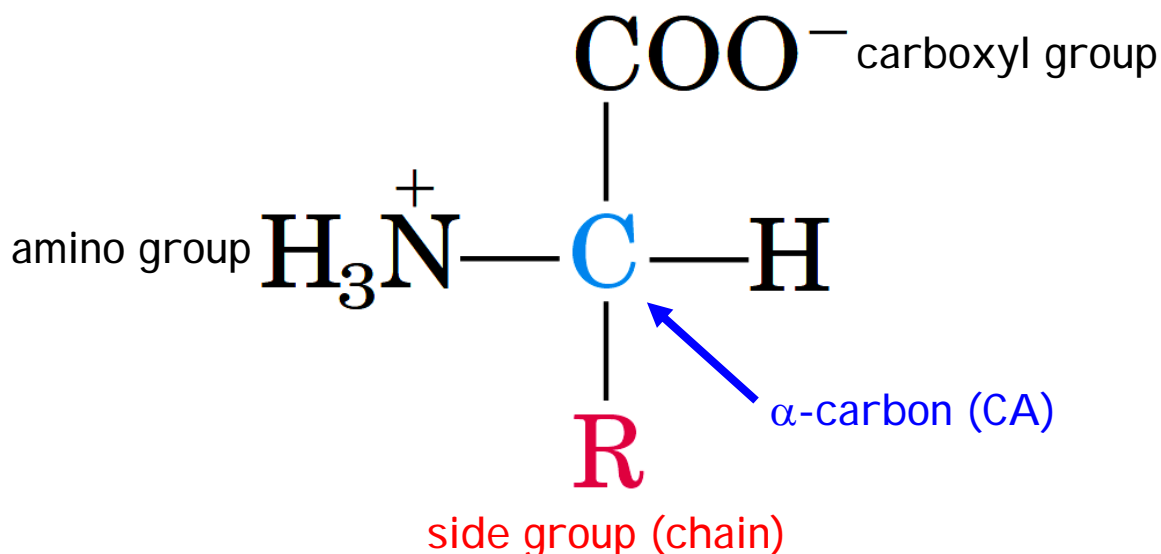# Basics of (Bio)Molecular Modeling

- Biopolymers: structure, function
- Amino acids and proteins
- Molecular visualization with VMD
- PDB files
- Proteins: conformation, dynamics
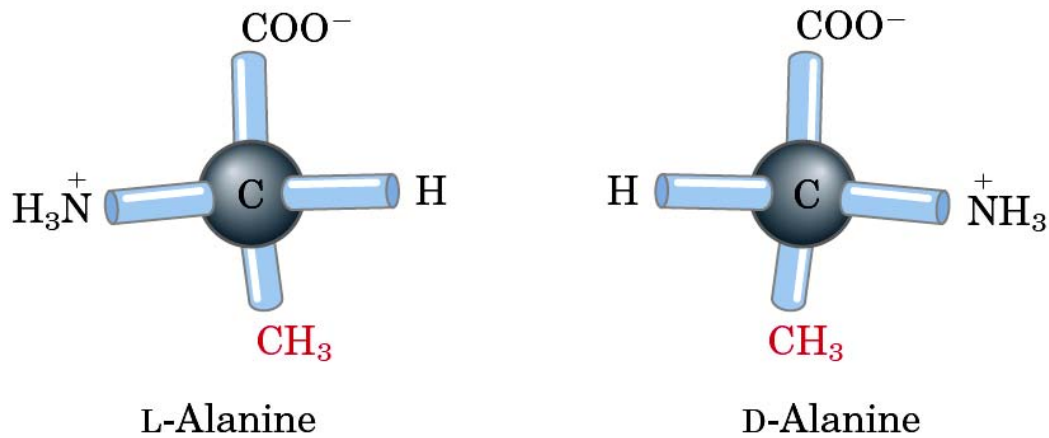- Computer simulation methods: MD, MC, QC

Hands-On

- Download protein structures from the Protein Data Bank
- VMD tutorial 1 (Basics)
- Tcl scripting (TclTutor)
- VMD tutorial 2 (Multiple molecules and scripting)

α-Amino Acids (AA)

