondary structure

- There are several less common secondary structures
- Regions connecting well-defined secondary structure elements are often referred to as “loops”



Loops connect different secondary structural elements

# BACKBONE DEGREES OF FREEDOM



- The torsion angle rotating about the N-CA bond is called  $\phi$  "Phi"
- The torsion angle rotating about the CA-C bond is called  $\psi$  "Psi"
- Together they are the  $(\phi, \psi)$  angles

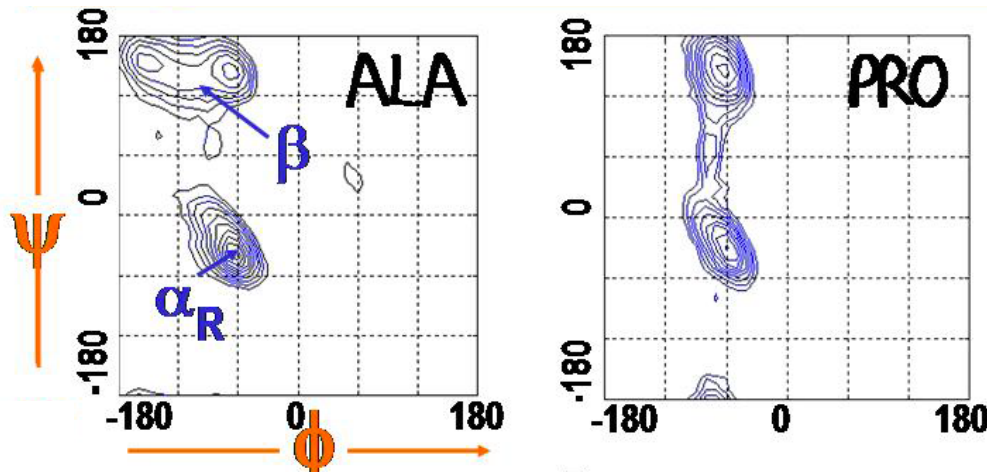
From Michael Levitt

- The remaining backbone bond (N-C, the "peptide bond") is rigid

Dihedral angles (aka torsion angles) are formed between 3 consecutive bonds in a molecule. They are defined by the angle created from the 2 outer bonds.

# Ramachandran diagrams

- A plot showing a distribution in the ( $\Phi$ ,  $\Psi$ ) plane is called a Ramachandran diagram
  - Such a diagram can be a scatterplot, or a two-dimensional histogram visualized as a contour map or heat map
  - For example, one might make a Ramachandran diagram for many residues of the same amino acid type
- Some amino acid types have distinctive Ramachandran diagrams



Ala is typical  
Pro is unusual

Image from  
Michael Levitt

- Alpha helices and beta sheets have characteristic Ramachandran diagrams

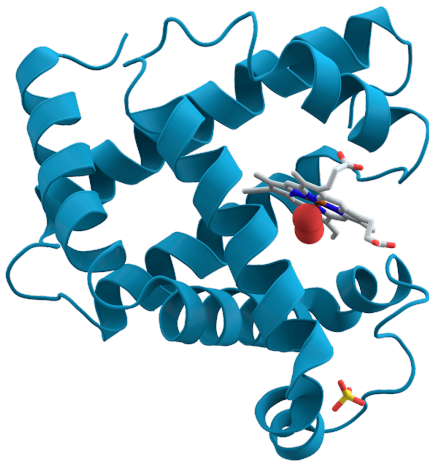
Protein structure: a more detailed view

**Tertiary structure, quaternary structure,  
and domains**

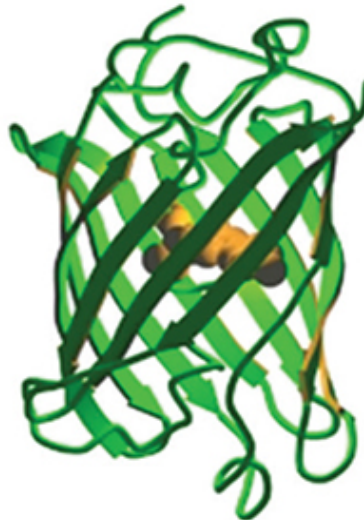
# Tertiary structure

- Tertiary structure: the overall three-dimensional structure of a polypeptide chain

