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PHI- PSI ANGLES

Proteins → polymers of amino acids → fold into a 3D structure → that has a function

Structure-Function Paradigm

Myoglobin - first structure to be solved

Kendrew & Perutz

↓ under L. Bragg.

started X-ray crystallography in the field of macromolecules

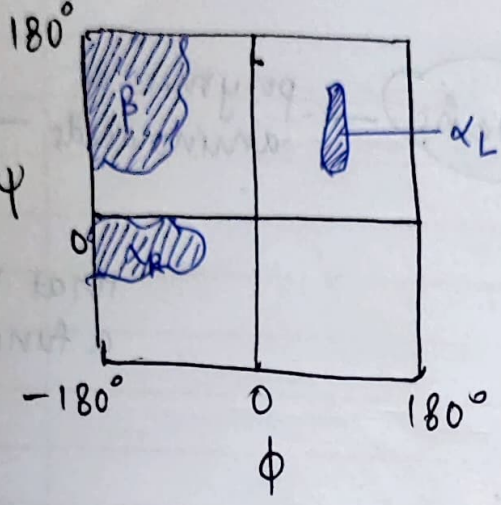
G.N. Ramachandran:

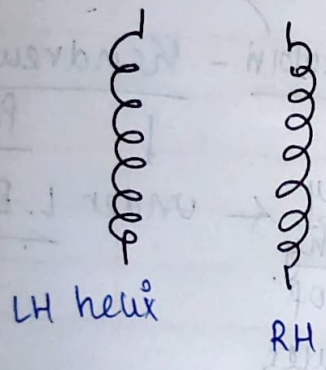
- di'hedral angles
- a few allowed angles
- also solved collagen

extrapolating X-ray crystal structures to solve new structures → structural biology

PDB: Protein Data Bank. – www.rcsb.org.

Ramachandran Plot





→ from right-hand thumb rule

Eg: P53

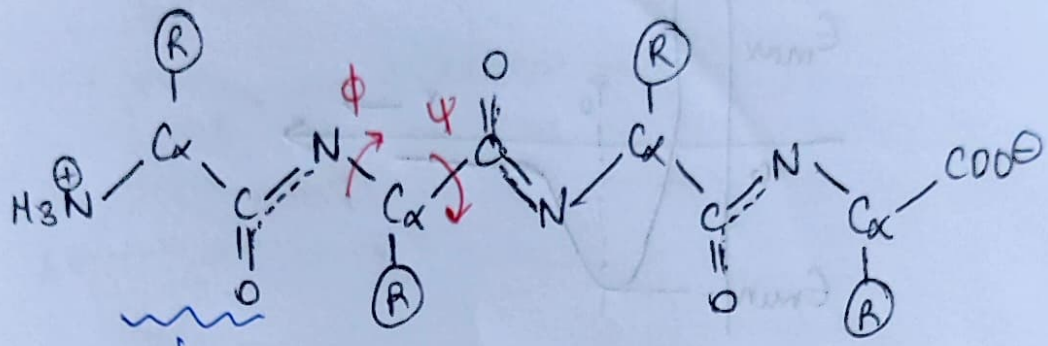
IDPs – intrinsically disordered proteins

structural polymorphism

not folded into a 3D structure in the native state → folds when it binds to any partner or conditions

↳ (exception of the structure-function rule).

N-terminal ——— L to R ———→ C-terminal



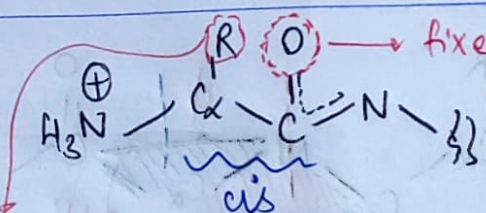
trans → R & O are opposite ~ 172.7°

Note:

- ✓ no diffraction data is available for H.
- ✓ due to its size & presence of only 1 electron
- ✓ as X-ray is diffracted by the electrons.
- ✓ electron density map → then you fit it in the model

CONS → proteins
CONF → nucleic acids
} the atoms that are shown in X-ray diffn.