▶ AA are the building blocks of proteins

▶ proteins are built from 20 AA
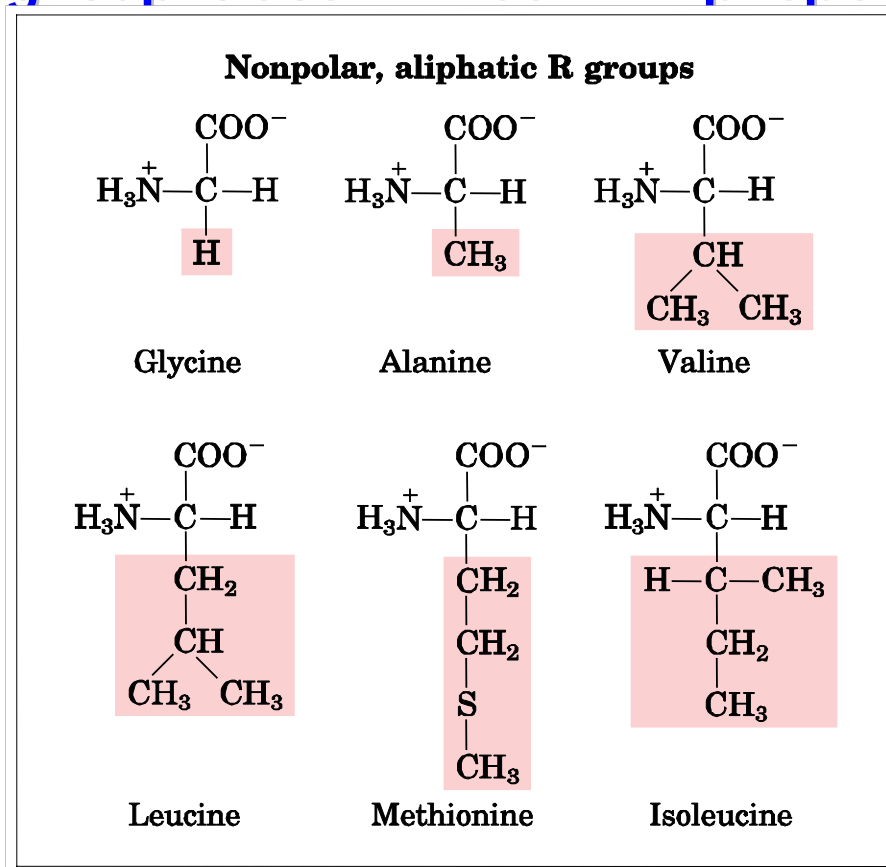
▶ common structure of AA (except *proline*)

amino group $H_3\overset{+}{N}$ — C — H   carboxyl group (COO$^-$)

α-carbon (CA)

R — side group (chain)
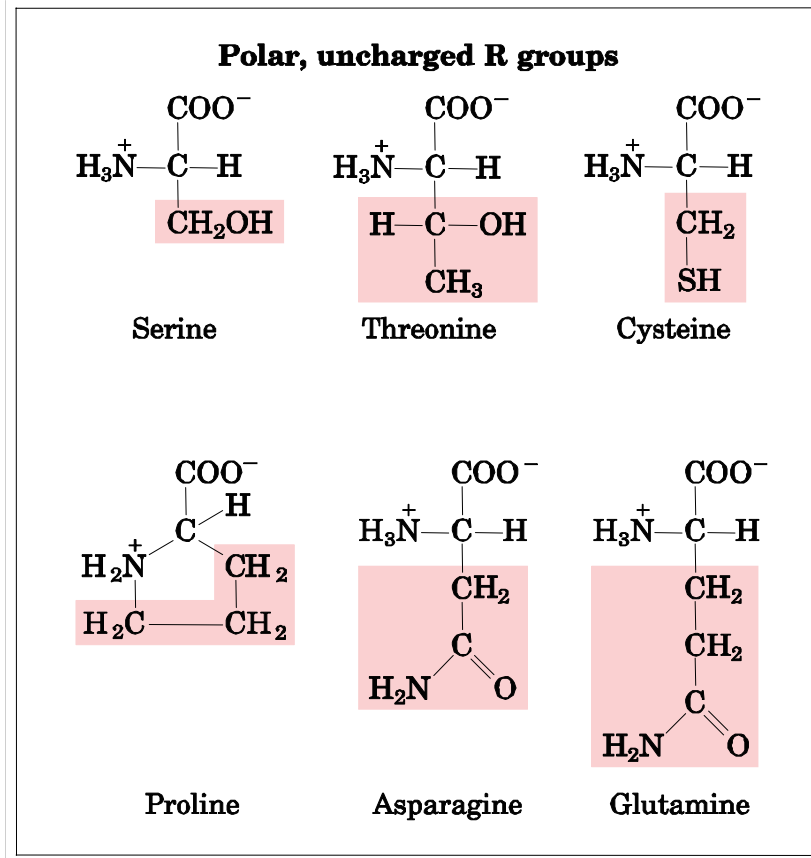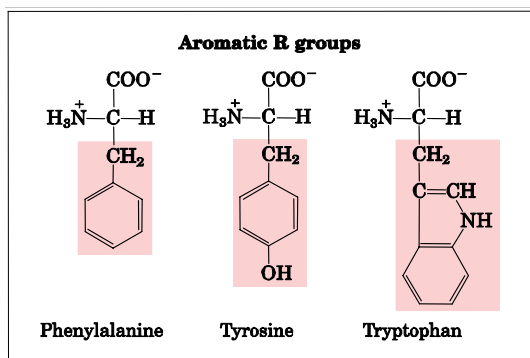
α-Amino Acids are Chiral