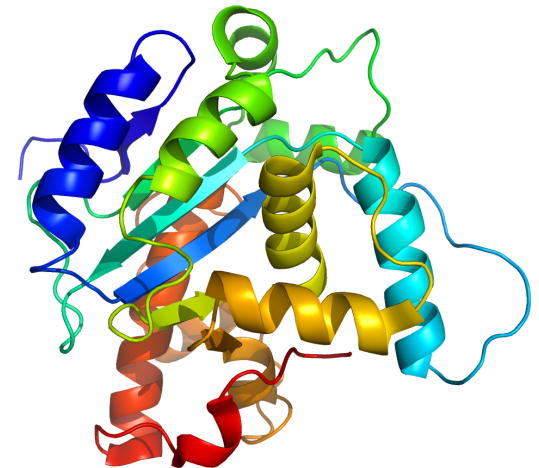
**Myoglobin**



**Green Fluorescent Protein**



**Pop2p**

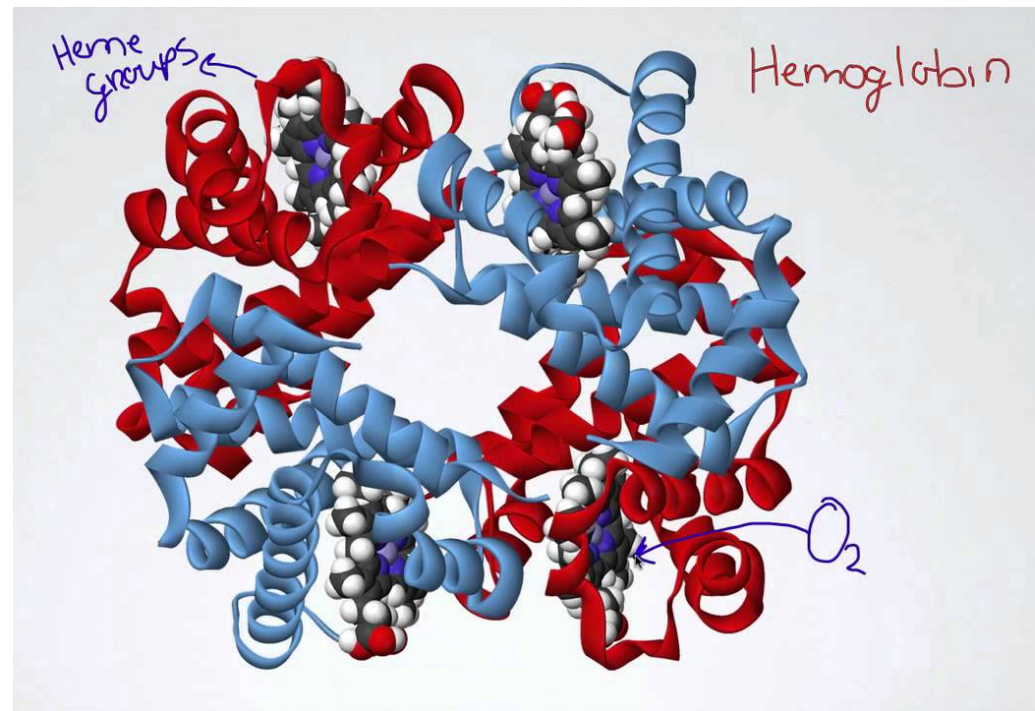
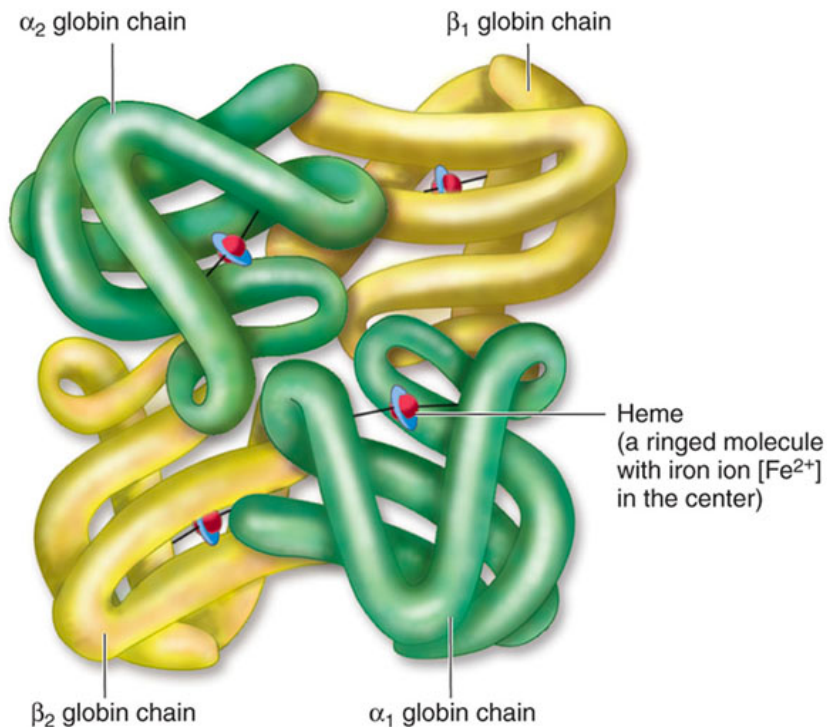


