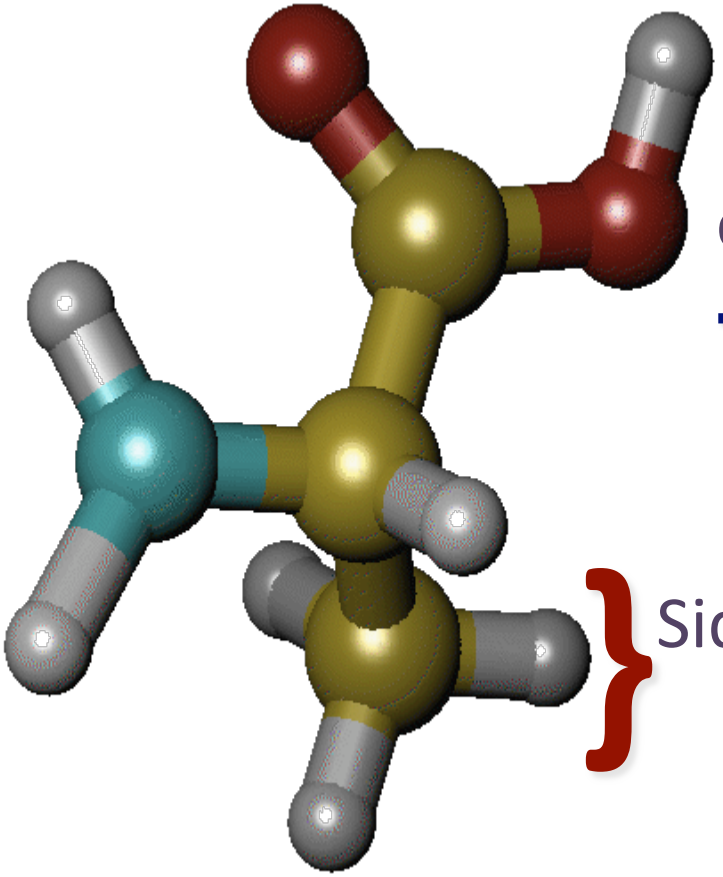
Principles of Protein Structure and Conformational Space

Protein structure

1. Introduction
    1. Amino acids
    2. Peptide bond
    3. Native conformation
    4. Levels of structure (1,2,3)
2. Energy
    1. Bonding energy terms
    2. Non-bonding terms
3. Secondary Structure
    1. Strands
    2. Helix
    3. Ramachandran Plot
    4. Aa propensities

