Lecture 2:
Amino Acid Structure & INTs

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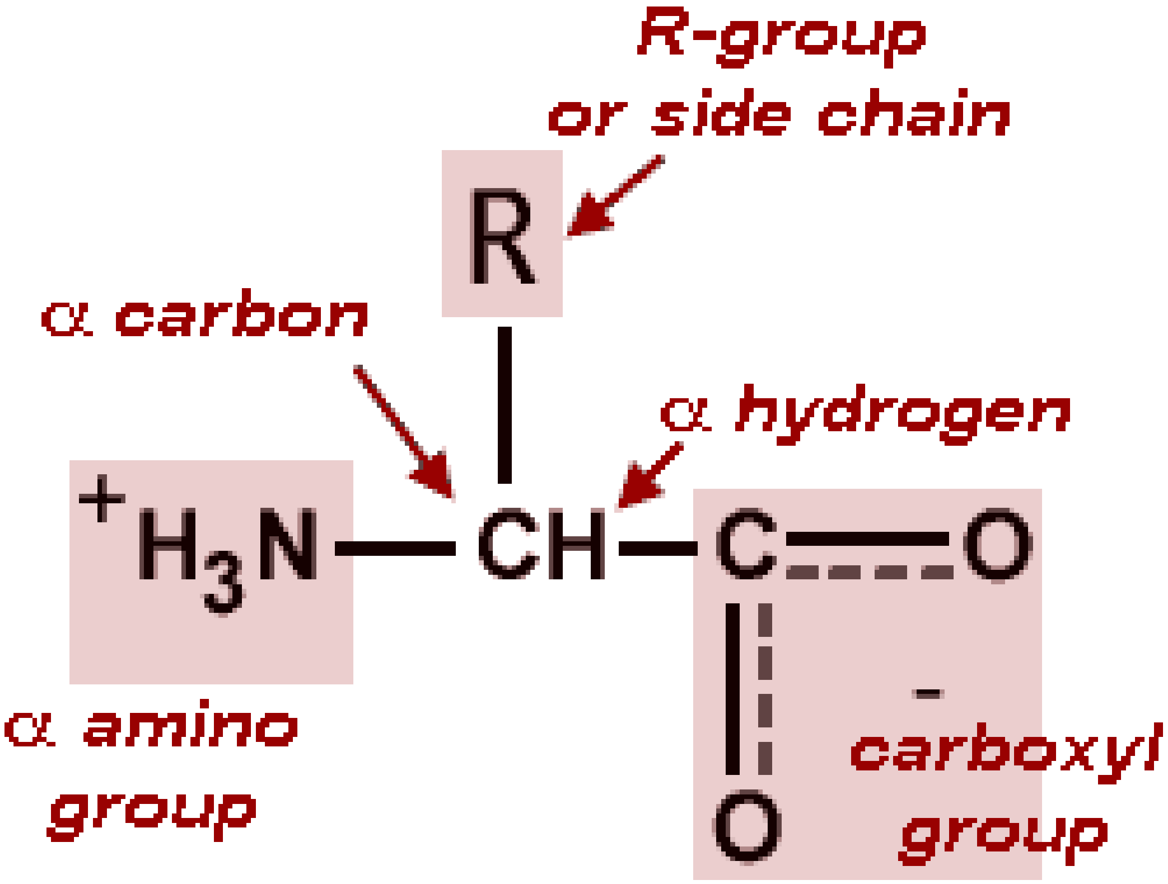
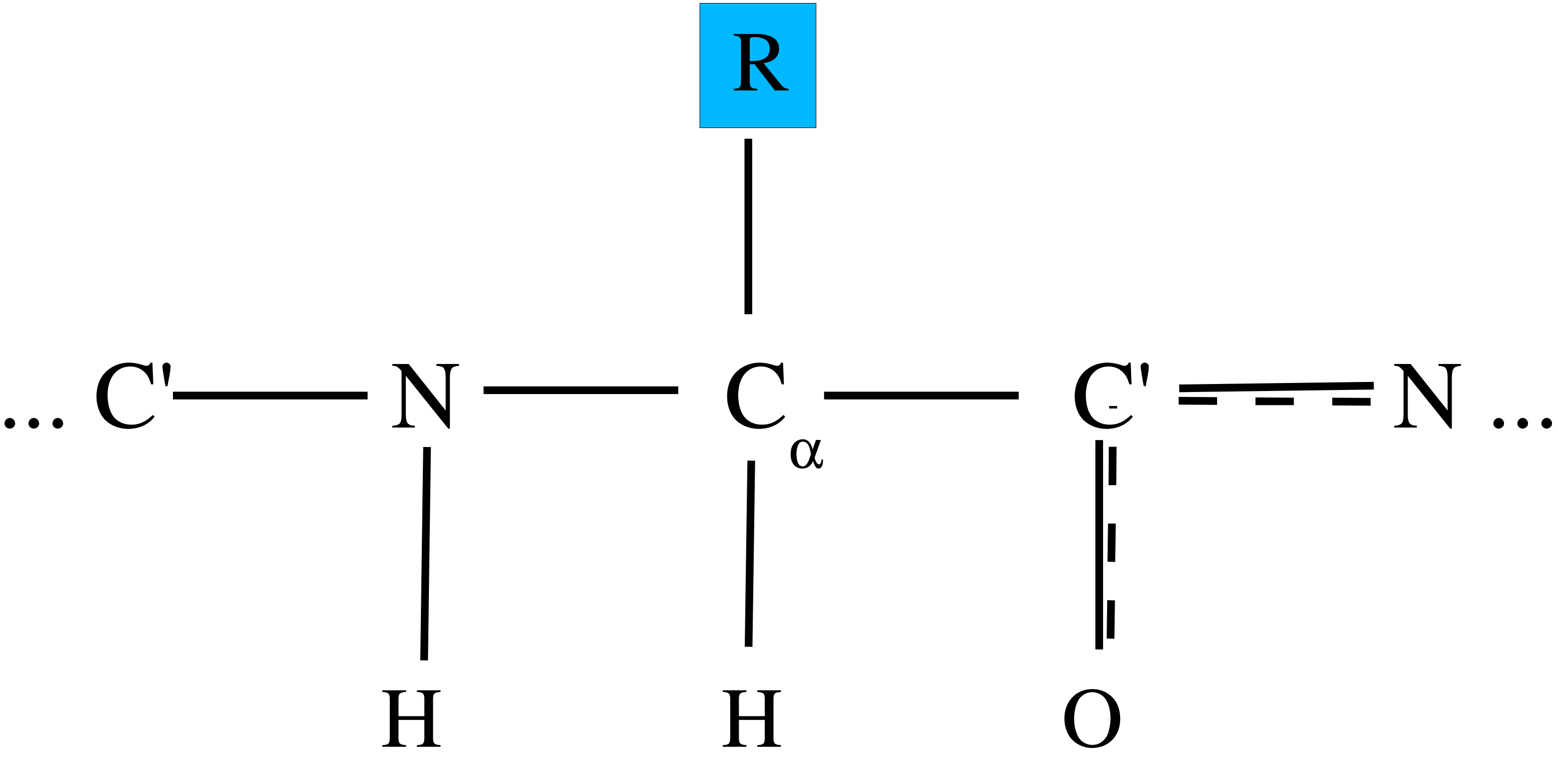
Structure & bonding within each amino acid