# Quaternary structure

- Quaternary structure: the arrangement of multiple polypeptide chains in a larger protein

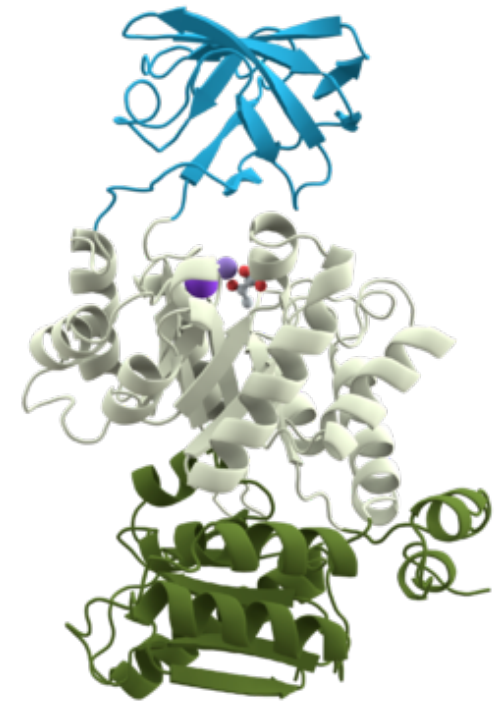
Hemoglobin is an oxygen carrier protein, made of 2 pairs of polypeptide chains called alpha and beta chains.

