# Notes from Voet & Voet — 8th chapter (3D structures of proteins)

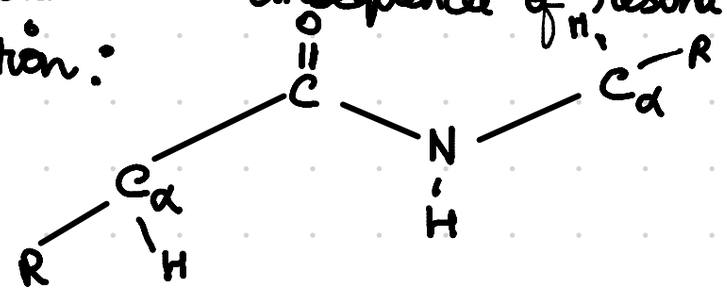
① 2° structure ② Fibrous proteins

## 2ndary Structure

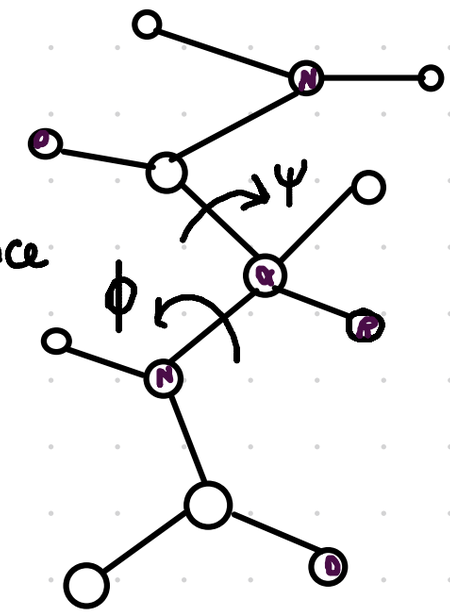
- Local conformation of its backbone — helices, pleated sheets, etc.

## Peptide group

- rigid planar structure — consequence of resonance interactions : 40 % double bond structure
- trans conformation :




most common — because of steric interference




- Torsion angles / dihedral angles : $C_\alpha - N$ bond — $\phi$ ; $C_\alpha - C$ bond — $\psi$ → both 180° when all-trans

substituents other than H hinder rotation, hence some conformations are prohibited

- Ramachandran Diagram

sterically allowed values of $\phi$ & $\psi$ — determined by calculating distances between the atoms of a tripeptide → for all values of $\phi$ & $\psi$ for the central peptide unit.

sterically forbidden conformation → when any non-bonding interatomic distance < Van der waals dist.

↳ Ramachandran map

→ 7+% is forbidden

→ allowed regions depend on the Van der waals radii chosen to calculate it

↳ for realistic values, one three small regions are accessible

• red → actual values | we find ones with forbidden values lie close to $\psi = 0$

↳ b/w two allowed regions

[twists of only a few degrees about the peptide bond]

Ramachandran plot for glycine

Glycine → X $C_\beta$ atom → ↓ sterical hindrance

↳ found in sharp turns of chains (less sterical hindrance)

Why is the Ramachandran diagram more restricted for all its $\phi$ and $\psi$ angles in >tripeptides