cis

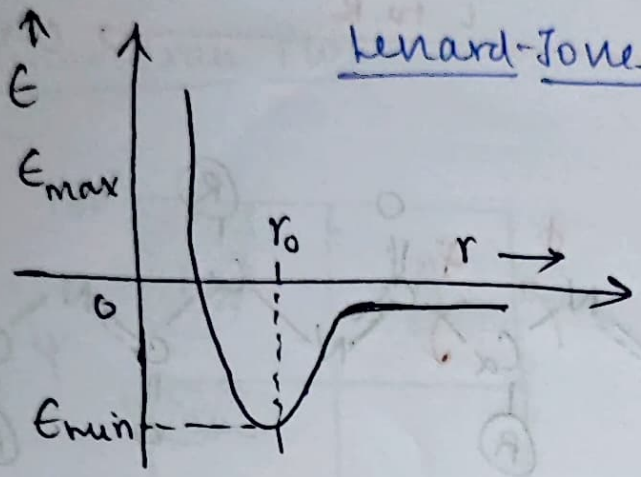


→ fixed van-der waals radii

depends on the side chain

- if Gly → no problem as only one hydrogen.
- If Arg (longest side chain) → will try to penetrate the vdw radii of O → steric hindrance

Lenard-Jones Potential

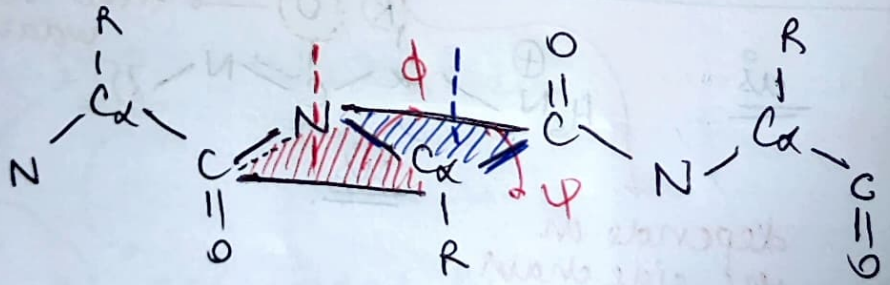


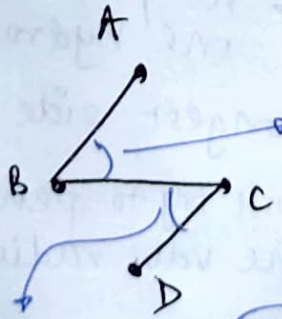
$$LJ = \frac{A_{ij}}{r^{12}} - \frac{B_{ij}}{r^{6}}$$

repulsive part — attractive part

as r ↓ → minus term ↑

overall LJ ↓

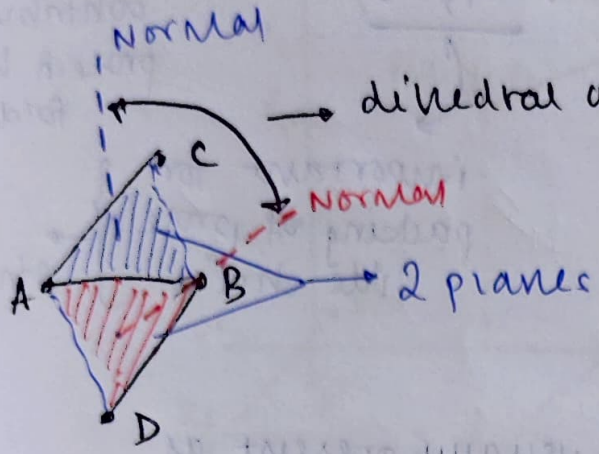




this angle can be considered for interⁿ between A & C

for interⁿ b/w B & D.