1. Introduction

1. Amino Acids



amino
$-NH_2$

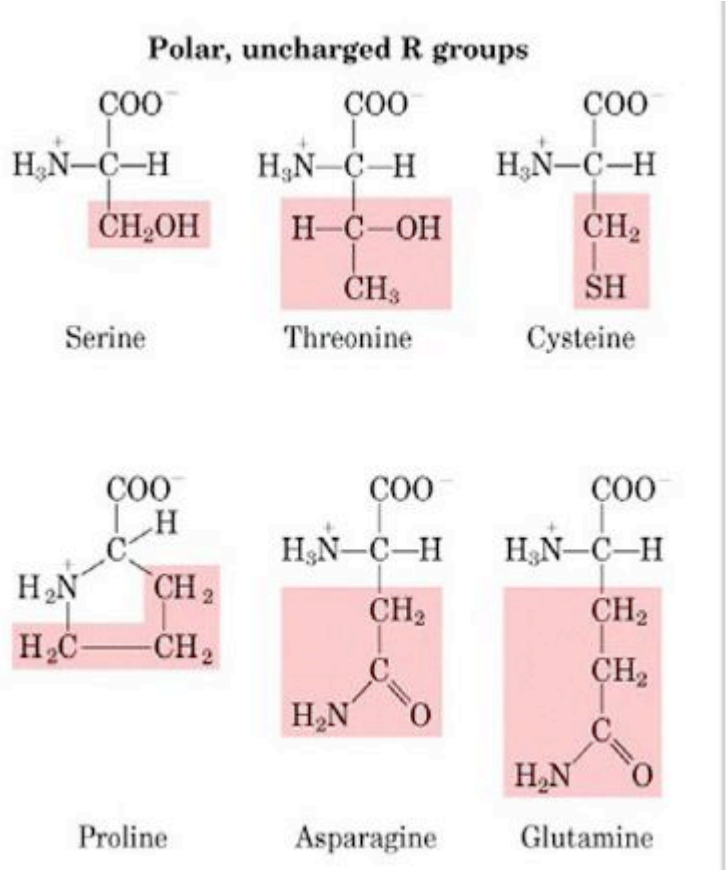
carboxyl
-COOH

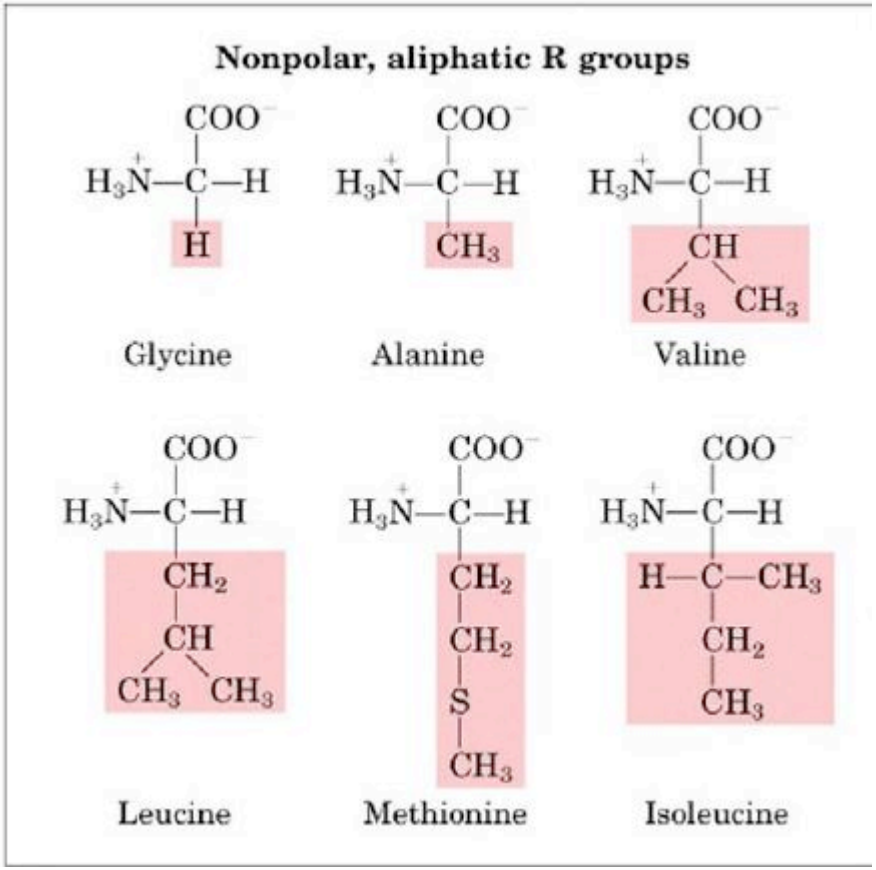
Side-chain **($-CH_3$)**

Estereoisomer L

1. Introduction

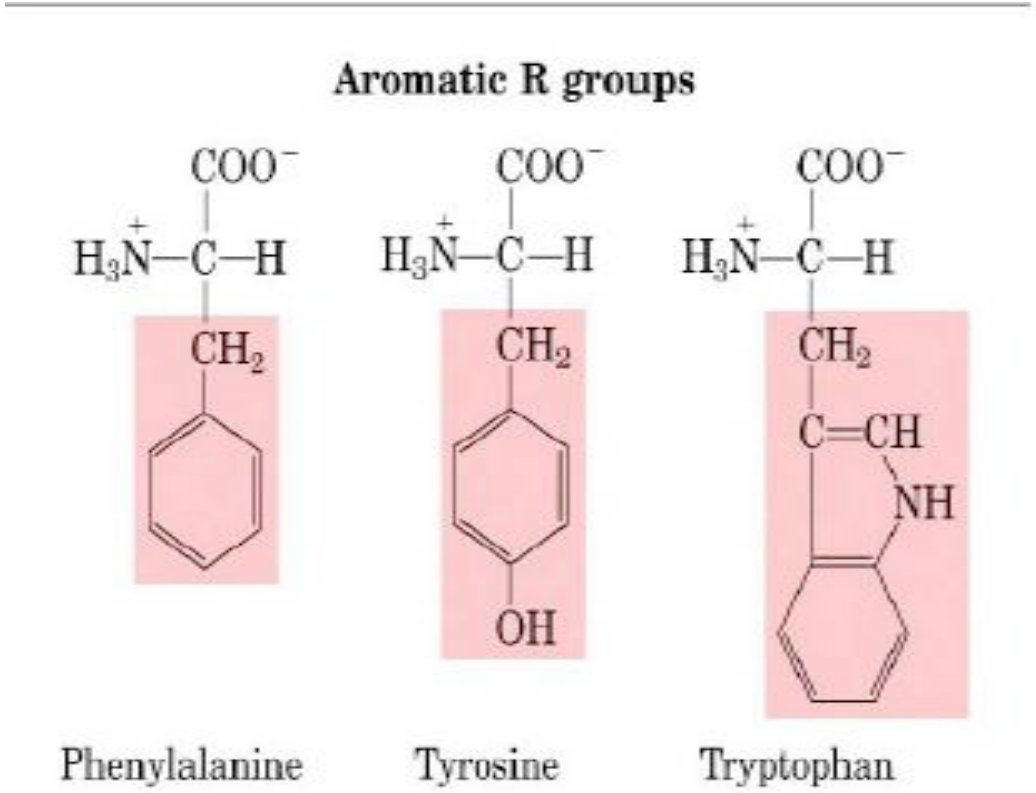
1. Amino Acids





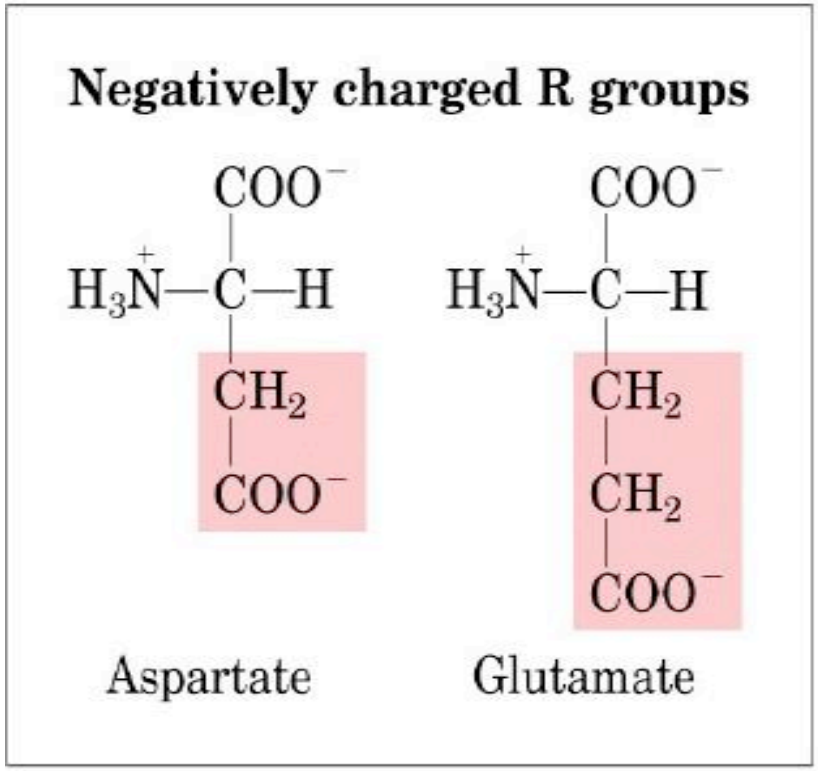
1. Introduction

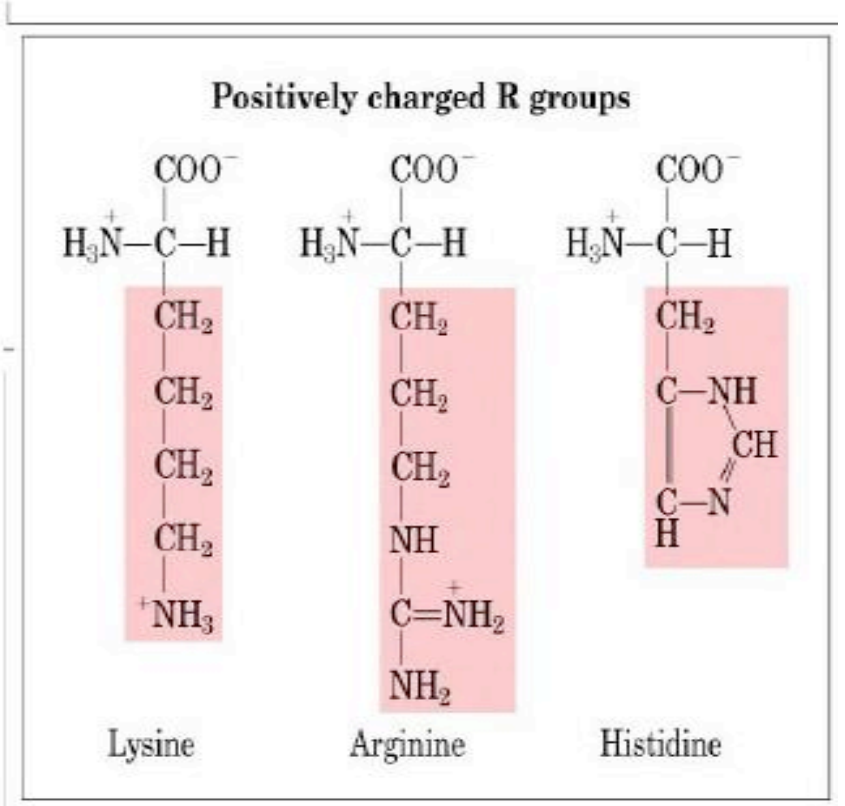
1. Amino Acids



1. Introduction

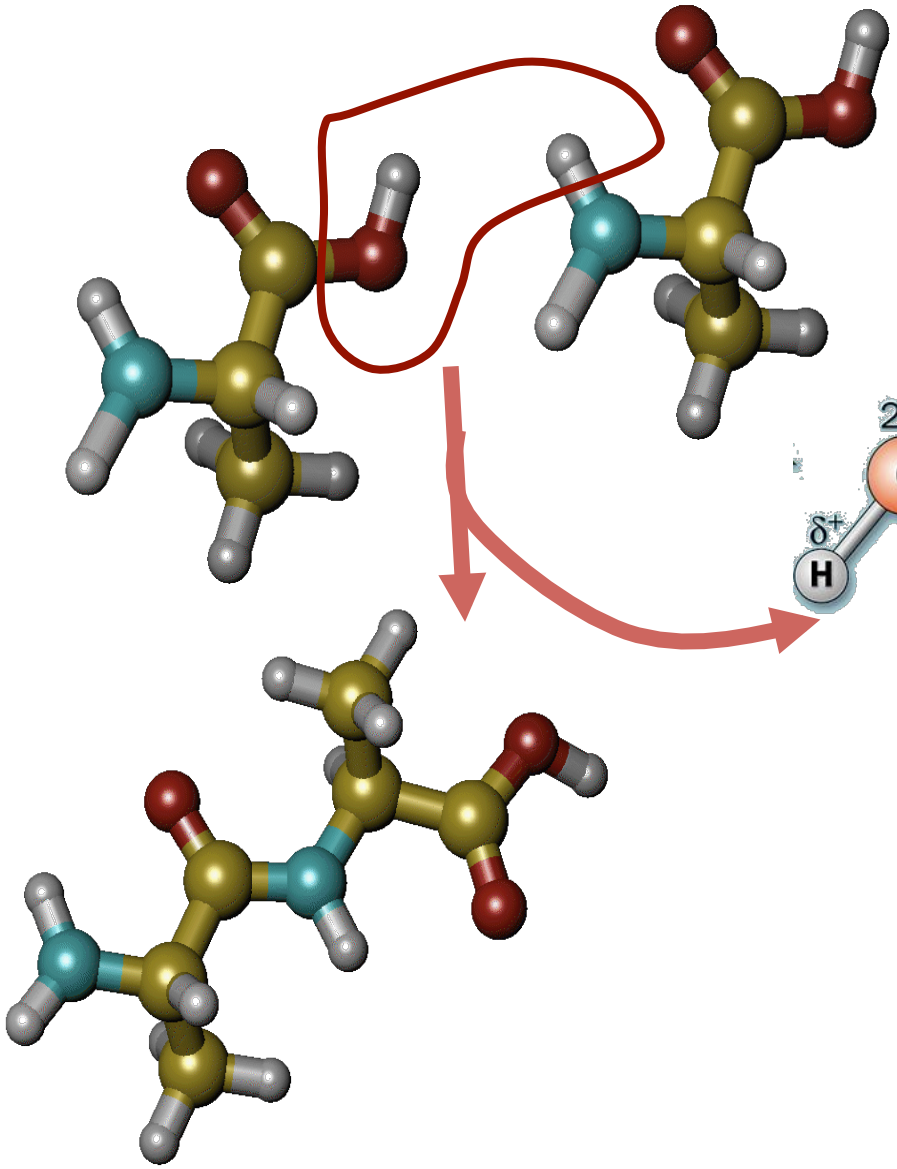
1. Amino Acids

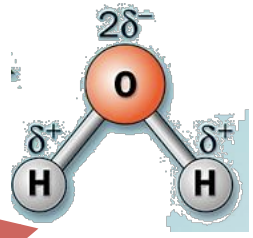




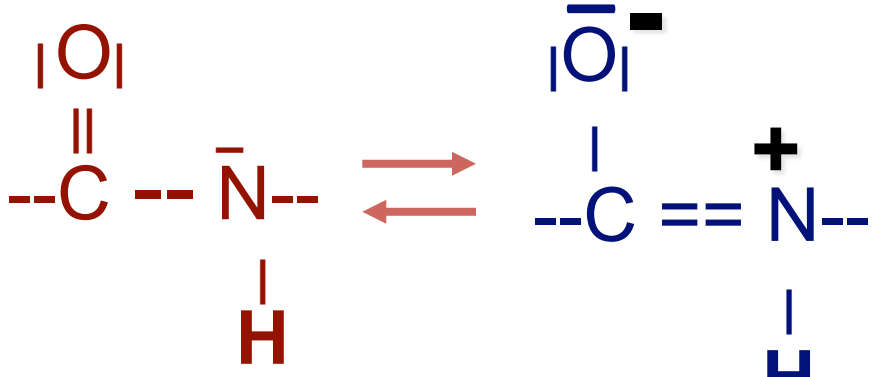