↳ because

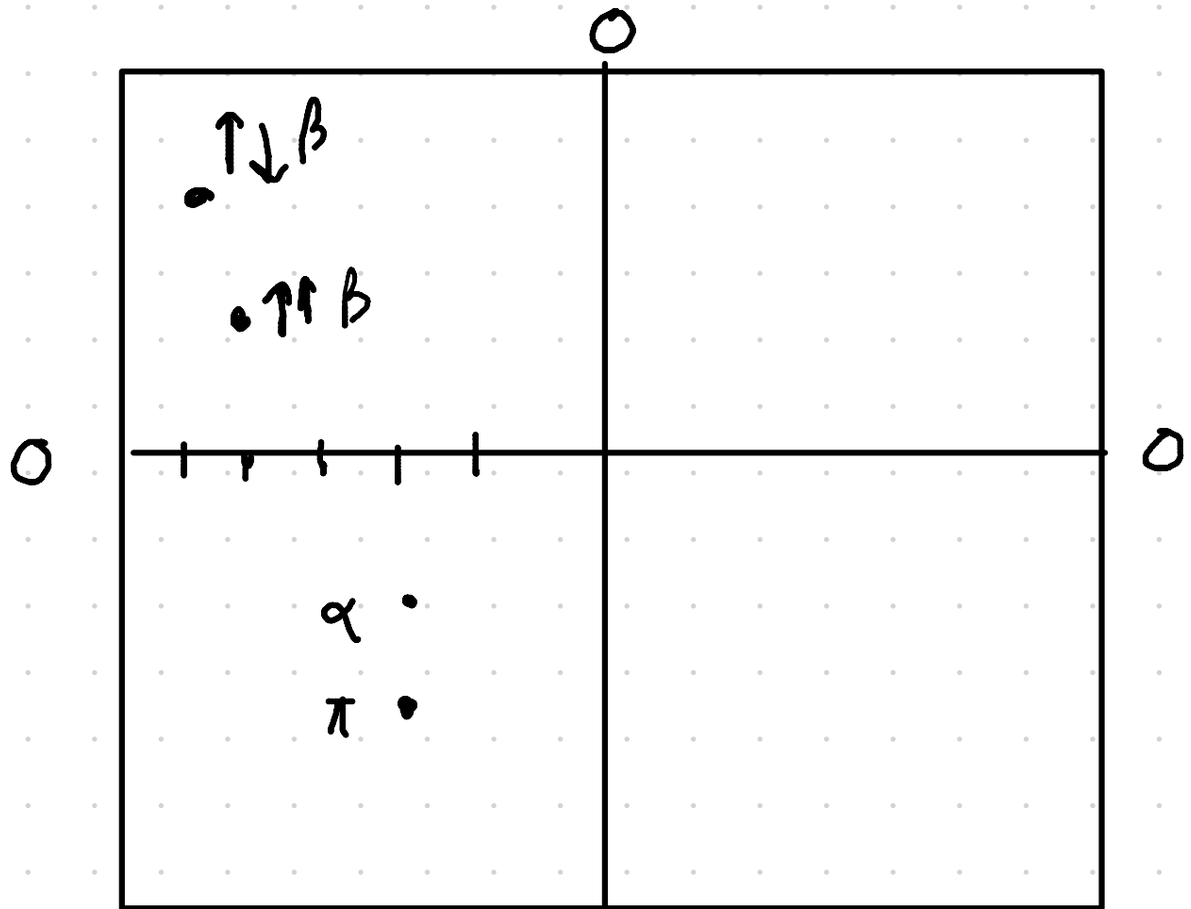
## Helical structures

helix → happens when polypeptide chain is twisted by equal amounts about each of its $C_\alpha$ atoms

↳ characterised by n → no. of peptide units per helical turn

p → pitch (distance helix rises per turn)

| | $\phi$ | $\psi$ | res./turn | |
|---|---|---|---|---|
| ↑↓ β-sheet | −140 | +135 | 2 | |
| ↑↑ β-sheet | −120 | +115 | 2 | |
| $3_{10}$ helix | −60 | 30 | 3 | |
| α-helix ($^{3.6}_{13}$-helix) | −60 | −50 | 3.6 | |
| π-helix ($^{4.4}_{16}$-helix) | −60 | −70 | 4.4 | |
| | | | | |




$3_{10}$ → tightly packed

π → loosely packed

In proteins, n is not an integer.
Conformations are greatly limited in accordance with the Ramachandran diagram

## (A) α-helix

- allowed conformation angles + favourable H-bonding pattern
- L-α aa residue → $\phi = -57°$, $\psi = -47°$ ; $n = 3.6$, $p = 5.4\,\text{Å}$