L-Alanine   D-Alanine

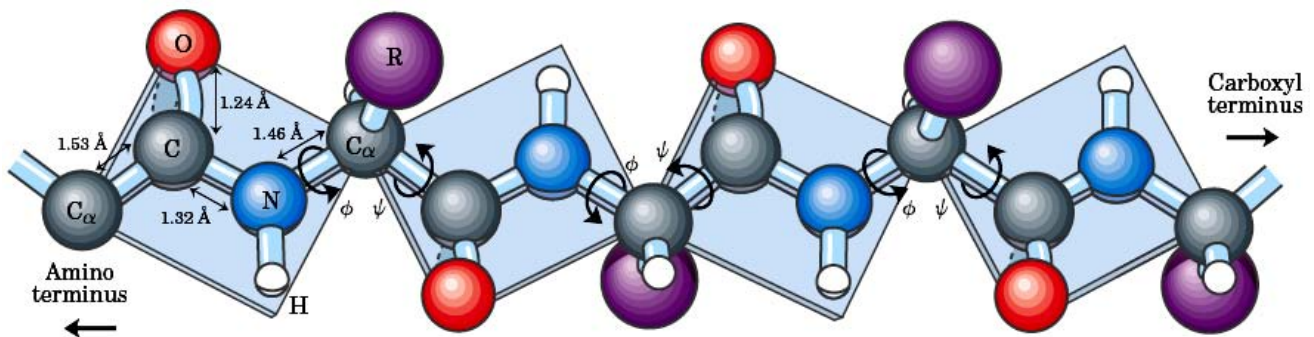▸ proteins are built from L amino acids

R-group determines AA properties

Nonpolar, aliphatic R groups

Glycine   Alanine   Valine

Leucine   Methionine   Isoleucine

R-group determines AA properties

Polar, uncharged R groups

Serine

Threonine

Cysteine

Proline

Asparagine

Glutamine

R-group determines AA properties

Negatively charged R groups

Aspartate

Glutamate

Positively charged R groups

Lysine

Arginine

Histidine

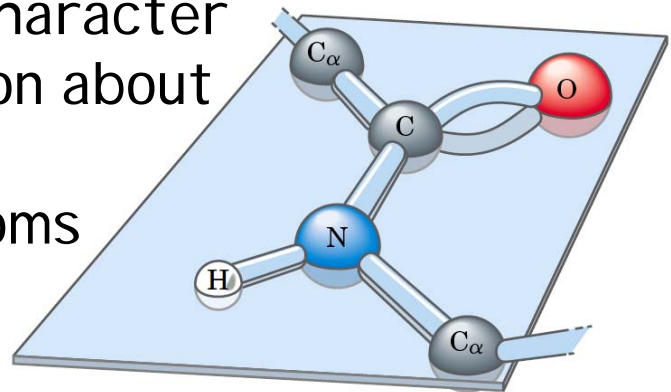**Aromatic R groups**

Phenylalanine

Tyrosine

Tryptophan

03

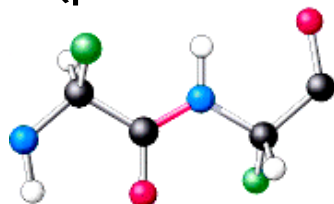# In Proteins (polypeptides) AA are Linked Through Peptide Bonds
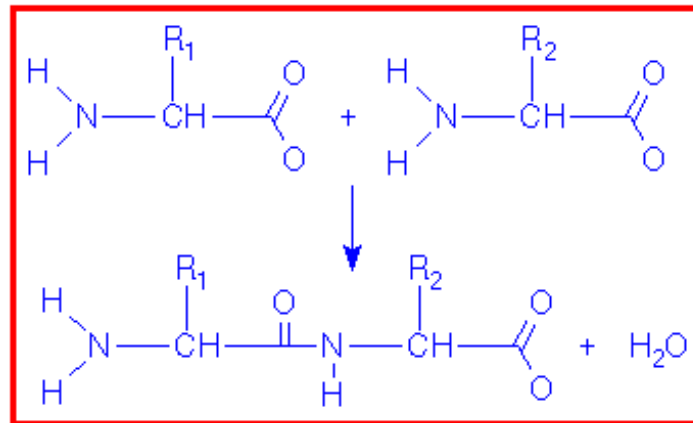
Properties of the Peptide Bond