## Molecular Structure of Hemoglobin



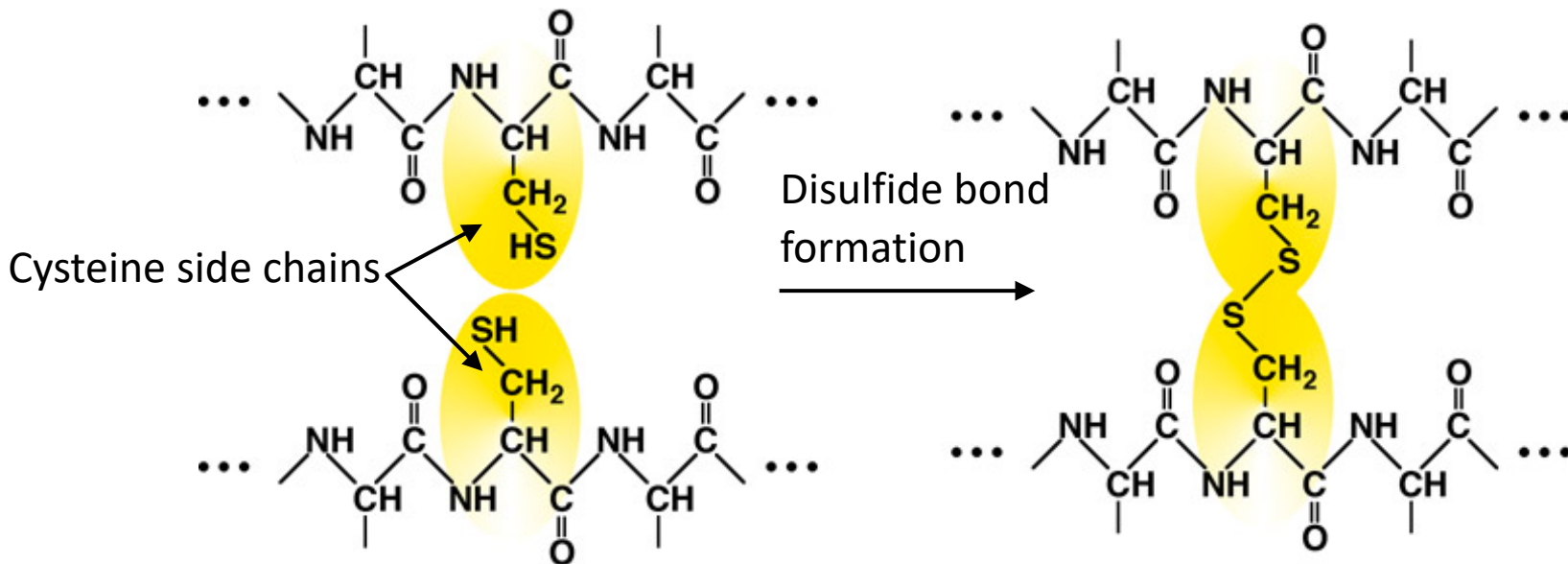
# Domains

- Large proteins often consist of multiple compact 3D structures called *domains*
  - Many contacts within a domain.  
Few contacts between domains.
  - “Domain  $\approx$  blob”
- One polypeptide chain can form multiple domains, and a single domain may include portions of several polypeptide chains



# Disulfide bonds

- One particular amino acid type, cysteine, can form a covalent bond with another cysteine (called a disulfide bond or bridge)
- Disulfide bonds can connect amino acid residues that are distant in the peptide chain
- In a typical cellular environment, disulfide bonds can be formed and broken quite easily