but for interⁿ b/w A & D? → Dihedral Angle



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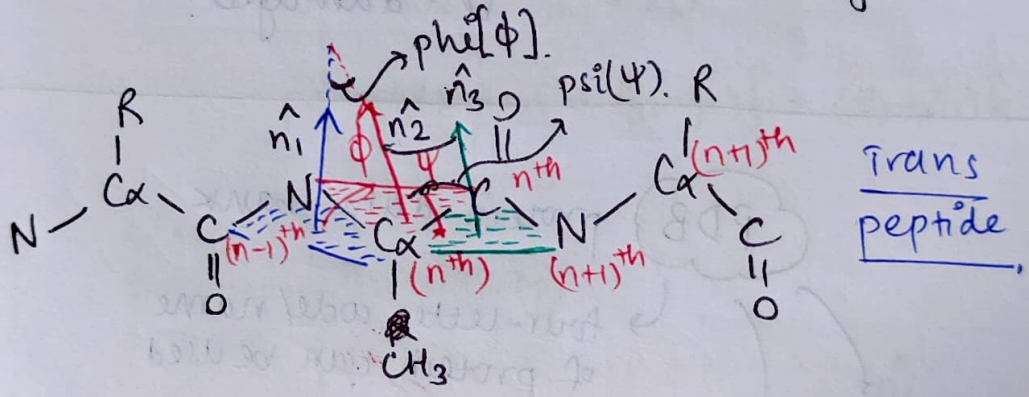
ϕ, ψ → backbone dihedral angles



trans peptide.

To calculate ϕ, ψ of n^{th} Ala residue.

$\hat{n}_1 \cdot \hat{n}_2 = |\hat{n}_1||\hat{n}_2|\cos\phi$

$= \cos\phi$

$\therefore \boxed{\phi = \cos^{-1}(\hat{n}_1 \cdot \hat{n}_2)}$

$\boxed{\psi = \cos^{-1}(\hat{n}_2 \cdot \hat{n}_3)}$

- coordinates of carboxyl C of $(n-1)^{th}$ residue & N of n^{th} residue.
- coordinates of carbonyl C of n^{th} residue & N of n^{th} residue.

(G)-(A)-(V)-(C)-(M)-(R)

∴ we cannot calculate ϕ for the 1st residue as no $(n-1)^{th}$ residue

Similarly, we cannot calculate ψ for the last residue as no $(n+1)^{th}$ residue

side-chain dihedral angles → χ_1, χ_2, etc. → do not really contribute to protein backbone folding

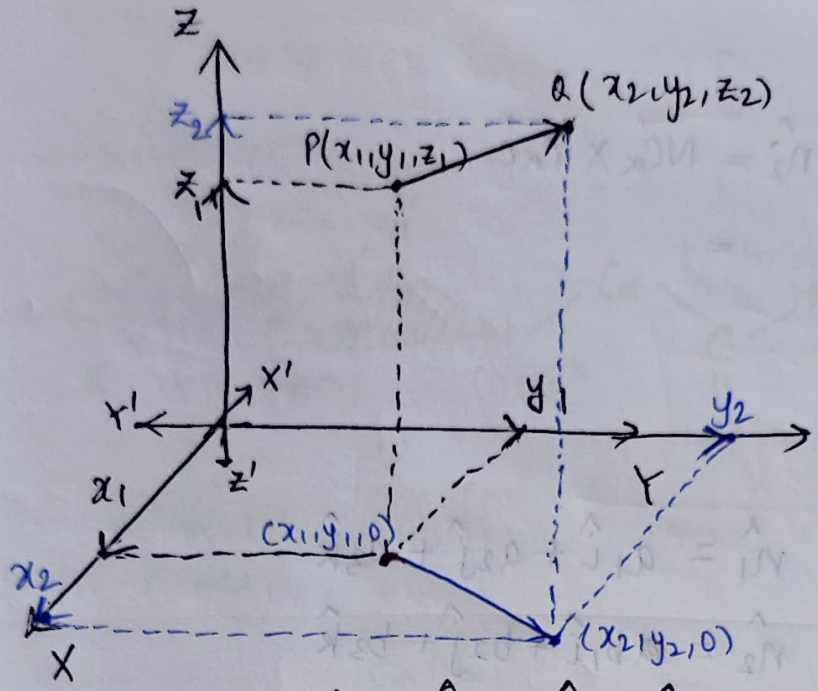
χ_1, χ_2 → important for packing of protein side chains → 3D structures

★ **Proline:** — usually present as helix-capping residues

if present in blw, the helix structure might be damaged.