  D-α aa residues → $\phi = 57°$, $\psi = 47°$ ; $n = -3.6$, $p = 5.4\,\text{Å}$

- $n^{th}$ $\underset{H}{N}$ – H bonding with $(n-4)^{th}$ $\overset{O}{\overset{\|}{C}}$ ($N \cdots O \rightarrow 2.8\,\text{Å}$)
- tightly packed core with R groups pointing outwards (minimising steric hindrance)
  - ↳ Left-handed helices are forbidden because of this reason

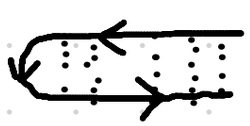
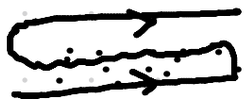
## (B) Other polypeptide helices

- $2.2_7$ ribbon & $3_{10}$ helix ($n_m \rightarrow n$ = no. of residues per helical turn and $m \rightarrow$ no. of atoms b/w H bond.
- $3_{10}$ helix mildly forbidden, so for π helix ($^{4.4}16$) → sometimes found.
- for $2.2_7$ helix, strongly forbidden → never found
- certain synthetic polypeptides (homo) like polyproline assume weird structures | polyproline → No H-bond, → steric hindrance
  - ↳ Yet. left-handed helix, with 3.0 res / helical turn and 9.4 Å pitch.

- polyproline and polyglycine helixes are almost identical - polyglycine can be right-handed or left-handed
  ↳ achiral

  polyglycine and polyproline } → basic structural motif of collagen

## © β-structures

- H-bonding occurs b/w neighbouring polypeptide chains
- Two kinds: ⓐ Antiparallel β-sheet : 
  ⓑ Parallel β-sheet : 

  } rippled, pleated appearance → pleated sheet

  ↳ 2 residue repeat distance of 7 Å, average 6 strands ~25 Å

  If mixed, only 20% have parallel as well as antiparallel

Parallel β-sheets are less stable (distorted H-bonds) : min. 5 strands

- In globular proteins, β-sheets form the central core & have pronounced right-handed twist - WHY?
  ↳ because of non-bonded interactions between chiral L-amino acid residues in the sheets extended polypeptide chains
  ↳ distorts and weakens interchain H-bonds — Tradeoff
- antiparallel β-strands are linked by what is topologically equivalent to a simple hairpin turn

parallel β-strands → crossover connection → out of plane
                                          → right-handed helical sense

## ① Non-repitive structures

- In globular proteins, 31% α helix, 28% β-sheet — rest **coiled / loop** structure
  - ↳ straight runs of secondary structure joined by **β-bends** (occuring at protein surfaces)
    - ↳ irregular, but not disordered random coil
    - ↳ four successive amino acid residues

β-bends → two types → Type I β & Type II β. (differ in peptide unit joining 2 & 3)

| Type I β | Type II β |
|---|---|
| $\phi_2 = -60^\circ$ | $\phi_2 = -60^\circ$ |
| $\psi_2 = -30^\circ$ | $\psi_2 = 120^\circ$ |
| $\phi_3 = -90^\circ$ | $\phi_3 = -90^\circ$ |
| $\psi_3 = 0^\circ$ | $\psi_3 = 0^\circ$ |

Residue 2 → Glycine

Residue 3 → Proline

- chains containing charged surface groups are usually disordered | sometimes proteins are disordered in one state and ordered in another

## ② Fibrous Proteins

We discuss structural-functional motifs in (A) Keratin (B) Collagen

- fibrous proteins do not crystallise, and contain little information if they do.