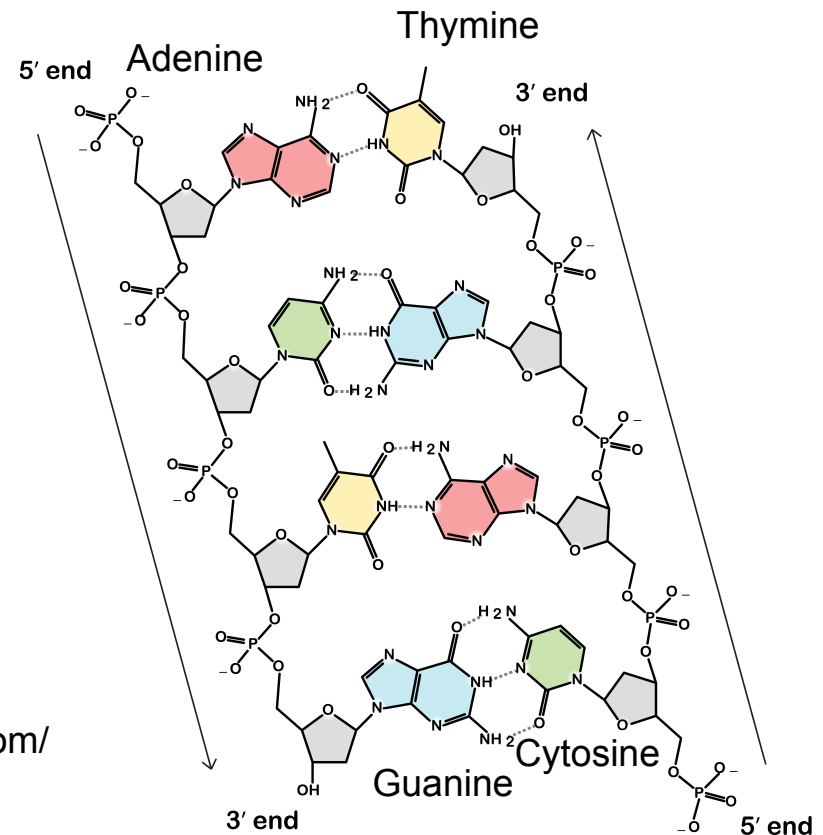
# Structures of other biomolecules

# What determines the structure of other biomolecules?

- The physical interactions that determine protein structure also determine the structures of other biomolecules
  - More generally, the great majority of the material covered in this course for proteins applies to other biomolecules as well

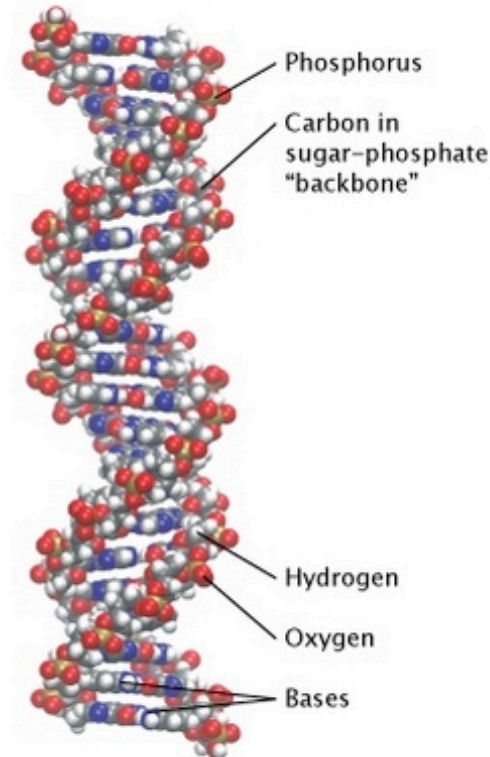
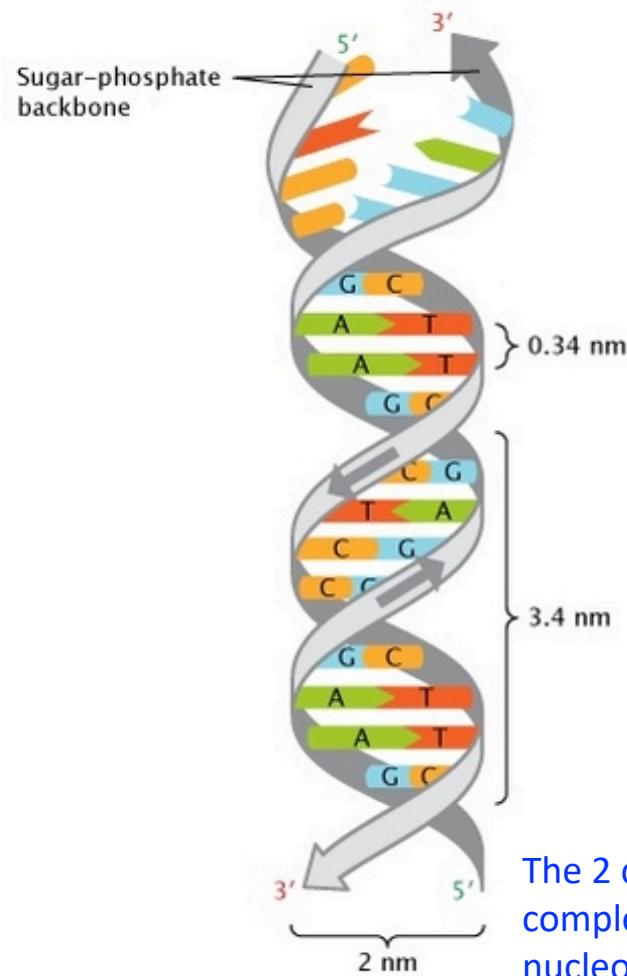
# DNA