1. Introduction

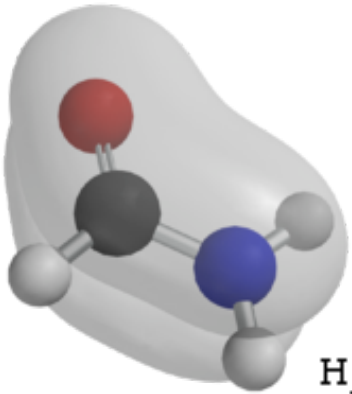
2. Peptide Bond

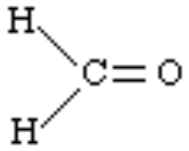


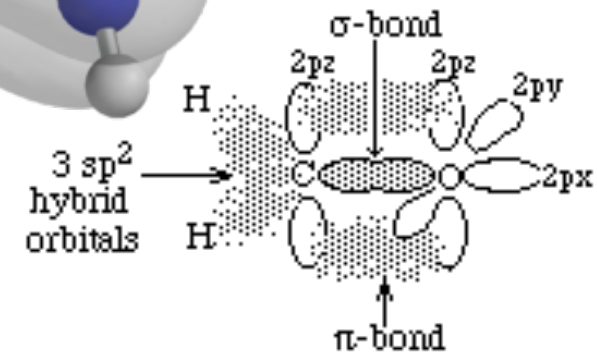


PLANE -CO-NH-

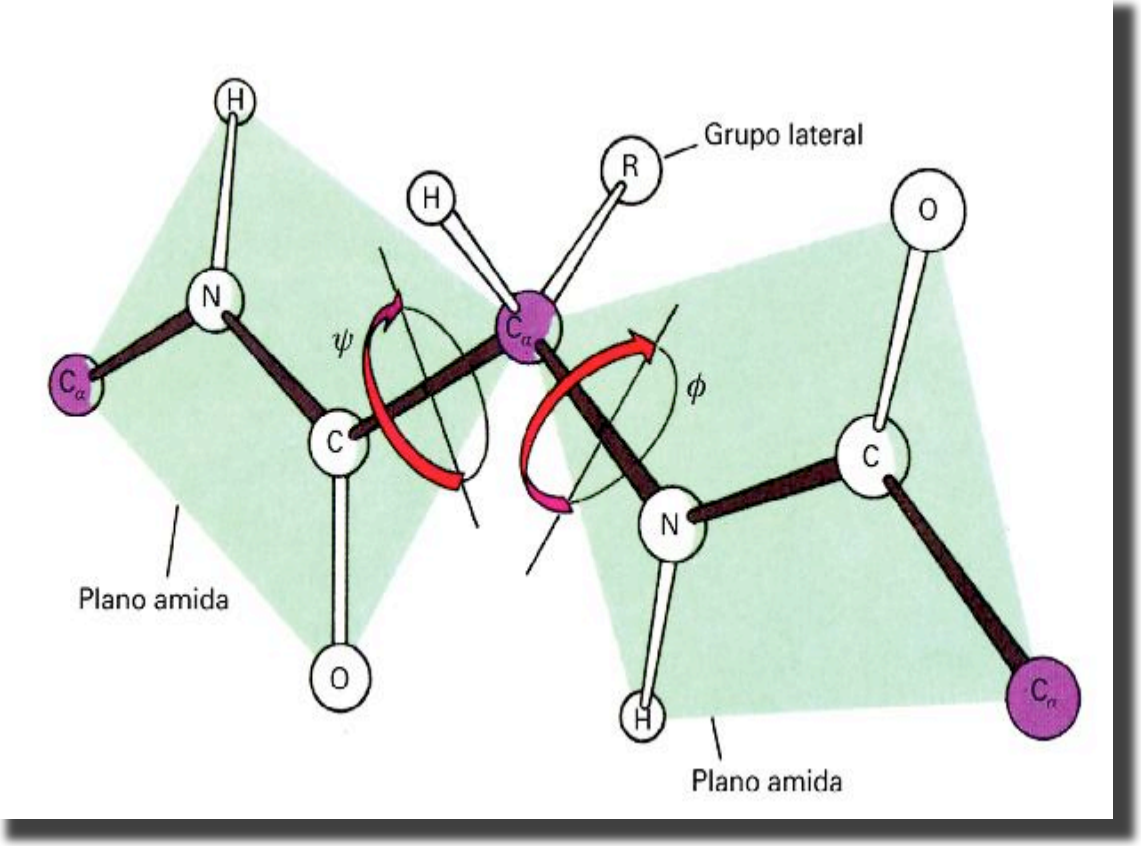








Angles ϕ & ψ



ψ = [-180º, +180º]

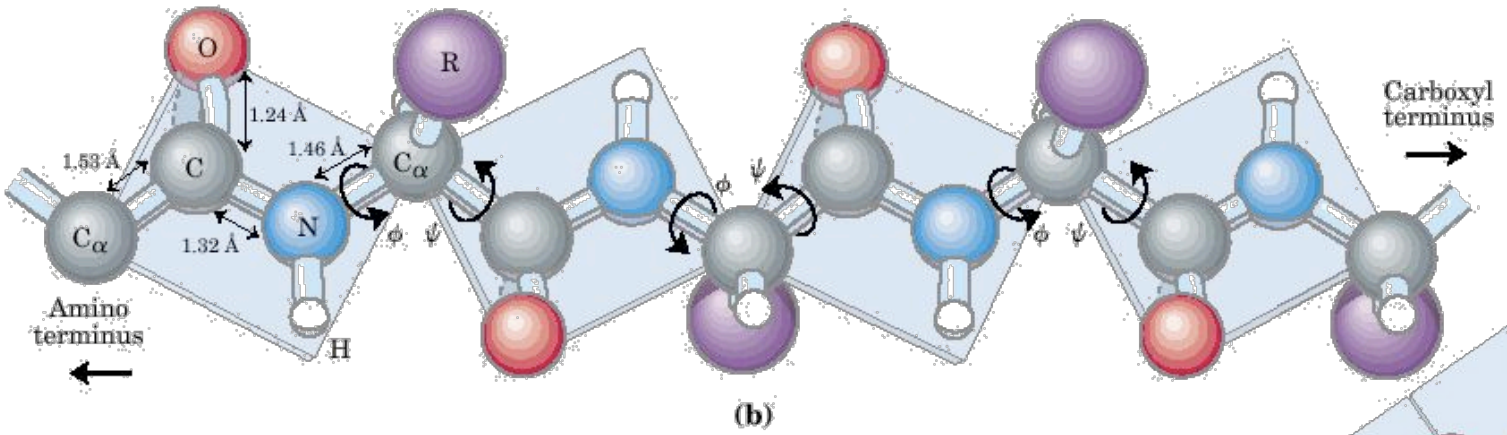
ϕ = [-180º, +180º]

1. Introduction

3. Native Conformation

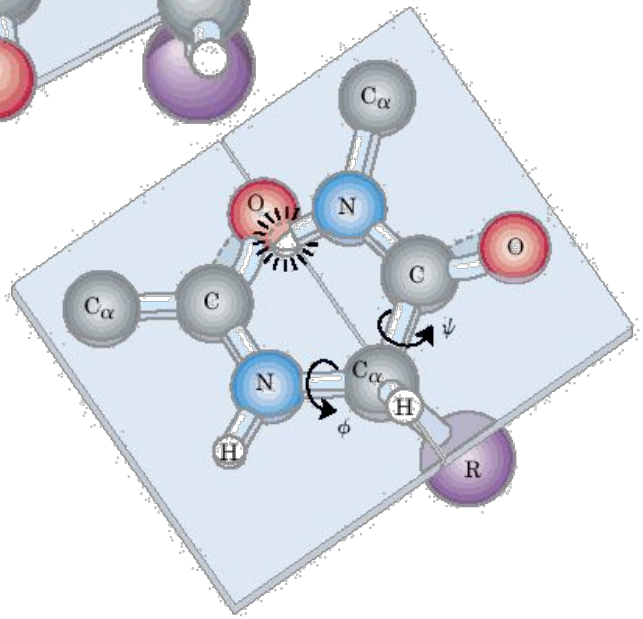
Native conformation:

1) Polipeptide + environment
2) Function & stability



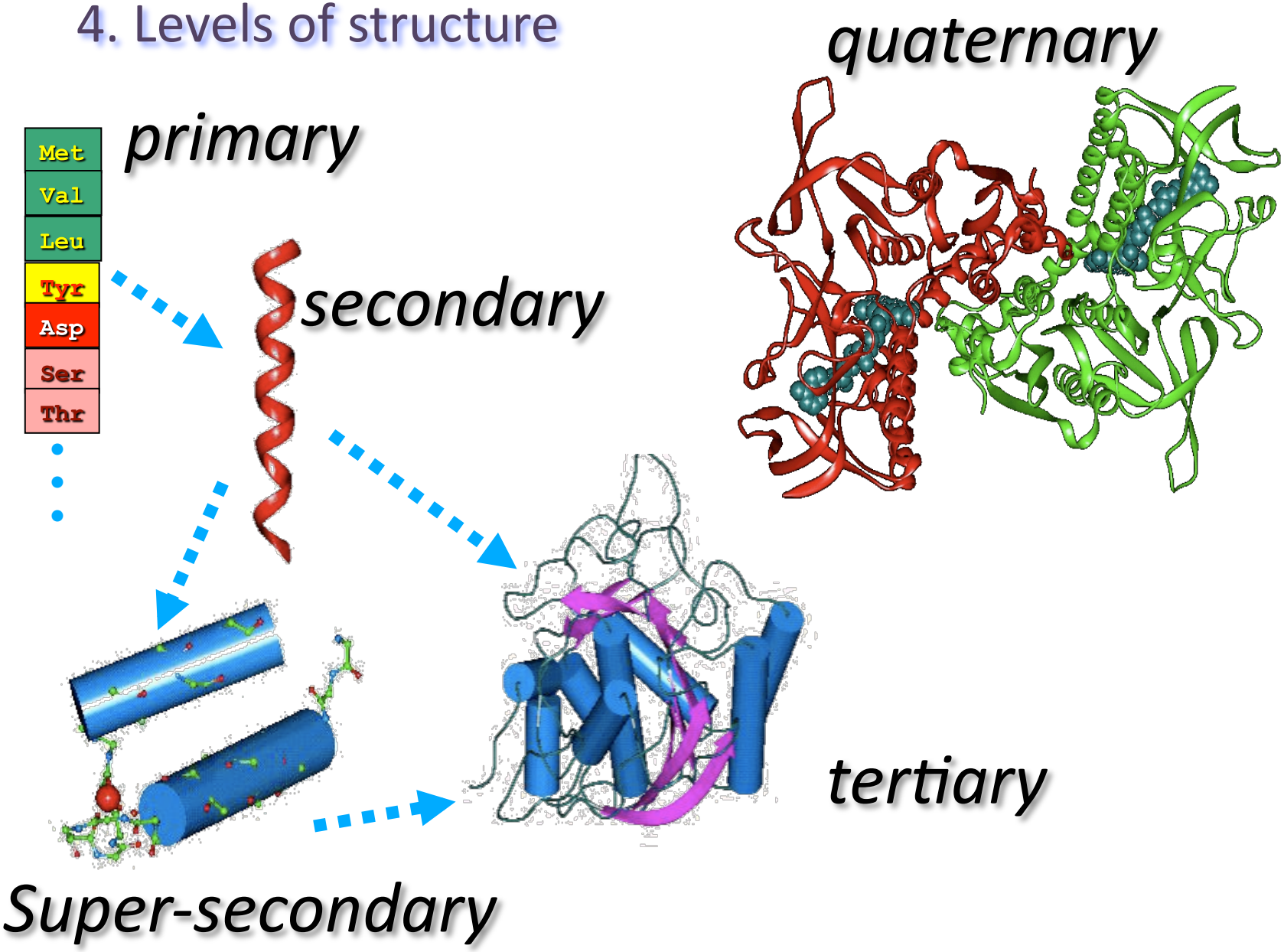
Conformational restraints:

1) Peptide bond planarity
2) The total space is not 360 x 360



1. Introduction

4. Levels of structure



2. Energy

1. Bonding energy terms

$$\vec{F} = m * \vec{a} = \sum_{i=1}^{N} \vec{F}_i$$

$$W = \int_{path} \vec{F} * d\vec{r}$$

2. Energy

1. Bonding energy terms

$$\vec{a} = \frac{\partial}{\partial t}\left(\frac{\partial \vec{r}}{\partial t}\right) = \frac{\partial \vec{v}}{\partial t}$$

$$d\vec{r} = \vec{v} * dt$$

$$\frac{\partial\left(v^2\right)}{\partial t} = \frac{\partial(\vec{v} * \vec{v})}{\partial t} = 2\left(\vec{v} * \frac{\partial \vec{v}}{\partial t}\right)$$

$$\vec{F} * d\vec{r} = \left(m * \frac{\partial \vec{v}}{\partial t}\right) * \left(\vec{v} * dt\right) = \frac{1}{2} m \frac{\partial\left(v^2\right)}{\partial t} dt$$

2. Energy

1. Bonding energy terms

$$W = \int_{Path} \vec{F} * d\vec{r} = \int_{Time} \frac{1}{2} m \frac{\partial\left(v^2\right)}{\partial t} dt = \frac{1}{2} m v^2 + C$$

$$Potential = E_p = -\int_{Path} \vec{F} * d\vec{r}$$

$$Kinetic = E_k = \frac{1}{2} m v^2$$

$$Total = U = E_p + E_k$$

2. Energy

1. Bonding energy terms

Molecular mechanics

$$V = \frac{1}{2}\sum_i K_i^{bond}\left(d_i - d_{0,i}\right)^2 + \frac{1}{2}\sum_i K_i^{angle}\left(\alpha_i - \alpha_{0,i}\right)^2 + \frac{1}{2}\sum_i K_i^{dihedral}\left(\omega_i - \omega_{0,i}\right)^2$$

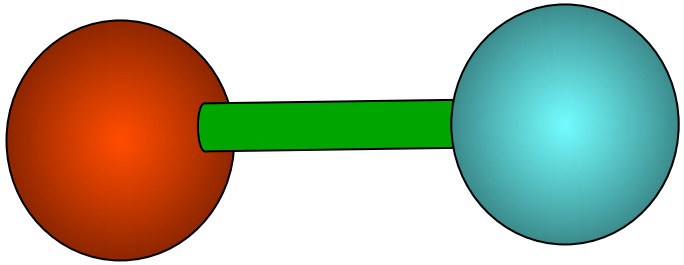
$$+\frac{1}{2}\sum_i K_i^{torsion}\cos\left(\lambda_i\phi_i + \delta_i\right) + \frac{1}{4\pi\varepsilon}\sum_i\sum_{j>i}\frac{q_i q_j}{r_{ij}} + \sum_i\sum_{j>i}\left(\frac{C_6(i,j)}{r_{ij}^6} - \frac{C_{12}(i,j)}{r_{ij}^{12}}\right)$$