Chirality & sp^3 versus sp^2 hybridization



sp^3 Hybridization: C_α (CH_4-methane)

→ **ground-state configuration of electrons in C:**

$1s^2\,2s^2\,2p^2$

→ **excited-state configuration of electrons in C^*:**

$1s^2\,2s^1\,2p^3$

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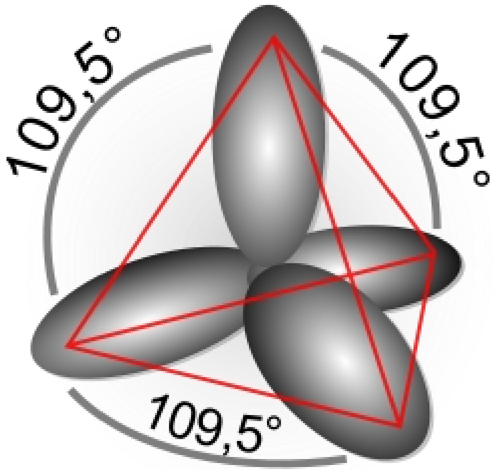
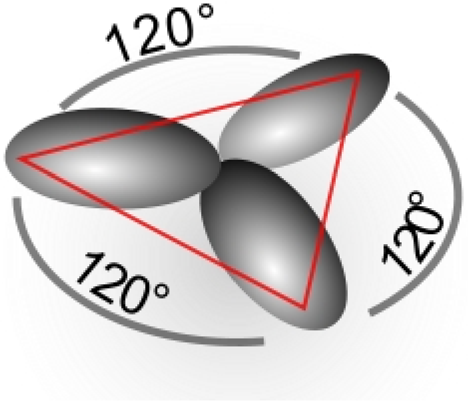


→ **4 hybridized (blended) sp^3-type orbitals composed of one s and three p electron "clouds"!**

sp^2 Hybridization: C'-O & C'-N (C_2H_4 - ethene)