- DNA (deoxyribonucleic acid) stores the genetic code
- DNA, like protein, is a string of units with a uniform backbone
  - The units are nucleotides, instead of amino acid residues
  - Different nucleotides contain different nucleobases (“bases”) instead of side chains
- Only four common DNA bases
  - Adenine pairs with Thymine
  - Guanine pairs with Cytosine



# DNA

- DNA forms one dominant 3D structure: a double helix
  - DNA usually acts more as information storage than as “machinery”
  - Long stretches of double helix can form coarser-scale structures



The 2 chains of DNA are complementary where the nucleotides pair up: adenine with thymine, guanine and cytosine



Cambridge, 1953. Shortly before discovering the structure of DNA, Watson and Crick, depressed by their lack of progress, visit the local pub.



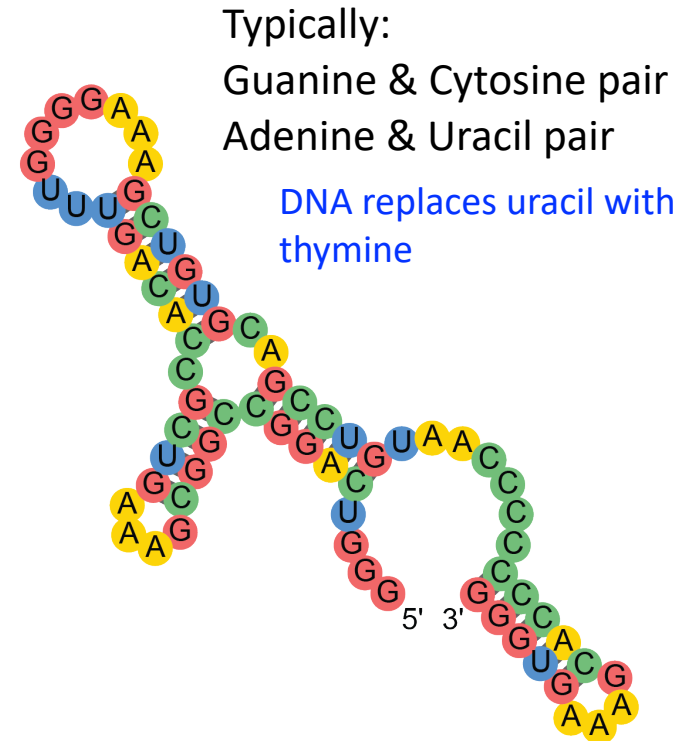
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"IT'S NOT SUPPOSED TO BE A  
TRIPLE HELIX, IS IT?"

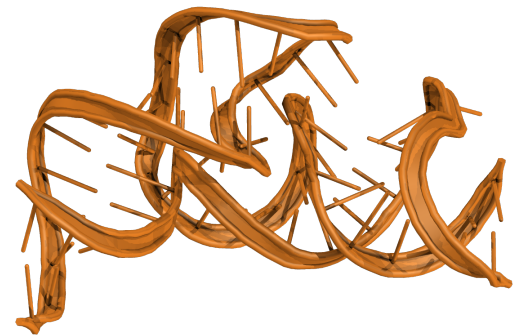
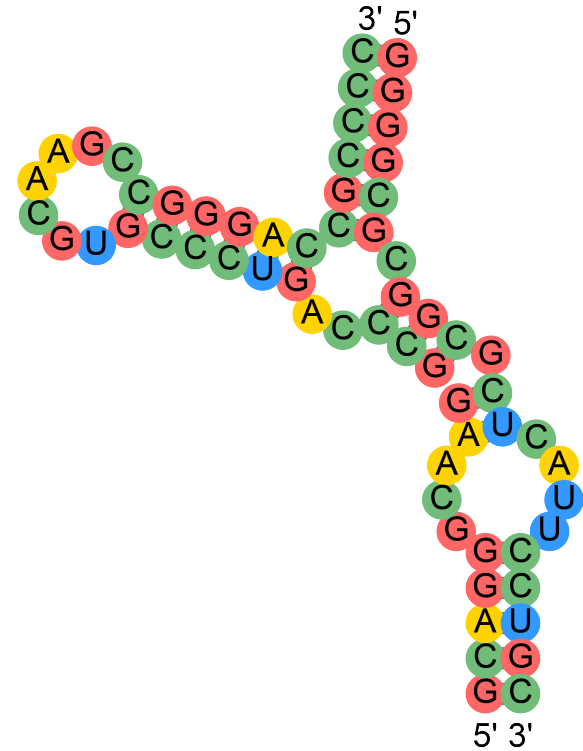
# RNA