$$+\sum_i\left(Hydrogen - Bonds\right) + \sum_i\left(\pi - \pi\right)$$

2. Energy

1. Bonding energy terms

Bond



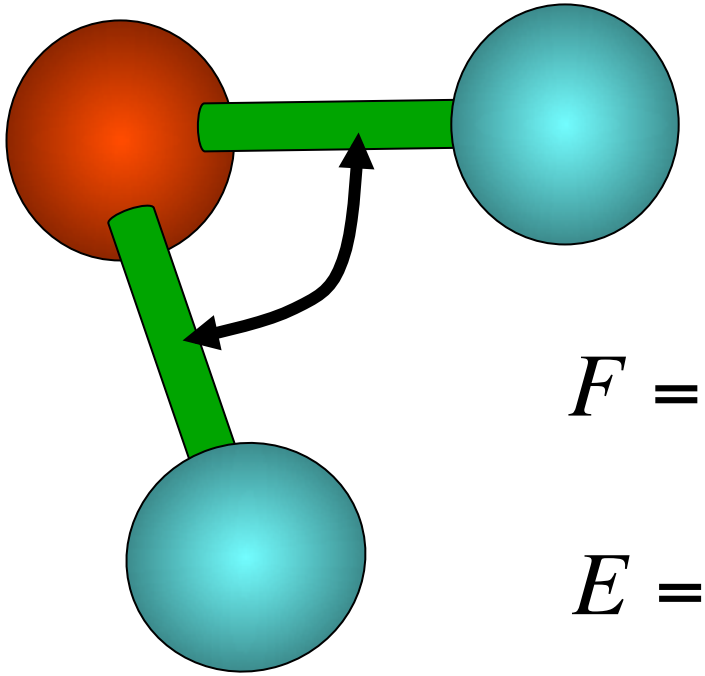
$$F = -k(d - d_0)$$

$$E = \frac{1}{2}k(d - d_0)^2$$

2. Energy

1. Bonding energy terms

Angle



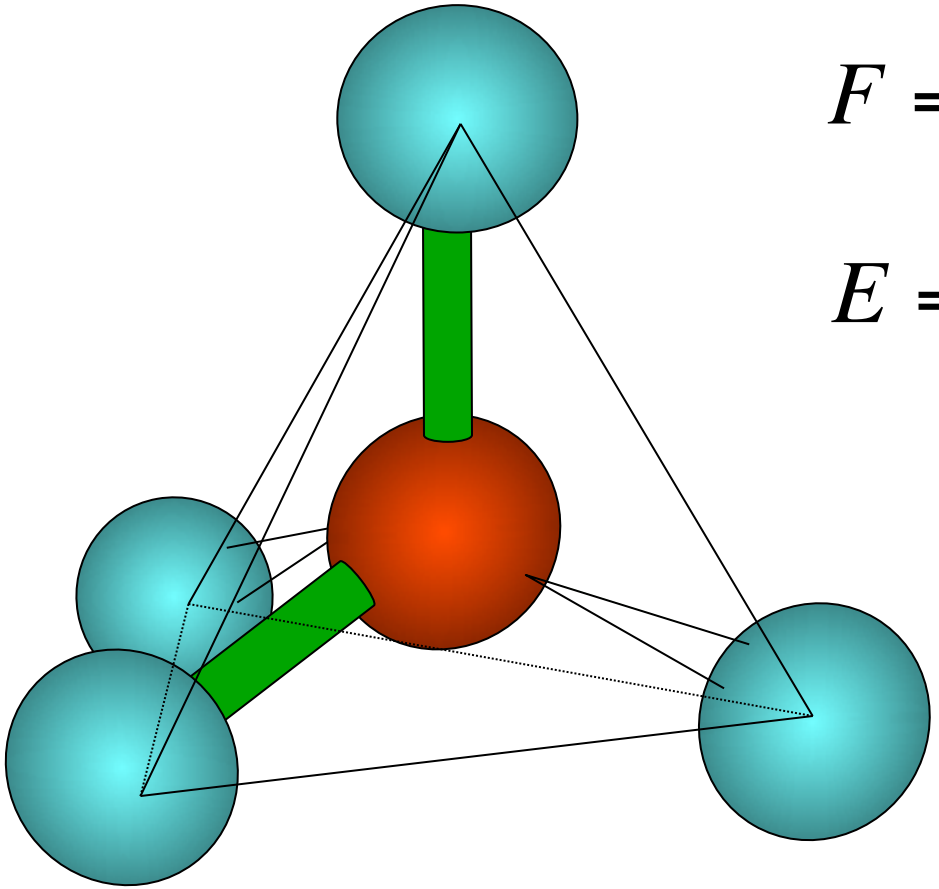
$$F = -k(\alpha - \alpha_0)$$

$$E = \frac{1}{2}k(\alpha - \alpha_0)^2$$

2. Energy

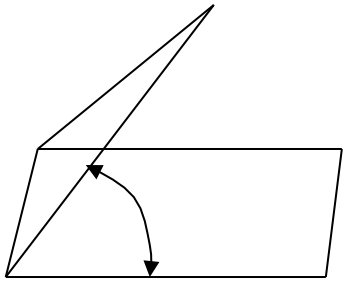
1. Bonding energy terms

Improper dihedral



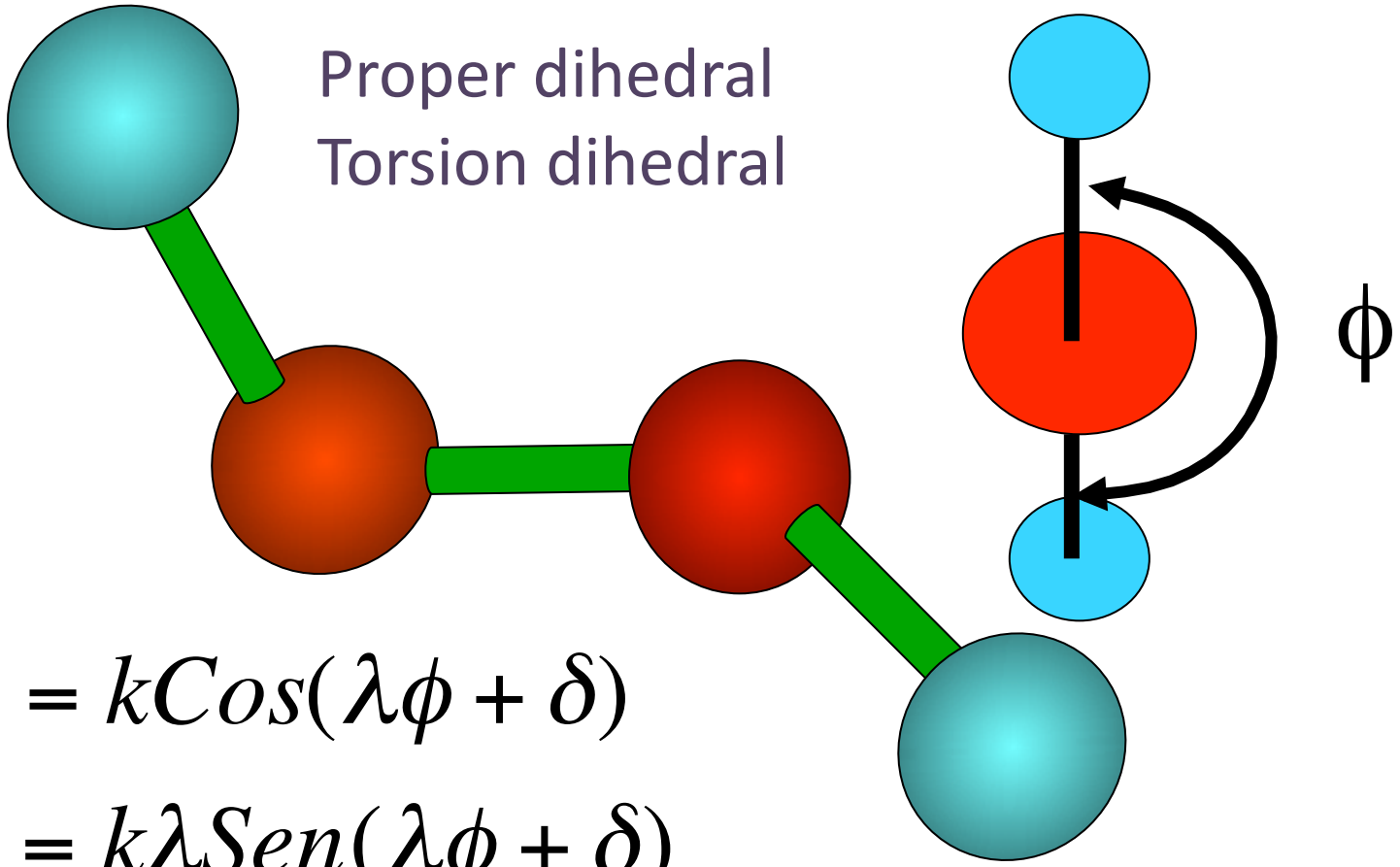
$$F = -k\left(\varpi - \varpi_0\right)$$

$$E = \frac{1}{2}k\left(\varpi - \varpi_0\right)^2$$



2. Energy

1. Bonding energy terms



$$E = kCos(\lambda\phi + \delta)$$

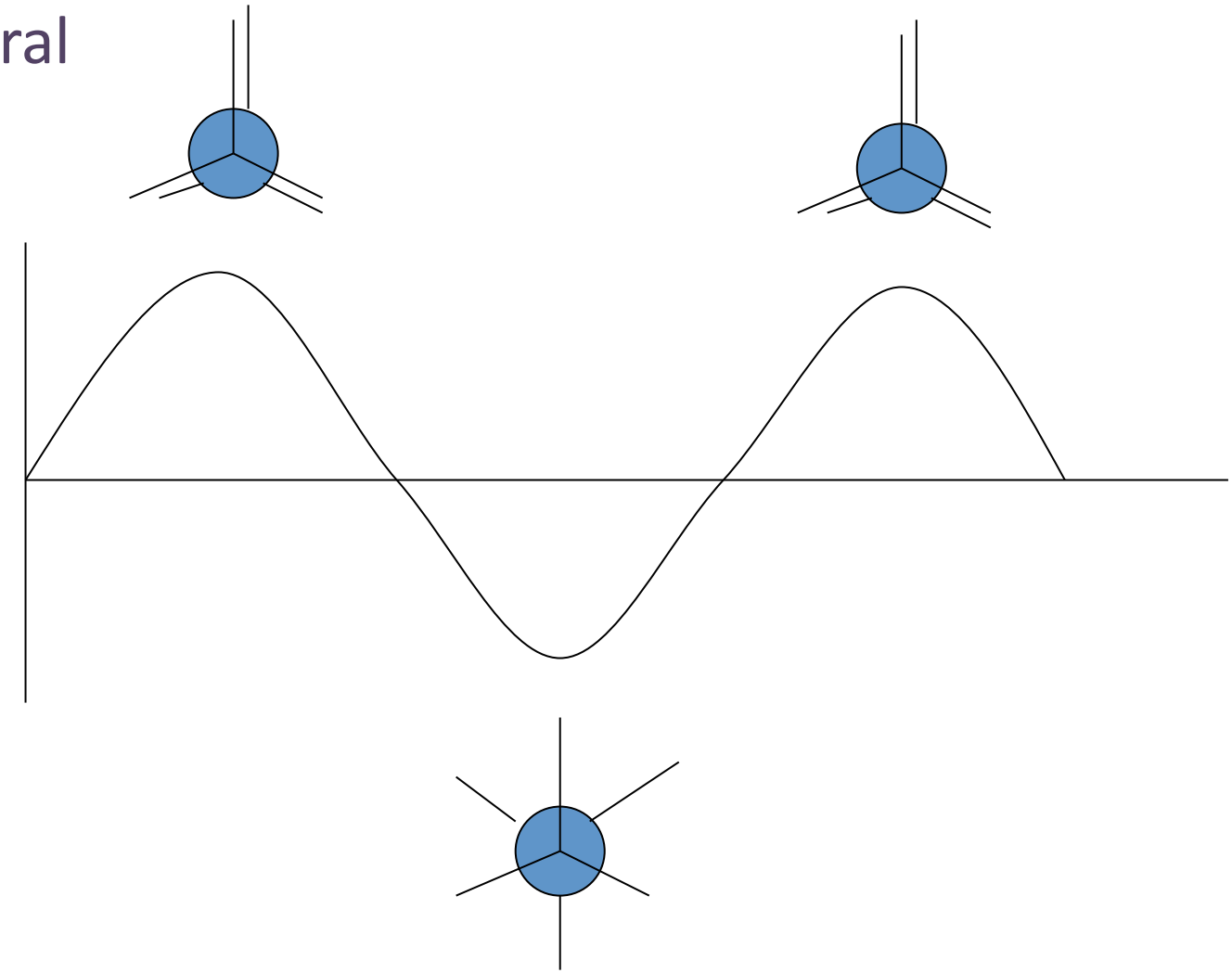
$$F = k\lambda Sen(\lambda\phi + \delta)$$

2. Energy

1. Bonding energy terms

Proper dihedral

Torsion dihedral



2. Energy

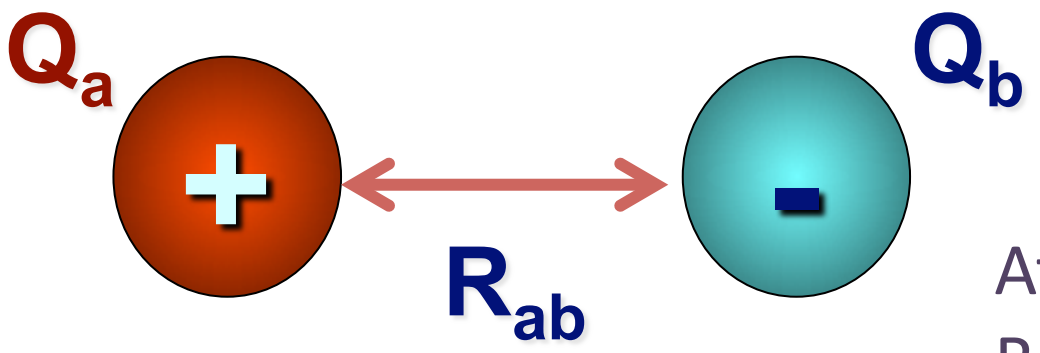
2. Non-Bonding terms

Electrostatic energy

Long range interactions
Involve in folding

$$\vec{F} = -\frac{1}{4\pi\varepsilon_0}\frac{Q_a Q_b}{r_{ab}^2}\left(\frac{\vec{r}_{ab}}{r_{ab}}\right)$$