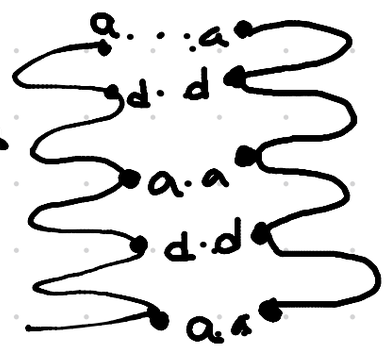
### (A) Keratin

- chemically unreactive

- α-Keratin - mammals, β-keratin — birds and reptiles
- In mammals, 50-keratin genes → Type I (relatively acidic) & Type II (relatively basic) → both present in keratin filaments
- # remember macrofibrils in hair are made from microfibrils cemented together by amorphous protein matrix of high sulfur content
- α-keratin because resembles α-helix in terms of diffraction pattern
  - ↳ Type I & Type II keratin chain twisted into parallel into left-handed coil (coiled coil)
- conformation of coiled coil is a consequence of its primary str.
  - ↳ central ~310 residue segment of each polypeptide chain contains heptad pseudorepeat with a & d as nonpolar residues.

α-helix : a and d line up forming hydrophobic strip ~ another hydrophobic strip.

↳ resulting in an 18° inclination of the α-helices | side chains fit into this groove




coiled coils are important parts of globular proteins as well

N & C terminals of polypeptide chains have flexible conformation → organised into 30 Å long protofilament

α keratin is rich in Cys residues → disulfide bonds b/w adjacent polypeptide chains → hard/soft (↑/↓)

↳ mercaptans are used to cleave disulfide bonds.