- RNA (ribonucleic acid) is a string of nucleotides, like DNA
- RNA, however, frequently occurs as a single string (strand) rather than paired strands
- RNA bases often pair with other bases in the same RNA strand
  - Much work on RNA structure focuses on the “secondary structure”: which bases pair with one another
  - Note that “secondary structure” has different meanings for RNA and protein
- Some RNAs store the genetic code of proteins, but most serve other functions
- RNAs usually form “machines” with well-defined, varied 3D structure



# RNA

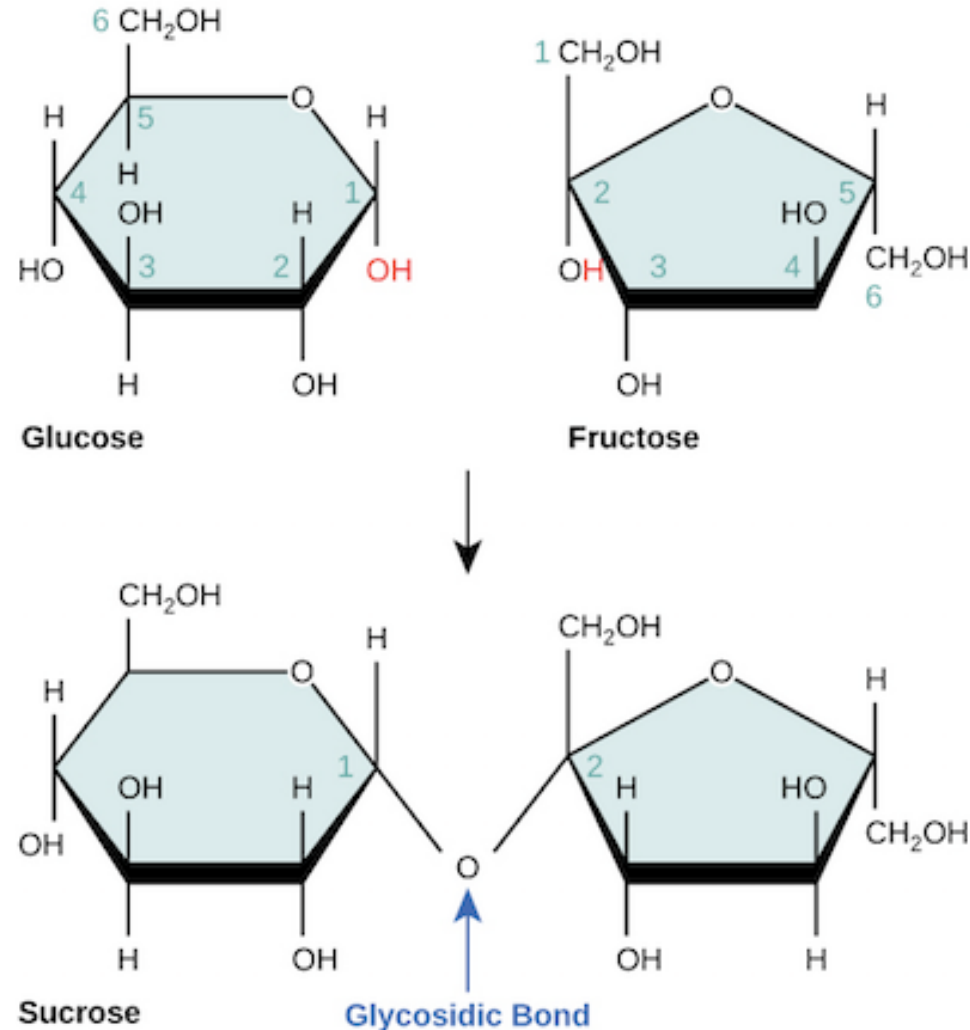
- Frequently, a single RNA is made up of multiple strands
  - Bases pair across strands
  - Secondary structure often includes multiple strands