▶ ~40% double bond character
  ⇒ restricted rotation about this bond
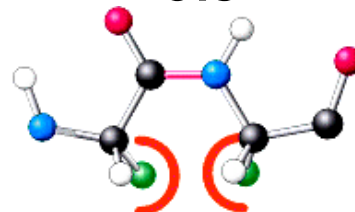 ⇒ the involved 6 atoms lie in a plane

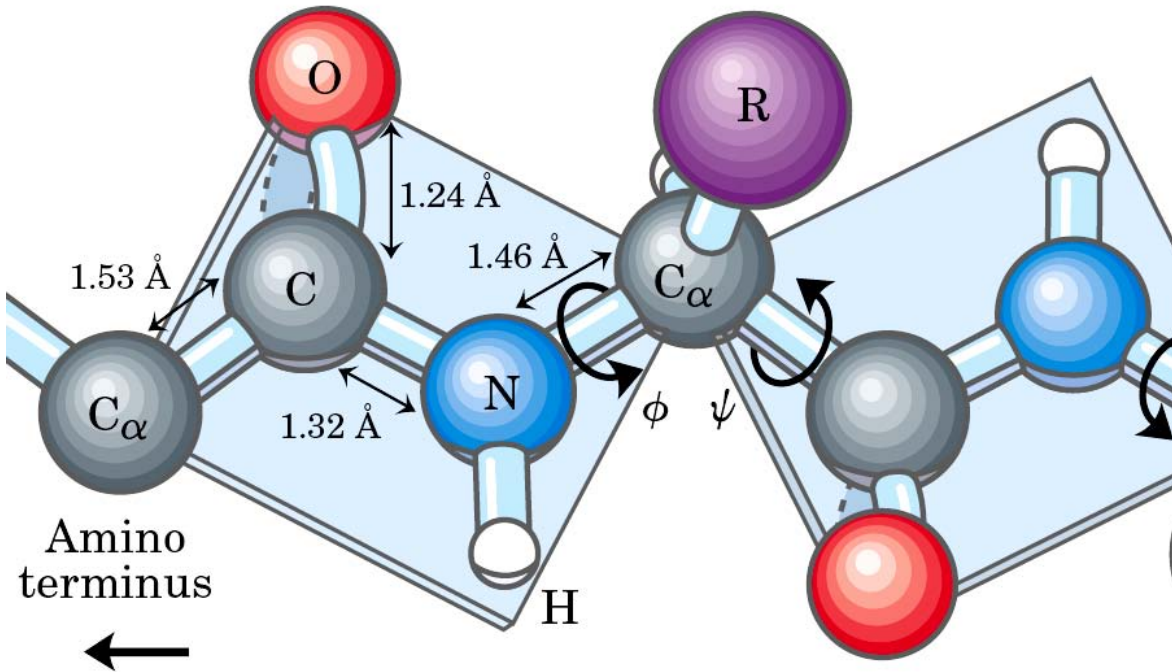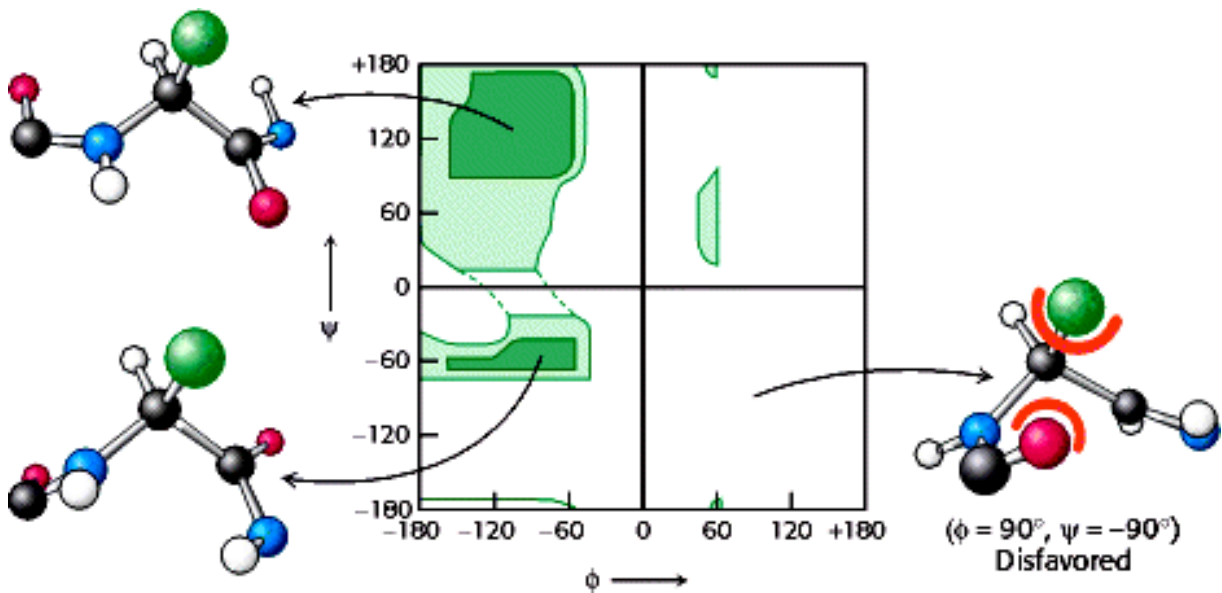▶ peptide bonds can have two forms:

Trans (preferred) & **Cis**

The ϕ and ψ angles

provide conformational freedom to proteins

Ramachandran plot/diagram/map

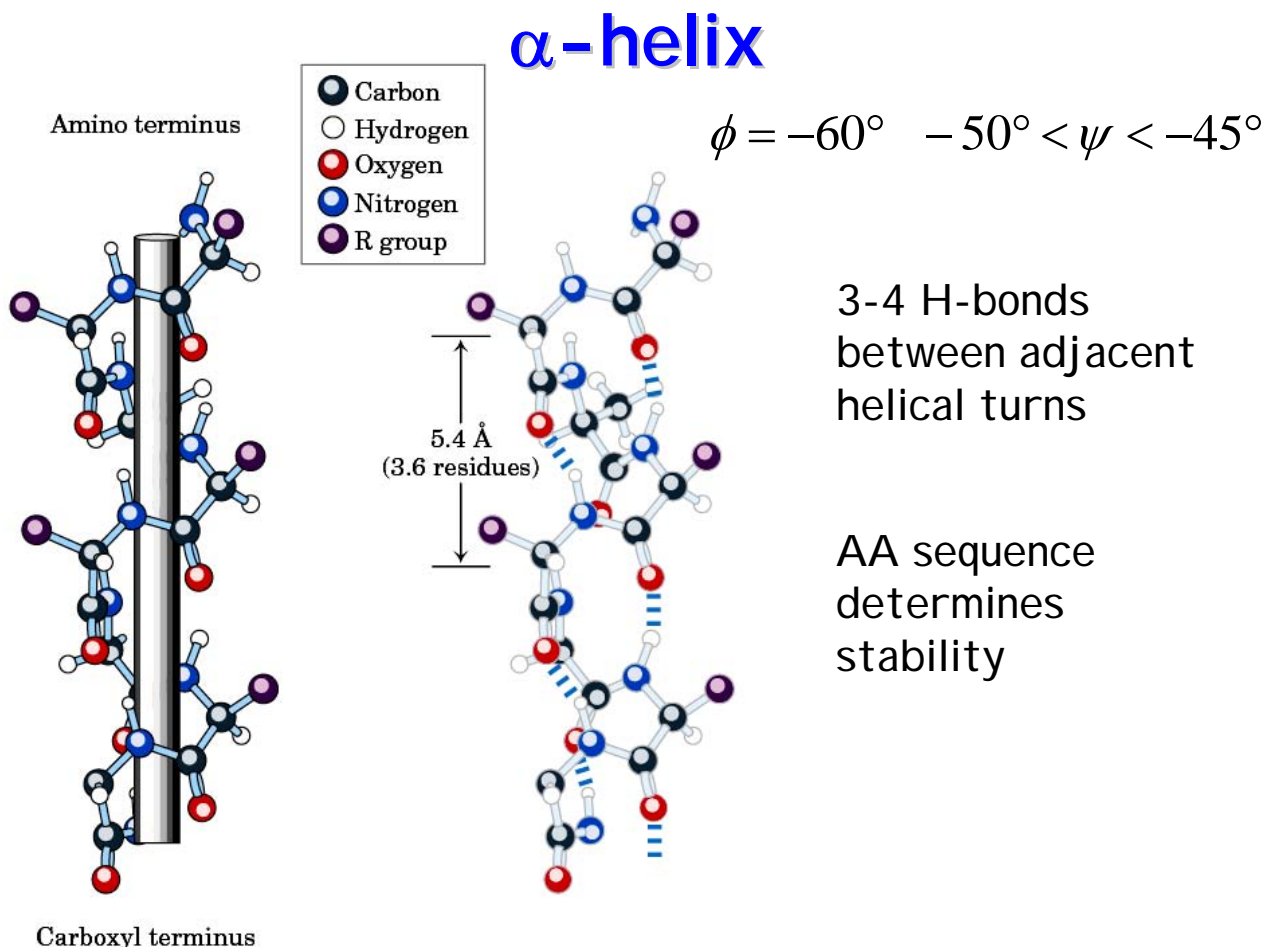▶ charts the domains with allowed/disallowed values of the angles ϕ and ψ