$$E = \frac{1}{4\pi\varepsilon_0}\frac{Q_a Q_b}{r_{ab}}$$



Atraction: opposite sign
Repulsion: same sign
Approx. 150 kcal/mol

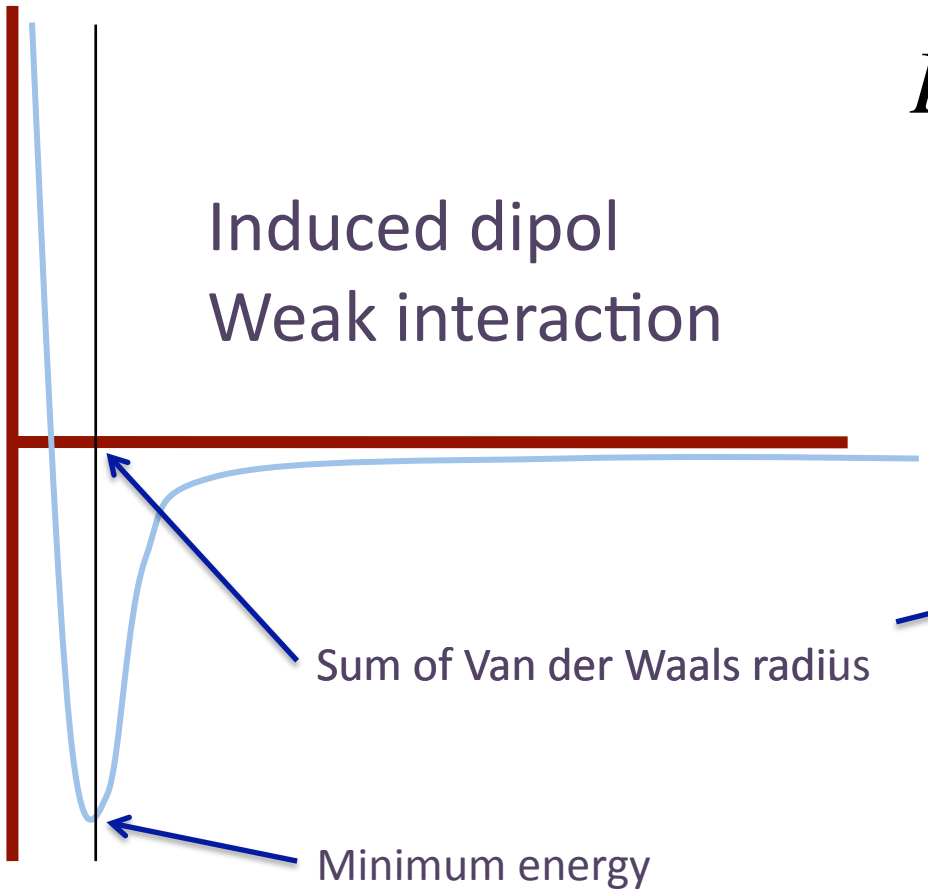
2. Energy

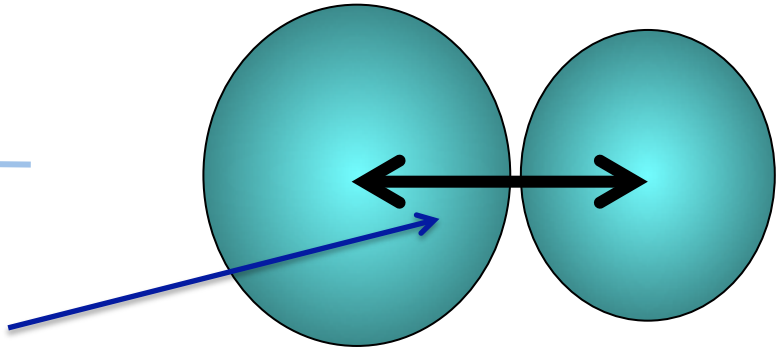
2. Non-Bonding terms

Van der Waals energy

Lennard-Jones equation

$$E = \frac{C_6(a,b)}{r_{ab}^6} - \frac{C_{12}(a,b)}{r_{ab}^{12}}$$



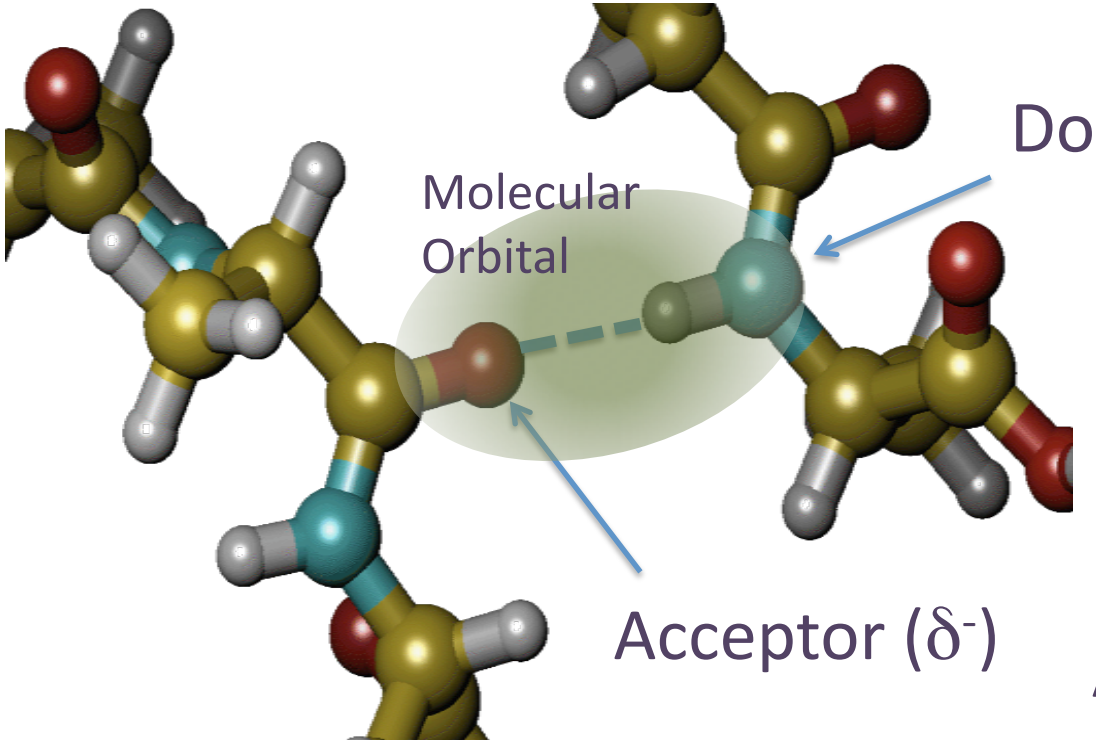


Avoids atoms collision

Approx. 2 kcal/mol

2. Energy

3. Hydrogen Bonds



Donor (H^+)

Acceptor (δ^-)

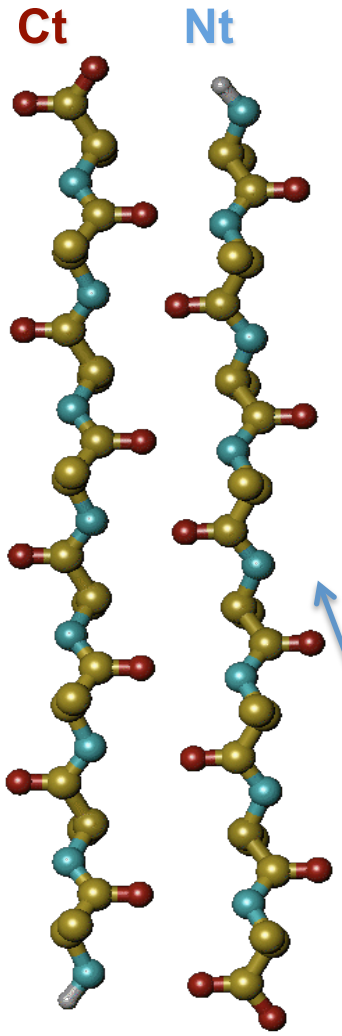
85% ionic bond
15% covalent
Approx. 4 kcal/mol

Restriction:
Angle OHN = 180^0+/-35^0
Distance ON = 2.8A

Inter-chain (long distance/short distance in sequence)
Intra-chain

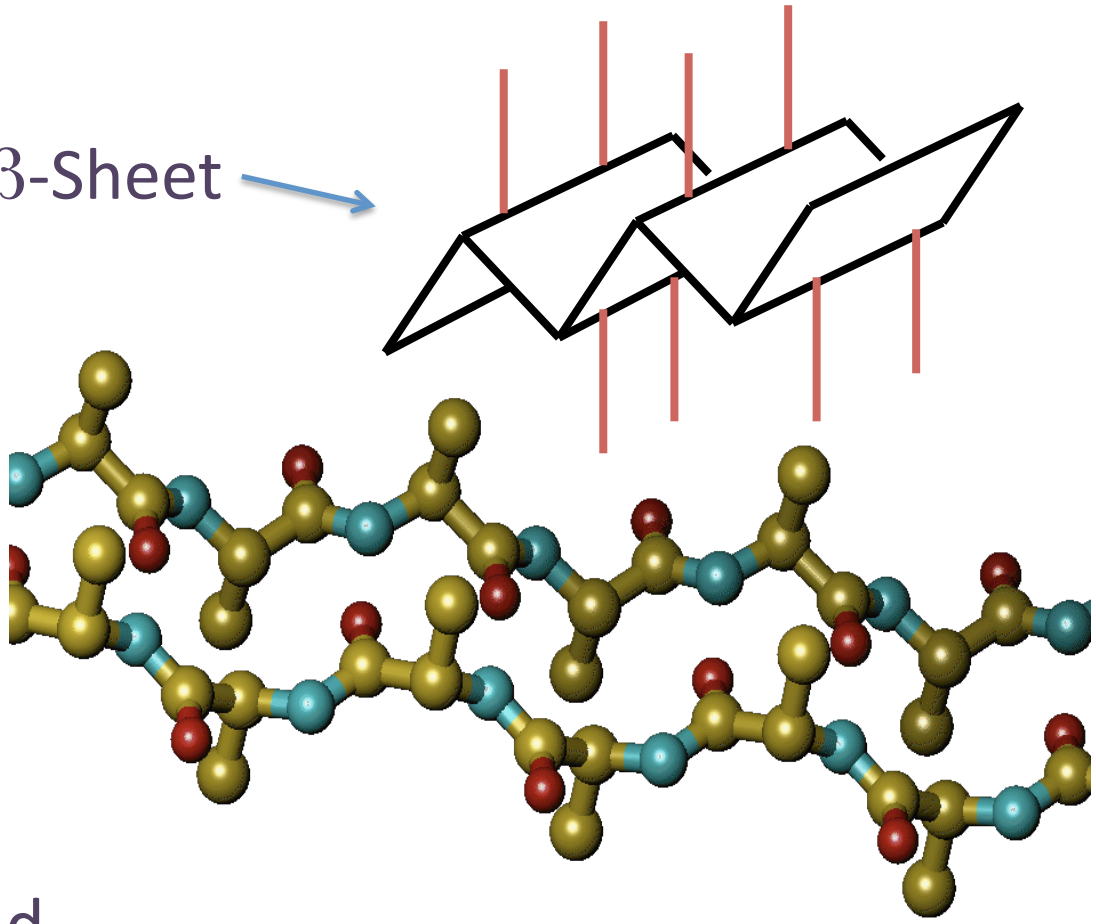
3. Secondary Structure

1. Strands



β-ladder

β-Sheet



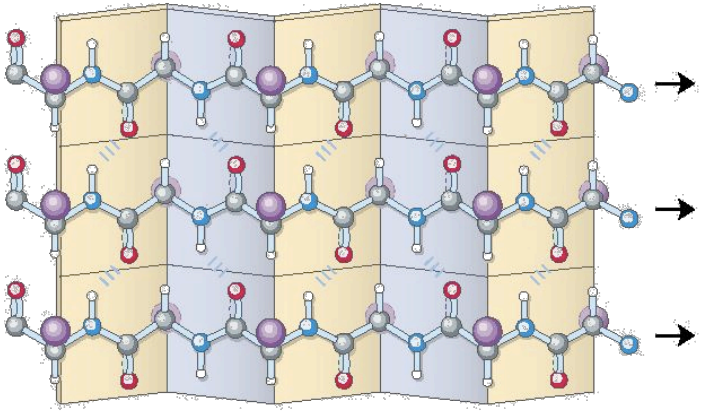
β-strand

- Hydrogen Bonds (HB) are long distance in sequence
- Side-chains are at both sides