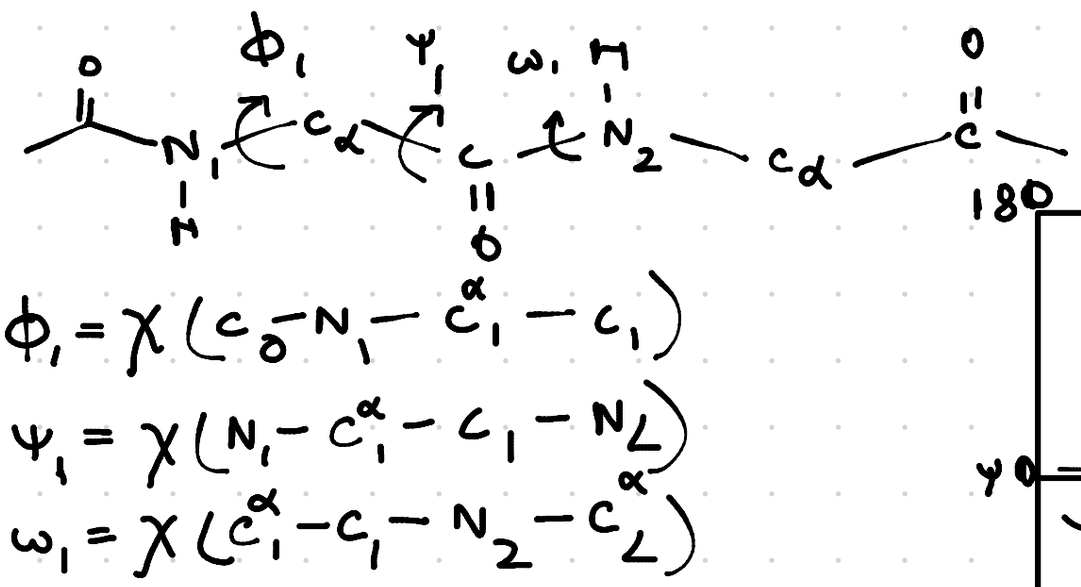
# Helix Designing

(a) Amino acids : Helix formers – Alanine, Leucine, Glutamate

Helix breakers – Proline, Glycine

charged residues at helix termini stabilise through electrostatic interactions

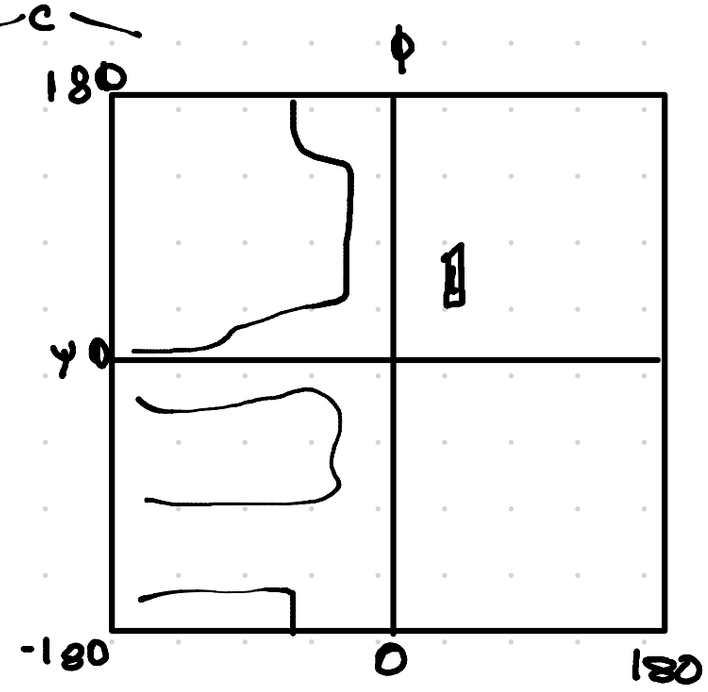
(b) Hydrogen bonding




$\phi_1 = \chi(C_0 - N_1 - C_1^\alpha - C_1)$

$\psi_1 = \chi(N_1 - C_1^\alpha - C_1 - N_2)$

$\omega_1 = \chi(C_1^\alpha - C_1 - N_2 - C_2^\alpha)$

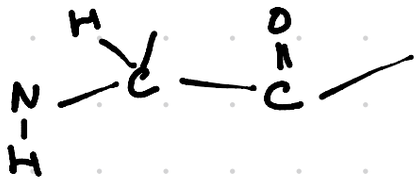


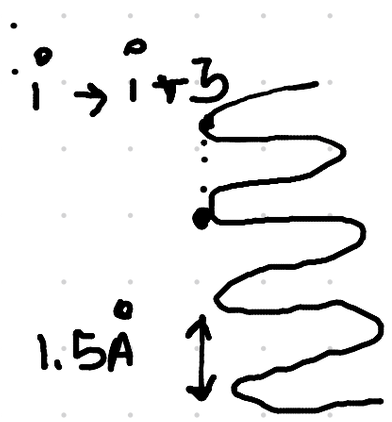

Helix Designing

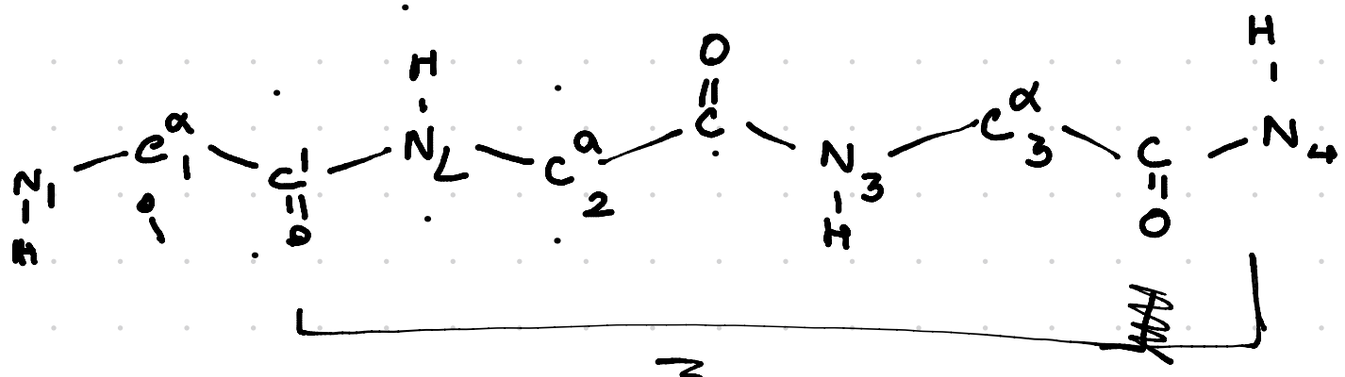
N-cap : Asparagine, Aspartate on glutamate, Proline, Glycine, Serine, Threonine