Hierarchical Structure of Proteins

▸ Primary structure: AA sequence
▸ Secondary structure: repeating structures
    e.g., α-helix, β-sheet, turns, ...
▸ Tertiary structure: folded protein
▸ Quaternary structure: protein complex

Why is this important ?

▸ AA sequence is encoded in a gene (piece of DNA)
▸ The 3D structure is determined by the AA sequence
▸ The function of the protein is determined by its 3D structure

α-helix

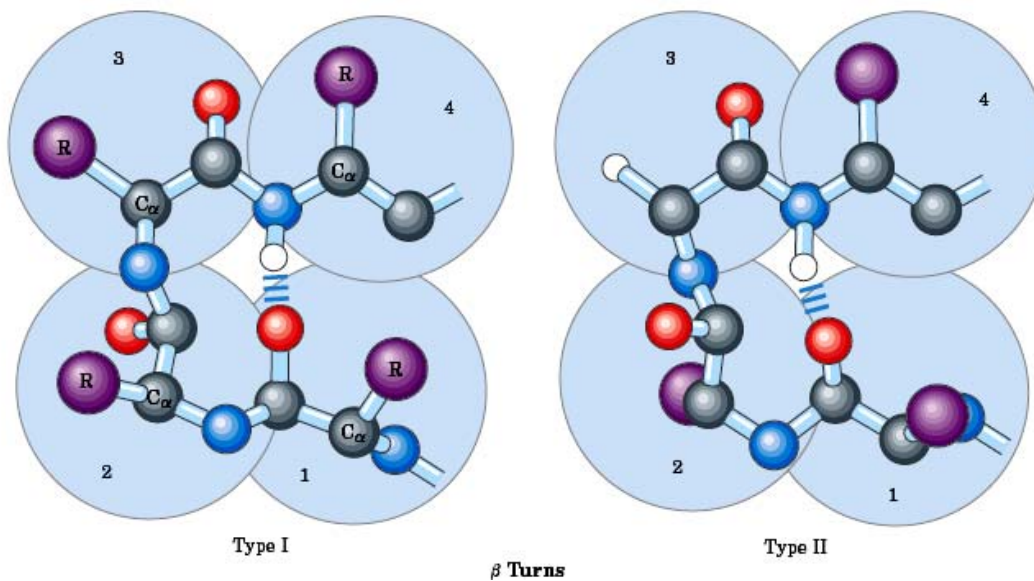$$\phi = -60° \quad -50° < \psi < -45°$$

3-4 H-bonds between adjacent helical turns

AA sequence determines stability

Amino terminus

Carbon
Hydrogen
Oxygen
Nitrogen
R group

5.4 Å
(3.6 residues)

Carboxyl terminus

β-sheet

the backbone of the polypeptide is extended into a zigzag (hairpin) and connected through H-bonds