- 3 hybridized planar sp^2 orbitals composed of one s and two p electron “clouds”
- one p electron “cloud” per atom (two per bond) ⊥ sp^2 plane



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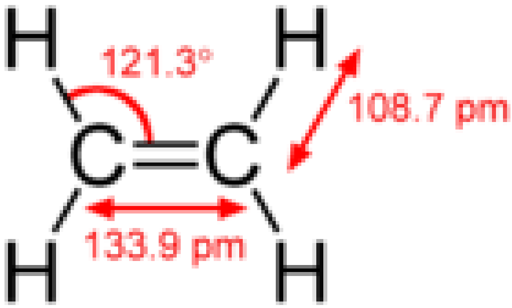
- double bond formation!



Why do chemical bonds form at all?

➔ **electron de-localization is energetically favorable**
➔ **electron transition from one atom to the other**

- **Heisenberg's uncertainty principle:** $\Delta x \, \Delta p \sim \hbar$

  $\Delta p \sim |p| \sim mv$

- **kinetic energy of the electron:** $E = \hbar^2/(m \, \Delta x^2)$

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The smaller the displacement (Δx), the lower the energy!

Lengths of chemical bonds in proteins:

- ➔ **C-H & N-H & O-H: 1 Å**
- ➔ **C=O & C=N & C=C: 1.2-1.3 Å**
- ➔ **C=C: 1.5 Å**
- ➔ **S-S: 1.8 Å**

Typical values of covalent angles:

- ➔ **120° (between sp^2 hybridized bonds)**
- ➔ **109.5°(between sp^3 hybridized bonds)**

Flexibility of the Protein Chain:

Thermal vibrations at room temperature T=300K:
- → covalent bonds
- → angles between covalent bonds

Vibrational frequencies (IR spectrum):
- → H-atoms: $\nu \sim 7 \times 10^{13}$ s^{-1} ($\lambda = 5\ \mu$m)
- → C-atoms: $\nu \sim 2 \times 10^{13}$ s^{-1} ($\lambda = 15\ \mu$m)

Thermal fluctuations at T=300K:
- → $k_B T \sim 2$ cal/mol K$^{-1} \times$ 300K = 0.6 kcal/mol

Calculate the characteristic ν_T of thermal motion:

- $k_B T = 0.6$ kcal/mol = 600 cal / (6×10^{23} particles)

  $= 10^{-21}$ cal/particle

- $h\nu_T = k_B T \rightarrow \nu_T = k_B T/h$

- $h = 6.6 \times 10^{-34}$ J s $= 6.6 \times 10^{-34}$ J s cal (4.2) J^{-1}

  $= 1.6\ 10^{-34}$ cal s

- $\nu_T = 7 \times 10^{12}\ s^{-1}$ → 10-fold too small to excite the covalent bonds

Covalent angles less rigid than covalent bonds:

➔ vibrate at T = 300K with $\nu = 10^{12}$ to 10^{13} s-1

➔ amplitude of vibrations small ~ 5° (4-5%)