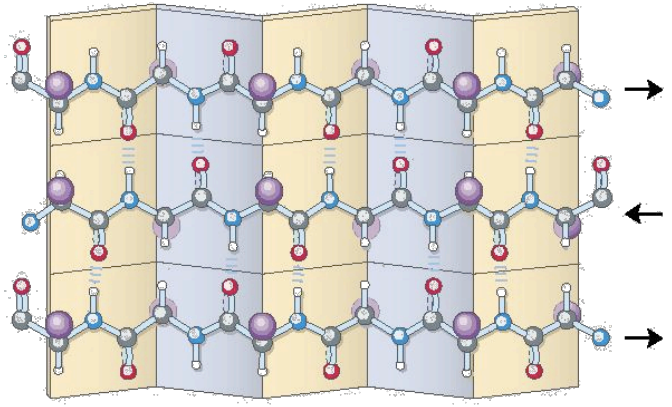
3. Secondary Structure

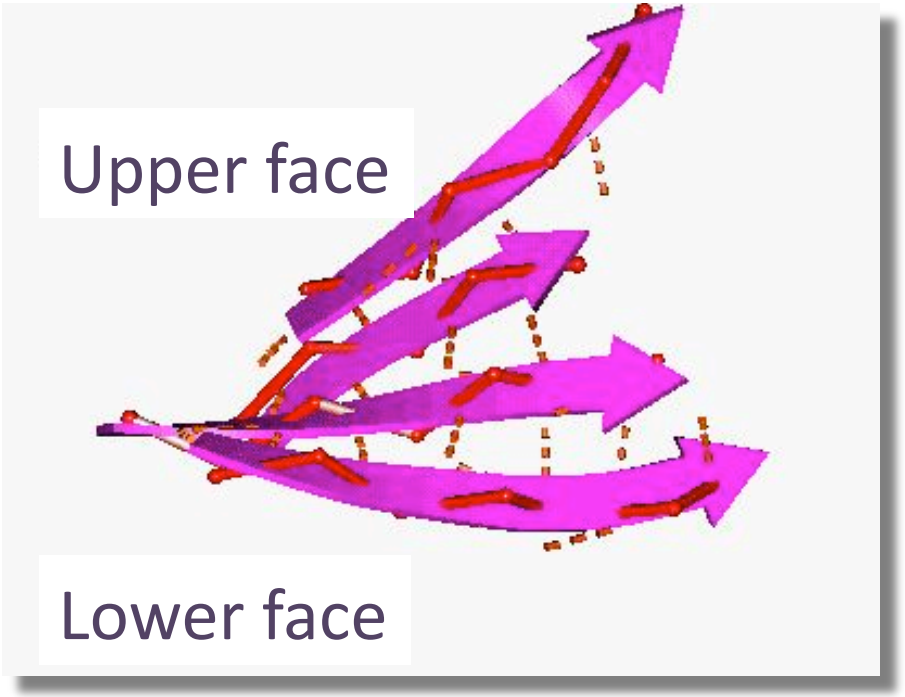
1. Strands

Parallel β−sheet



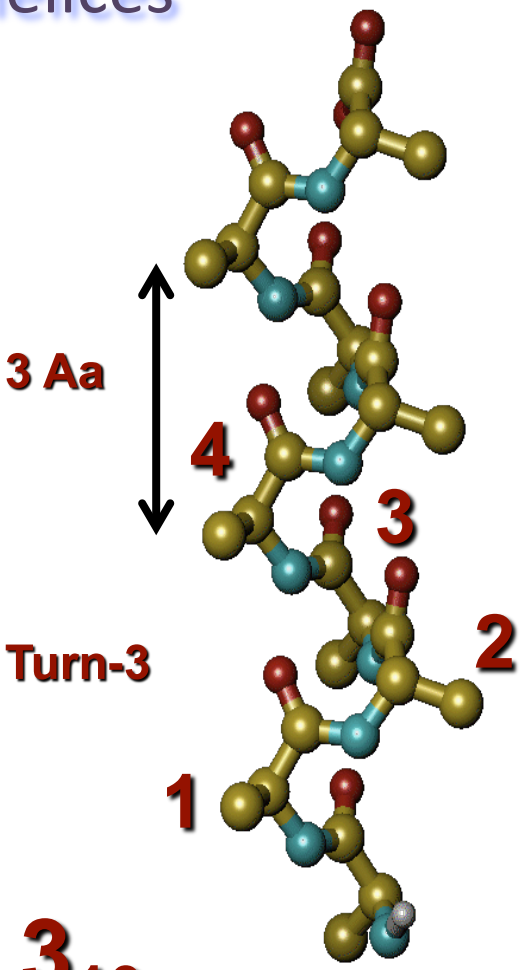
Anti-parallel β−sheet



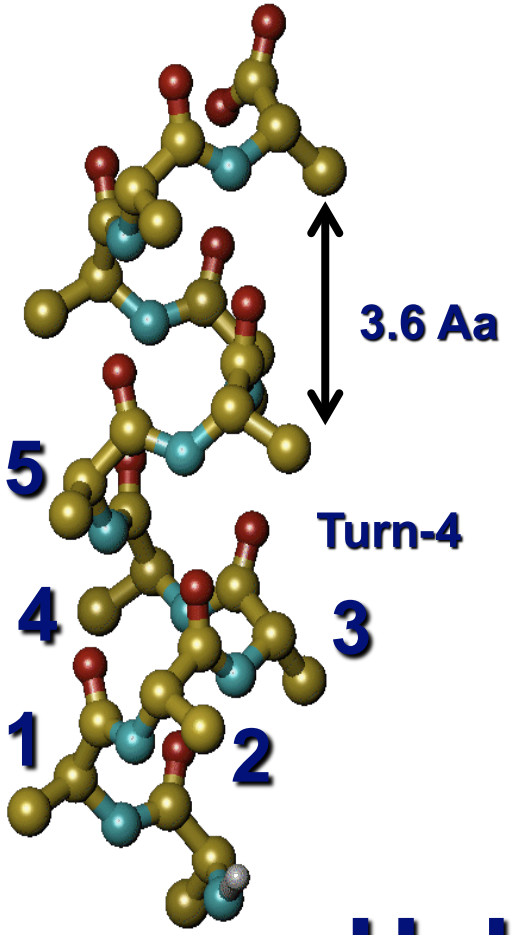


3. Secondary Structure

2. Helices



Helix 3_{10}

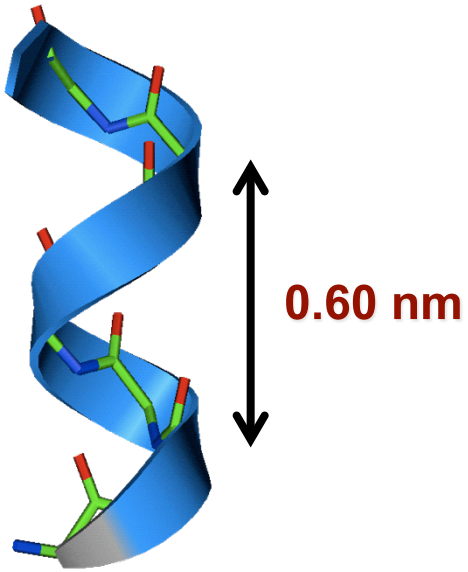


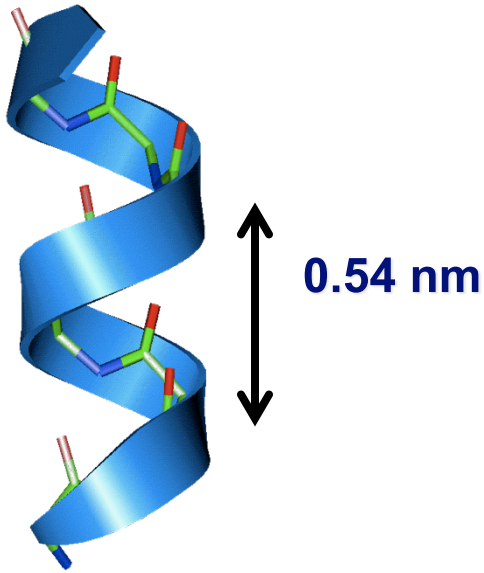
Helix α

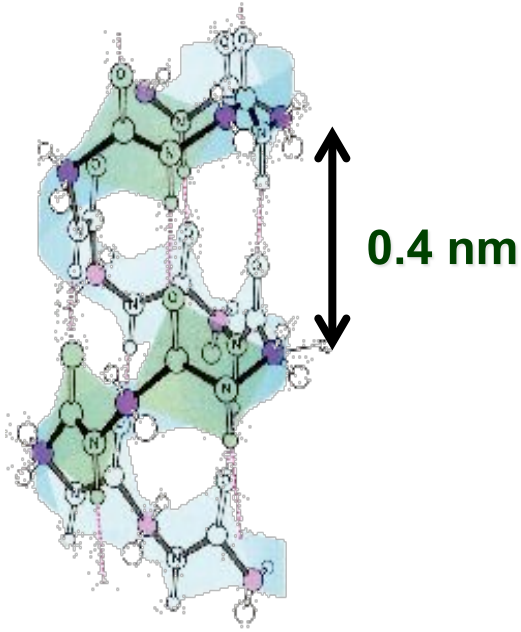
- HB are short distance in sequence
- Side-chains protrude out of the helix