Glycans are long chains of sugars linked by glycosidic bonds

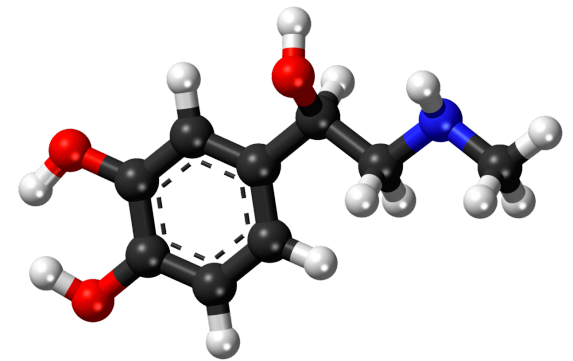
# Glycans (e.g. carbohydrates)

- The base units are called “mono-saccharides”
- When they are linked through glycosidic bond, they are called glycans
- Examples: starch, cellulose, chitin
- In cells, glycans are often attached to proteins (“glycosylation”)



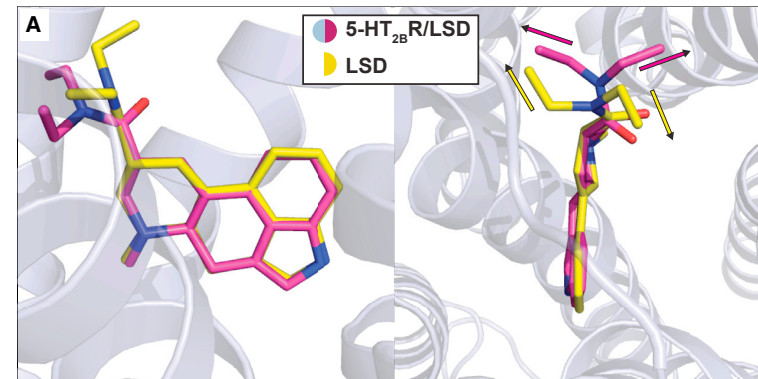
# Small molecules

- Most drugs and many hormones, neurotransmitters, and other natural signaling molecules are “small molecules” (~100 atoms or fewer)
- Cambridge Structural Database is a repository of small molecule 3D structures, generally from x-ray crystallography
- However, these molecules are usually highly flexible and thus likely to take on a different 3D structure when bound to a protein



Adrenaline (epinephrine)

[https://upload.wikimedia.org/wikipedia/commons/thumb/7/76/Epinephrine\\_ball-and-stick\\_model.png](https://upload.wikimedia.org/wikipedia/commons/thumb/7/76/Epinephrine_ball-and-stick_model.png)



LSD on its own (yellow) and receptor-bound (magenta)

Wacker et al., *Cell* (2017)

Because these molecules are small, it is difficult to determine 3D structures because there are many conformations with similar energy levels.

# Clarifications

(based on great questions from students)

- When you load into PyMol a PDB file that doesn't list covalent bonds, how can PyMol display the covalent bonds?
  - It infers them automatically
- What does “solving” a structure mean?
  - Determining it experimentally (which requires “solving” a computational problem to get atomic coordinates)

# Assignment 1

- Available on website
- Due Tuesday of next week
  - Congrats to those who have already started!
  - If you haven't, please start soon, and ask TAs if you need help.
- Options for computer use:
  - If you live on or near campus, we strongly recommend using one of many physical LTS clusters that have all necessary software pre-installed.
  - Otherwise, you can use LTS machines remotely—but start early, due to the limited number available for remote use.
    - Please avoid using this pool if you live on campus.
  - If you're experienced at command-line software installation, you can install the software on your own Mac (OSX) or Linux computer.