antiparallel   parallel
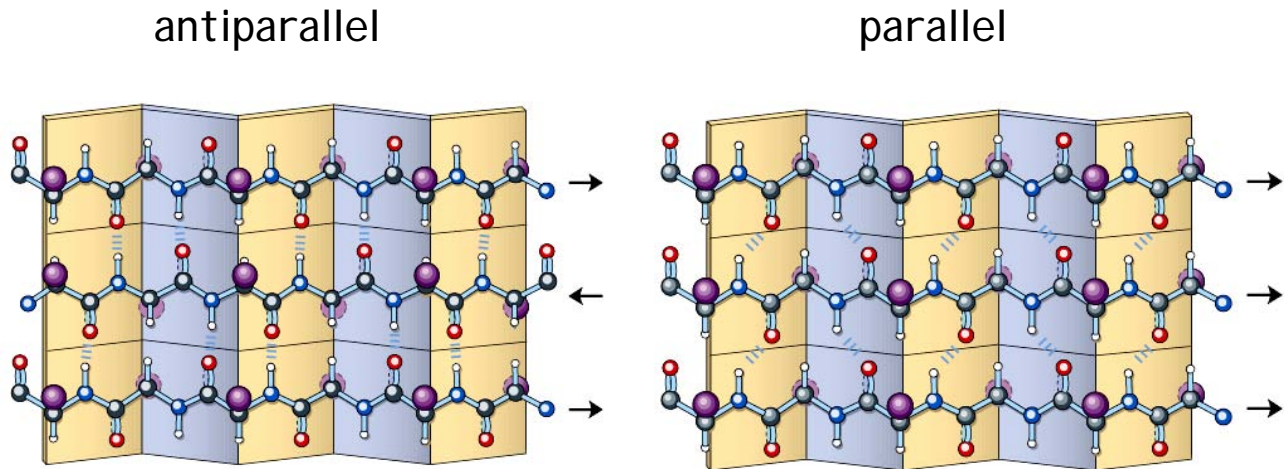
Turn/Loop

linking elements that connect α-helices and β-sheets
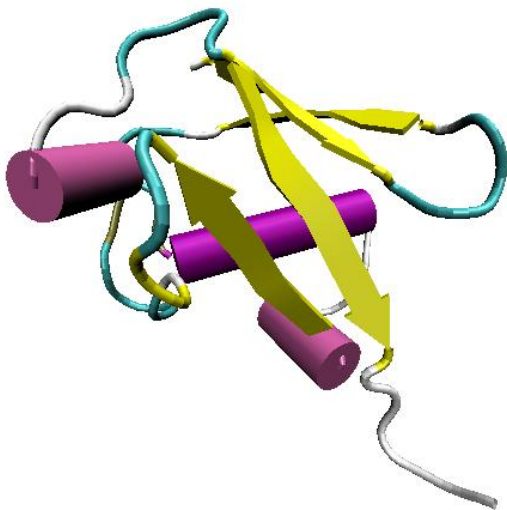
exp: β-turns

Type I   Type II

β Turns

Common 2nd-ary Structures Have:

▶ characteristic bond angles ϕ and ψ

▶ characteristic AA content

occurrence probability of AA in secondary structures

	α Helix	β Conformation	β Turn
Glu			
Met			
Ala			
Leu			
Lys			
Phe			
Gln			
Trp			
Ile			
Val			
Asp			
His			
Arg			
Thr			
Ser			
Cys			
Asn			
Tyr			
Pro			
Gly			
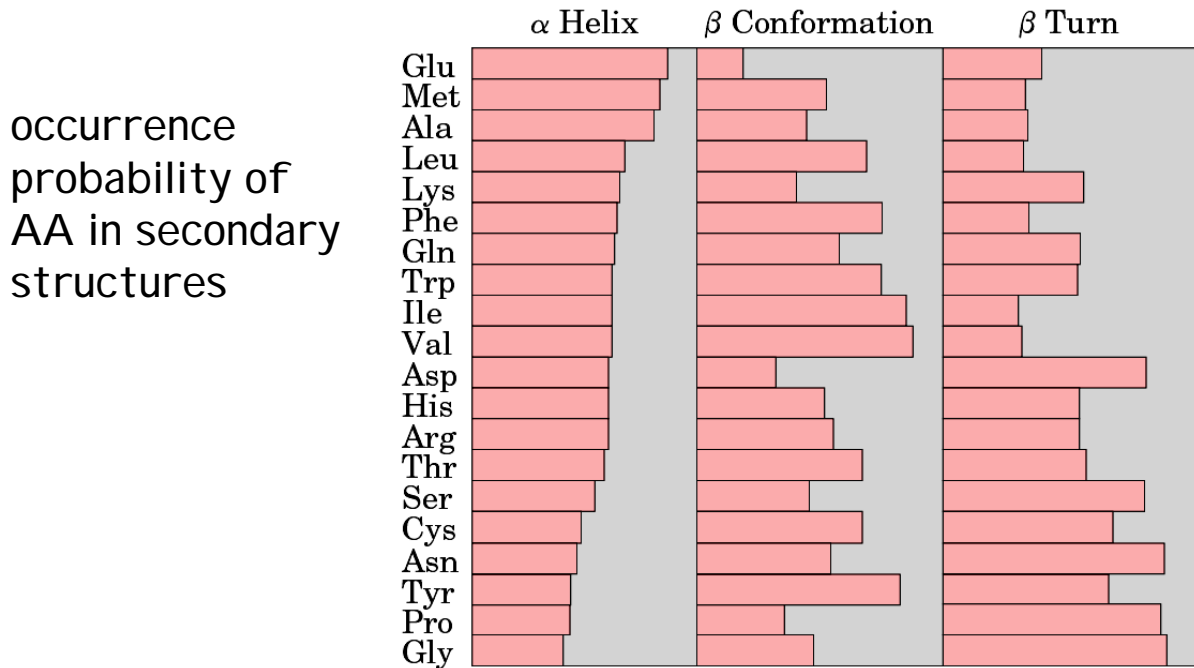
Tertiary Structure of Proteins