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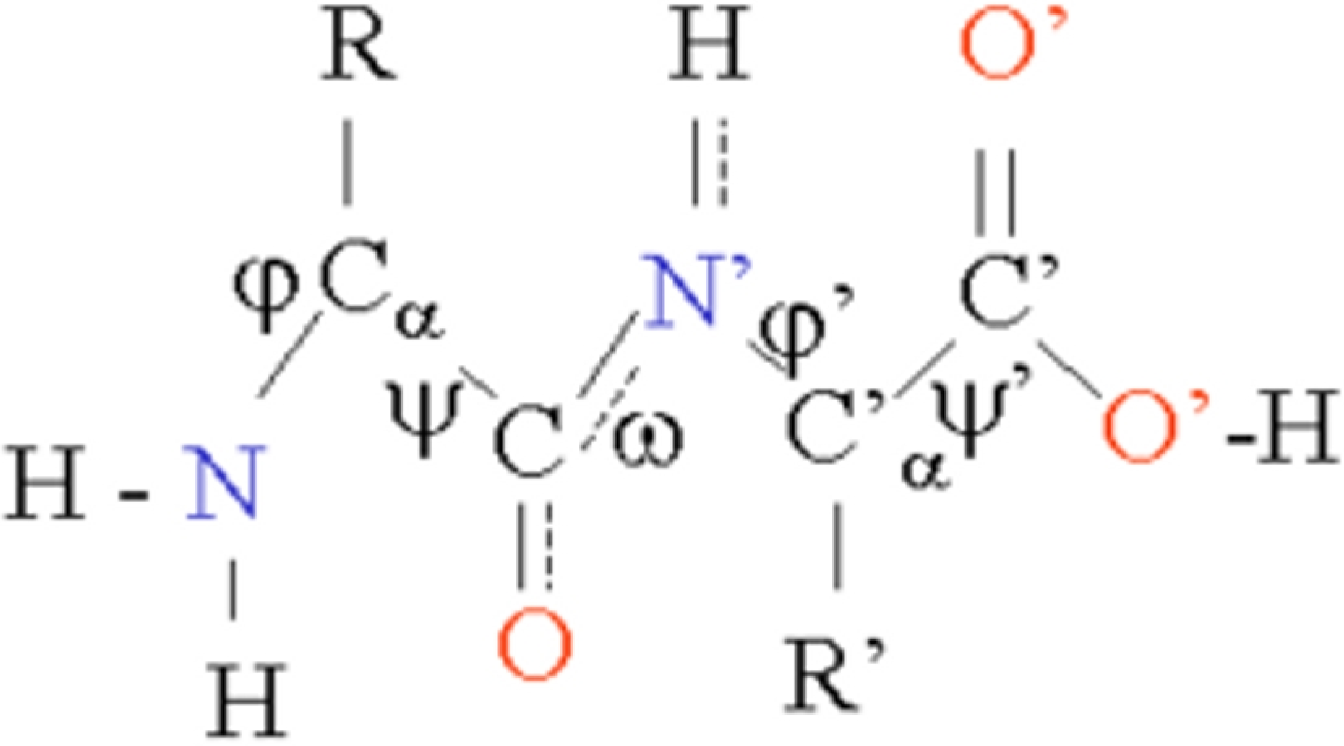
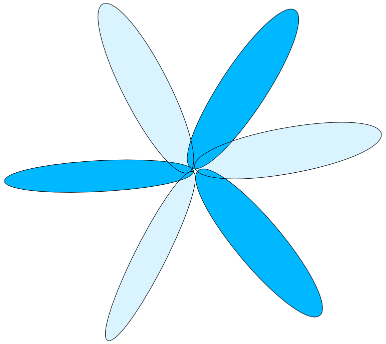
➔ flexibility of a peptide chain (needed for secondary structure formation) is provided by rotation AROUND covalent bonds

➔ angles ϕ, ψ, and ω define protein conformation (synonymous with structure)

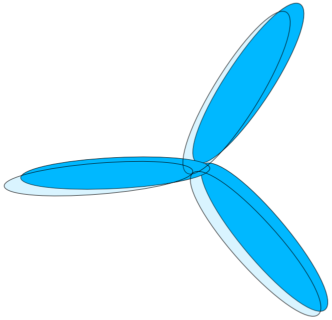
Di-peptide (two amino acids long peptide): Definition of angles ϕ, ψ and ω



Potential of rotation:
between two sp^3 atoms (aliphatic side chains):



- crossed orbitals (at 60°, 180°, 300°)
- electron clouds do NOT overlap: potential minima



- eclipsed orbitals (at 0°, 120°, 240°)
- electron clouds overlap: potential maxima

Barrier: 3 kcal/mol; Thermal fluctuations 15-20°

Potential around two sp^2 hybridized atoms (C' and N):

- ➔ a global minimum at 180°
- ➔ additional minimum at 0° (higher energy than at the global minimum due to repulsion between two neighboring massive C_α atoms)

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- ➔ angle ω distinguishes between trans and cis conformations almost all peptide groups are in trans conformation (proline exception)

Potential between sp^2 and sp^3 hybridized atoms
(ϕ around N-C_α & ψ around C_α-C'):

- ➔ potential has 6 minima and 6 maxima on [0°, 360°]
- ➔ low potential barriers of ~1kcal/mol ($k_B T \sim$ 0.6 kcal/mol)