Body : Alanine, Aib, Methionine, Leucine, Glutamate ($\phi = -60°, \psi = -30$)

AiBn $+60^\circ, +30^\circ$






$\alpha$ $i^{th}$ C=O to $i+4^{th}$ NH $\rightarrow \phi = -60^\circ, \Psi = -50^\circ$

$3_{10}$ : $i^{th}$ C=O to $i+3^{th}$ NH $\rightarrow \phi = -60, \Psi = 30^\circ$

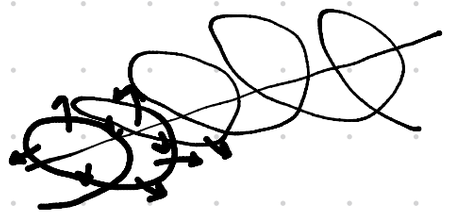
$\pi$ : $i^{th}$ C=O to $i+5^{th}$ NH $\rightarrow \phi = -60, \Psi = -70^\circ$

$\uparrow\downarrow\beta$ : $\phi$: -140 $\Psi$ : 135°

$\uparrow\uparrow\beta$ : $\phi = -120^\circ, \Psi$ : 115°

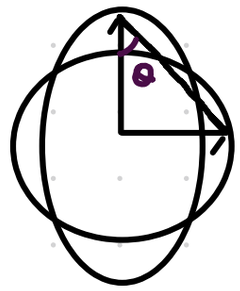
## Circular Dichroism

optically active chiral molecules absorb different amounts of LCP and RCP



$$\Delta A = A_L - A_R$$

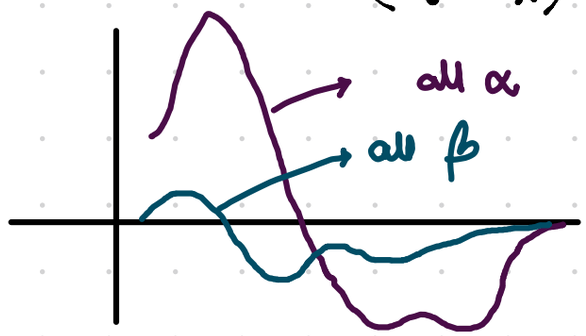
## Molar Ellipticity



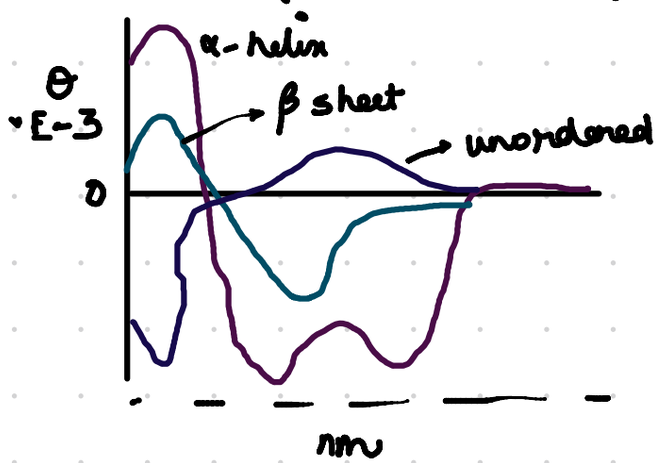

CD spectrum → reported in degrees of ellipticity : $\tan\theta = \frac{E_L - E_R}{E_L + E_R}$

$$[\theta] = 3298\,\Delta\epsilon = 3298(\varepsilon_L - \varepsilon_R) = 3298\left(\frac{\Delta A}{c}\right)$$

We notice that $\theta \uparrow\downarrow$ from all β to all α




Conformational analysis of 2° Str. of macromol.