Ubiquitin
(1UBQ)
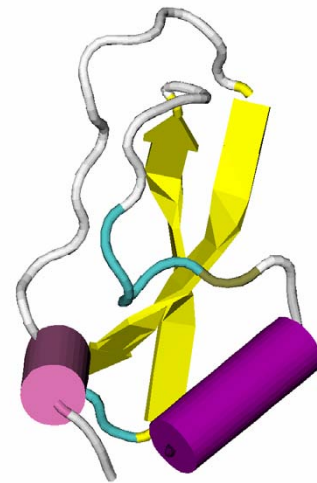
BPTI
(6PTI)

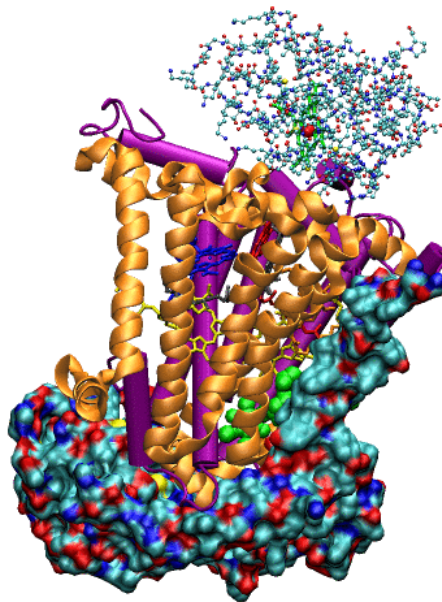Protein Structure DataBank: http://www.rcsb.org/pdb/

Basics of VMD

VMD
Visual Molecular Dynamics

Hands-On: VMD Tutorial – Part 1

Basics of VMD

Create Representation (a) → Create Rep

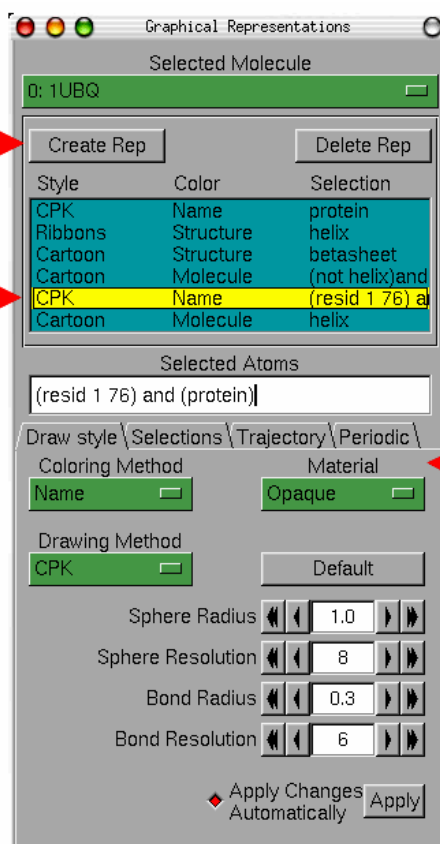(b) → Delete Representation

Current Representation (d) →

Multiple representations

(c) → Material

VMD Sequence Window

List of the residues (e)

Zoom (f)

Beta Value

Structure

T: Turn
E: Extended conformation
H: Helix
B: Isolated Bridge
G: 3-10 helix
I: Phi helix

Discover BPTI (6PTI) on your own!

BPTI = bovine pancreatic trypsin inhibitor

• Small (58 amino acids)

• rigid

• Binds as an inhibitor (blocks the active site) to Trypsin (a serine proteolytic enzyme, that appears in digestive system of mammalians)