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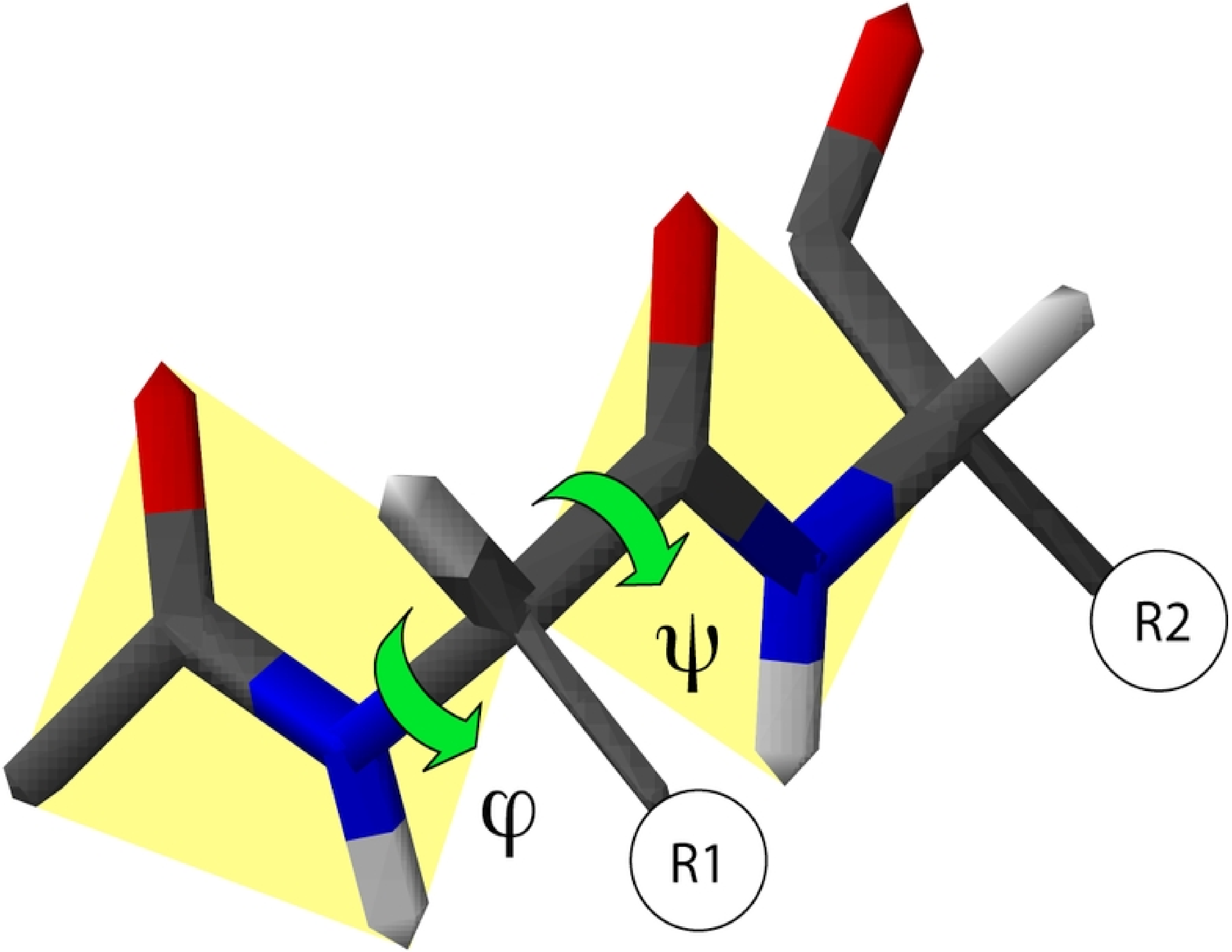
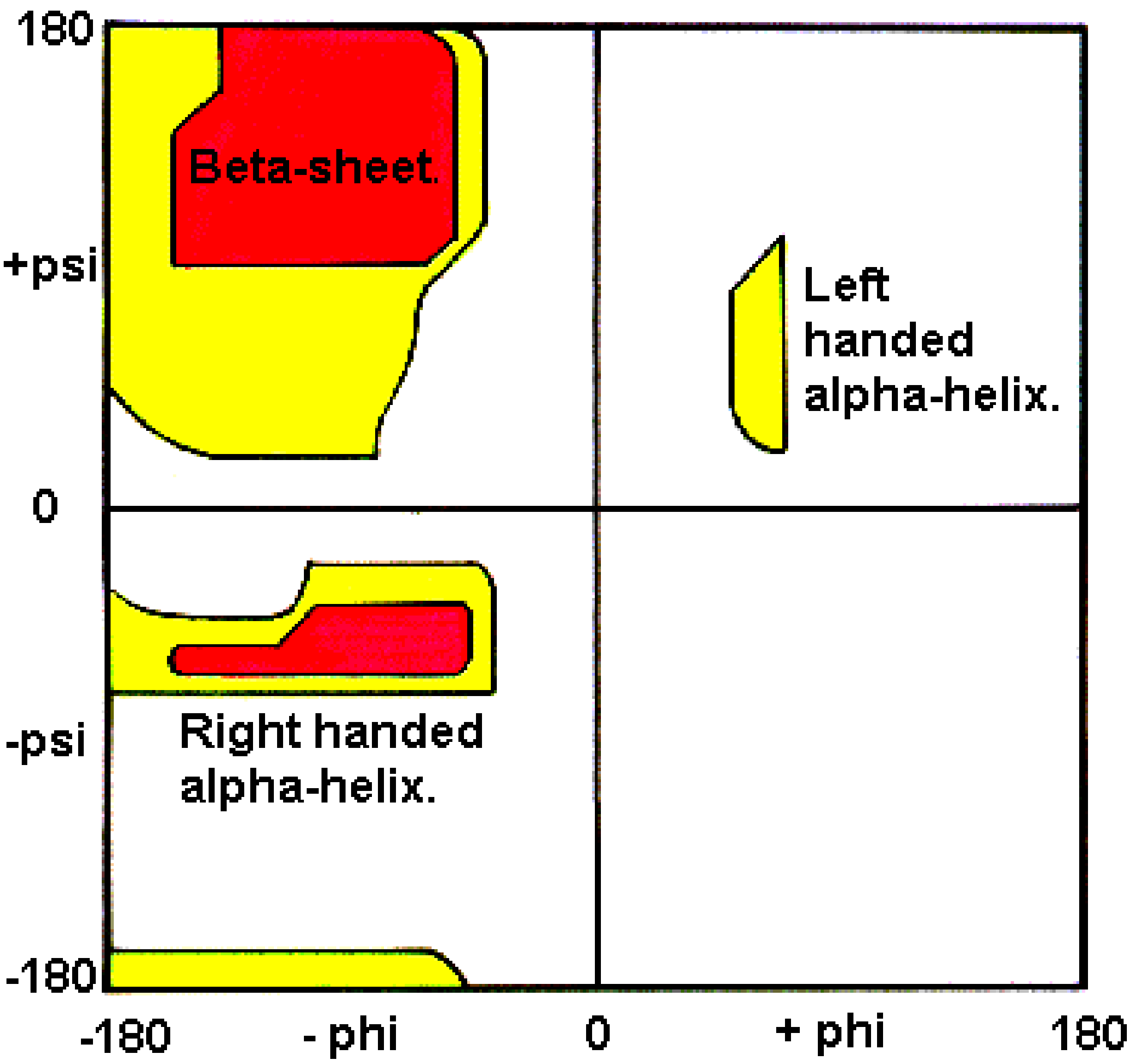
- ➔ nearly free rotations around ϕ and ψ !