Dichroism is measured as mean residue ellipticity (degrees-cm²/dmol)

In molecules it happens because of chirally active molecules → structure → placed in an asymmetric environment
→ covalently linked to chiral centre

## Optical rotation:

Specific rotation $[\alpha] = \frac{\alpha}{dc}$

Molar rotation $[\phi] = \frac{100\psi}{LM}$

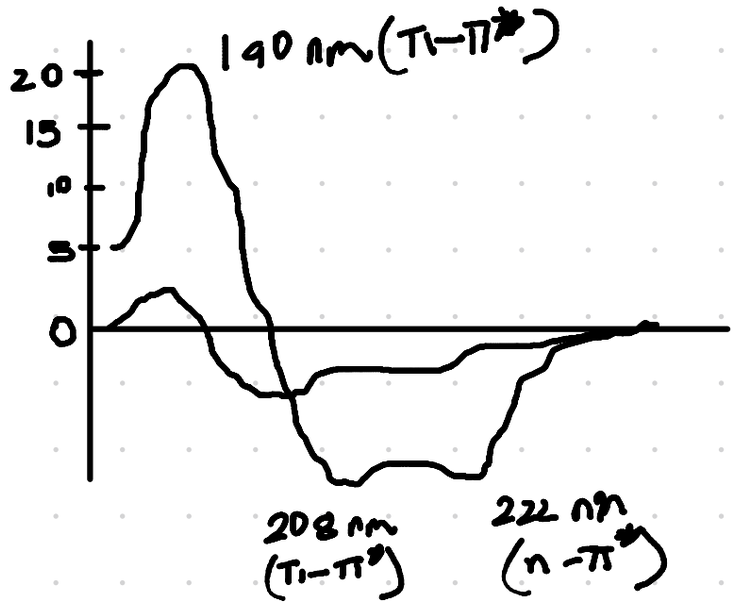
## Circular dichroism

Molar ellipticity $[\theta] = \frac{100\psi}{LM}$

$LM$ = path length [m] × conc [mol/L]

Circular Dichroism: $\Delta\varepsilon = \varepsilon_L - \varepsilon_R = \frac{A_L - A_R}{LM}$

$\psi$ = ellipticity (in degrees)

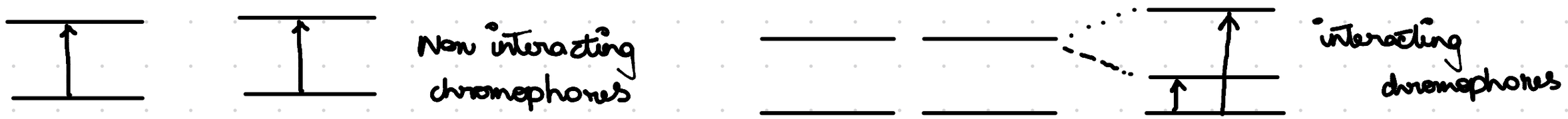



exciton interactions → peaks at 195 nm and 175 nm

nπ* transition → peaks at 215 nm

## Exciton Splitting

splitting of electronic absorption bands of a population of chromophores that are arranged in space st. two or more chromophores are in close proximity




$\Delta A = A_L - A_R$ => $A_L > A_R$ → maxima, $A_L < A_R$ → minima

↓

circular dichroism (e.g., ds dNA)

In helical structures, two kinds of chromophores → intramolecular H bonds
→ amide chromophores

In beta sheets, the individual dipole of the two kinds of chromophores are not closely packed → smaller amplitude of exciton splitting

## Nuclear Magnetic Resonance (NMR)

Nuclear spin: most elements; at least one isotope, with a non-zero spin angular momentum, $I$, and mag. moment $\mu$.