3. Secondary Structure

2. Helices







Helix 3_{10}

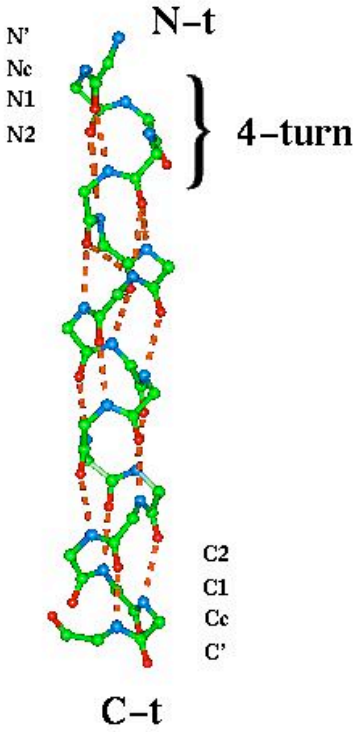
Helix α

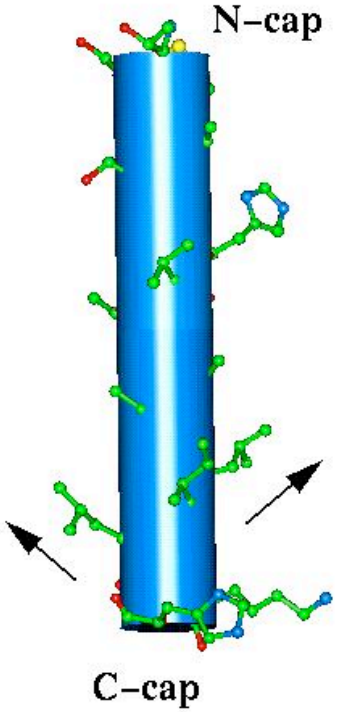
Helix π

UNSTABLE

3. Secondary Structure

2. Helices

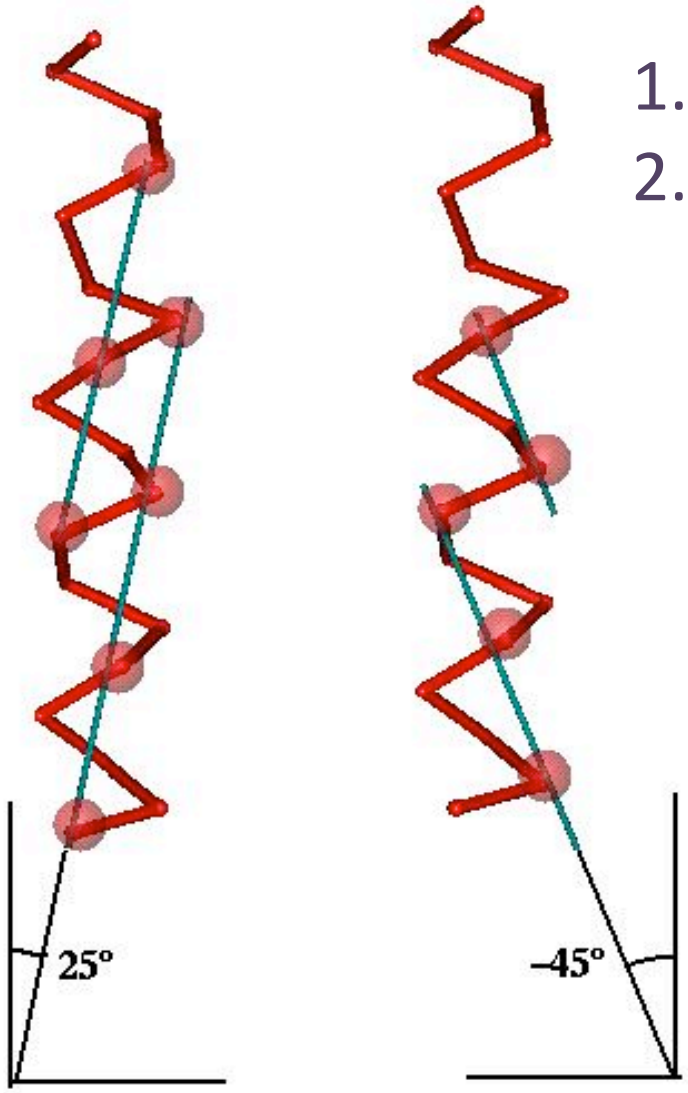




	Hbond	Hidrofobic
N-cap box	N_c-N_3	N'-N_4
Big box	N_c-N_3	N''-N_4
Shellman	C''-C_3 C'-C_2	C''-C_3
α_L	C'-C_3	C''-C_3

3. Secondary Structure

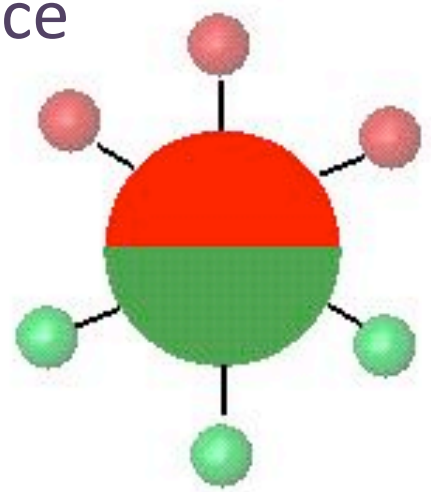
2. Helices



Side-chains location in the helix:

1. Groove formation as in a screw
2. Amphipathic helix: two faces with different solvation properties

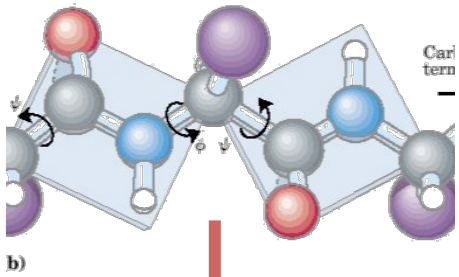
Polar face



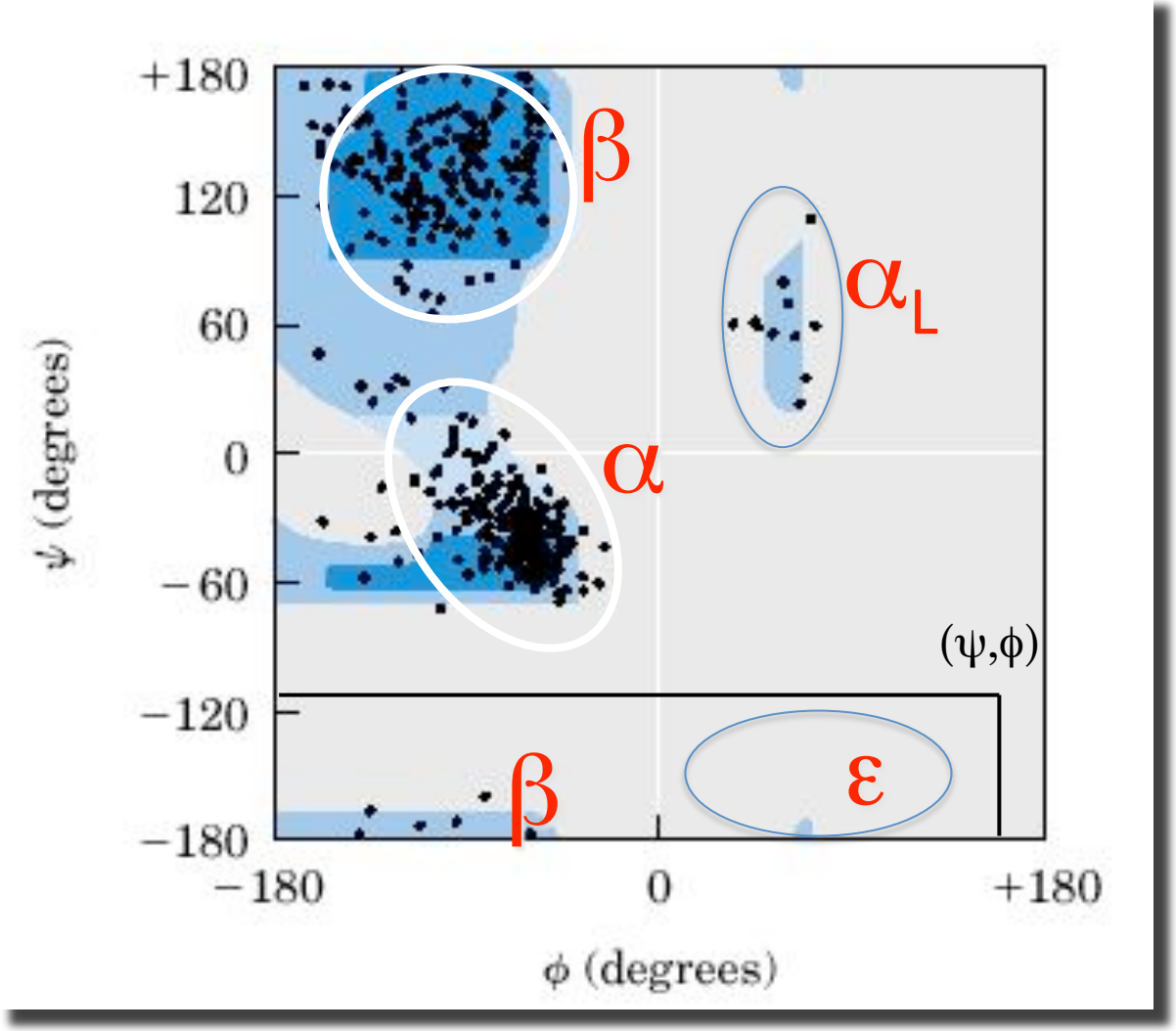
Non-polar face (hydrophobic)

3. Secondary Structure

3. Ramachandran Plot



(ψ,ϕ)



3. Secondary Structure

4. Aa propensity