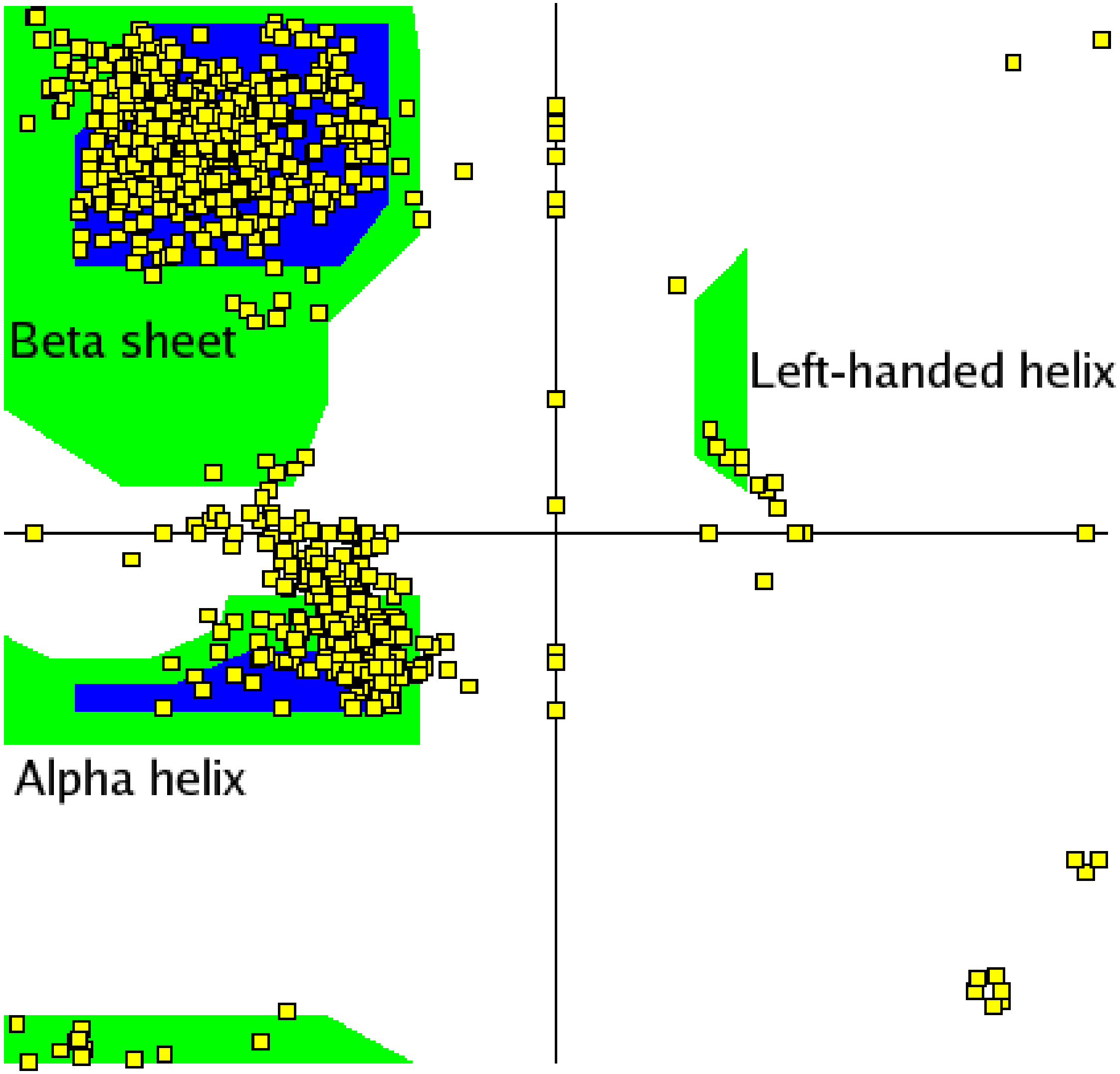
Dihedral angles (ϕ, ψ)





The Ramachandran Plot.

For protein **PCNA**, a human **DNA clamp** protein (**PDB** ID **1AXC**)



Elementary non-covalent interactions

- **Pauli's exclusion principle: up to two “paired” electrons per orbital that envelops two atoms & forms a covalent bond**

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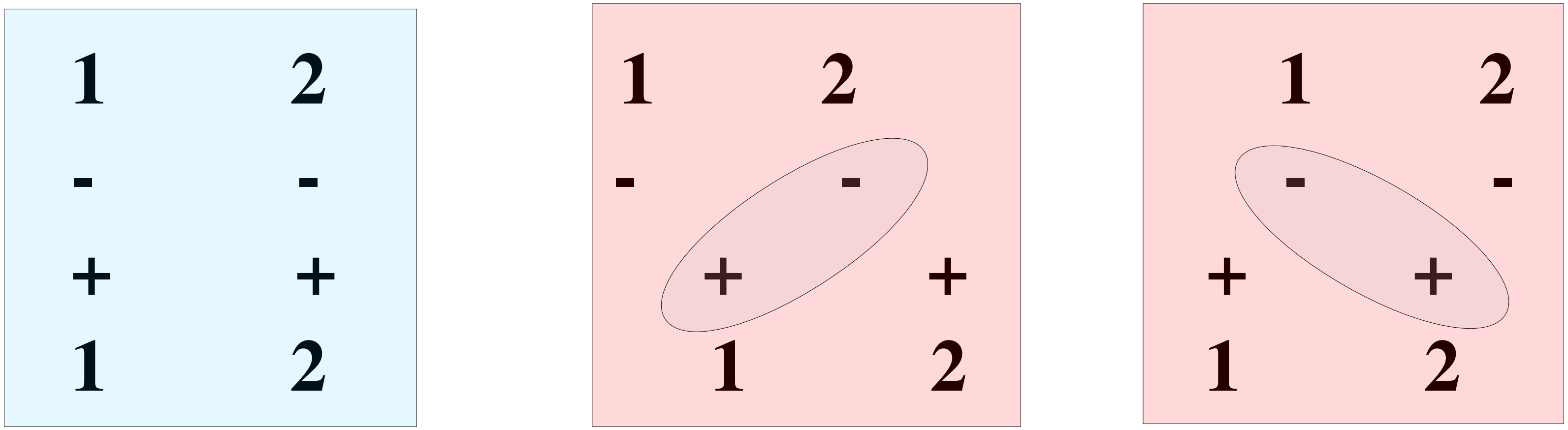
- **approaching atoms with saturated orbitals feel repulsion when their electron clouds begin to Overlap**
- **at greater distances all atoms & molecules attract each other → purely quantum mechanical effect!**

Coordinated vibrations of electrons of two atoms:

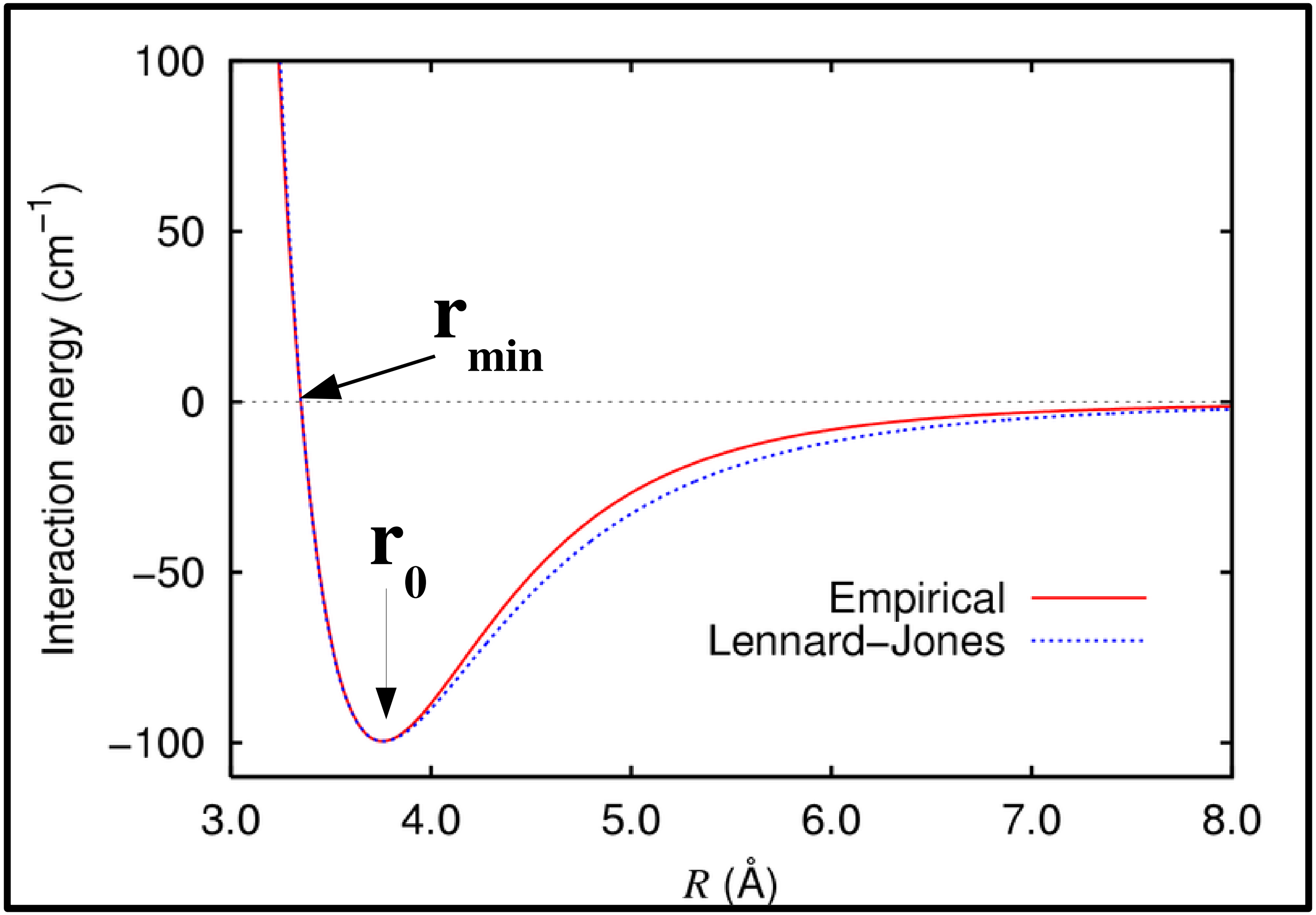


Electrostatic potential energy V(r) ~ 1/r:

→ the closer the two opposite charges the lower the electrostatic energy (negative sign-attraction)

Lennard-Jones Potential (12-6 Potential):

$$U_{LJ} = E_0 \left[(r_0/r)^{12} - 2\,(r_0/r)^{6}\right]$$



r_{min}

r_0

Characteristics of the LJ potential:

- spherically symmetric (approximation---p orbitals are in fact highly directional!)
- 2 “free parameters”, E_0 and r_0, to fit to exp. data
- strong repulsion at short distances (Pauli's exclusion principle)
- attraction at intermediate distances (Van der Waals)

Typical values of van der Waals interaction potential:

INT	E_0[kcal/mol]	r_0[Å]	r_{min}[Å]
H- -H	0.12	2.4	2.0
H- -C	0.11	2.9	2.4
C- -C	0.12	3.4	3.0
O- -O	0.23	3.0	2.7
N- -N	0.20	3.1	2.7
CH_2 – CH_2	0.5	4.0	3.0