PDB — protein data bank

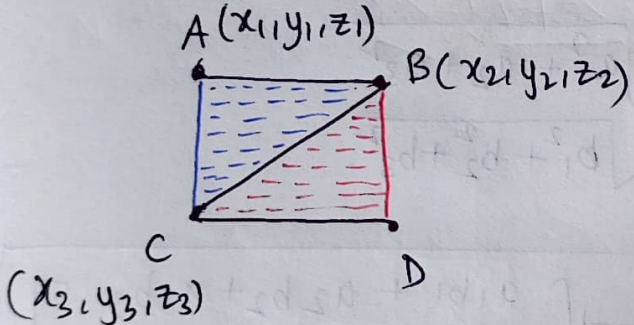
- four-letter code/ name of protein can be used
- orthogonal coordinate system
- gives us the coordinates of each & every atom except H atoms.

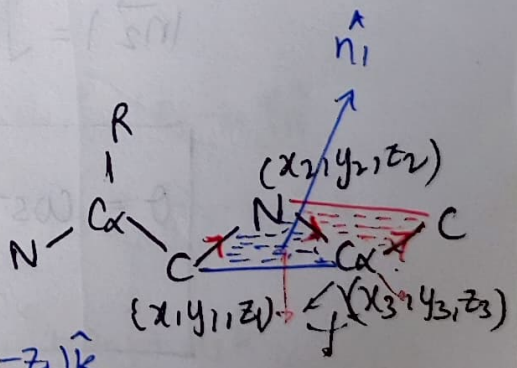


$$\vec{P} = x_1\hat{i} + y_1\hat{j} + z_1\hat{k}$$

$$\vec{Q} = x_2\hat{i} + y_2\hat{j} + z_2\hat{k}$$

$$\vec{PQ} = (x_2-x_1)\hat{i} + (y_2-y_1)\hat{j} + (z_2-z_1)\hat{k}.$$





$$\vec{CN} = (x_2-x_1)\hat{i} + (y_2-y_1)\hat{j} + (z_2-z_1)\hat{k}$$

$$\vec{NC_\alpha} = (x_3-x_2)\hat{i} + (y_3-y_2)\hat{j} + (z_3-z_2)\hat{k}$$

$$\boxed{\hat{n}_1 = \vec{CN} \times \vec{NC_\alpha}} = \begin{vmatrix} \hat{i} & \hat{j} & \hat{k} \\ (x_2-x_1) & (y_2-y_1) & (z_2-z_1) \\ (x_3-x_2) & (y_3-y_2) & (z_3-z_2) \end{vmatrix}.$$

$$\hat{n}_1 = \hat{i}\left[(y_2-y_1)(z_3-z_2) - (y_3-y_2)(z_2-z_1)\right] \quad \} N_1\hat{i}$$
$$-\hat{j}\left[(x_2-x_1)(z_3-z_2) - (x_3-x_2)(z_2-z_1)\right] \quad \} N_2\hat{j}$$
$$+\hat{k}\left[(x_2-x_1)(y_3-y_2) - (x_3-x_2)(y_2-y_1)\right] \quad \} N_3\hat{k}$$

$$\hat{n_2} = \overrightarrow{NC_\alpha} \times \overrightarrow{C_\alpha C}$$

$$\hat{n_1} = a_1\hat{i} + a_2\hat{j} + a_3\hat{k}$$

$$\hat{n_2} = b_1\hat{i} + b_2\hat{j} + b_3\hat{k}$$

$$\hat{n_1} \cdot \hat{n_2} = |\vec{n_1}||\vec{n_2}|\cos\theta$$

$$\boxed{\theta = \frac{\cos^{-1}(\hat{n_1} \cdot \hat{n_2})}{|\vec{n_1}||\vec{n_2}|}}$$

$$|\vec{n_1}| = \sqrt{a_1^2 + a_2^2 + a_3^2}$$

$$|\vec{n_2}| = \sqrt{b_1^2 + b_2^2 + b_3^2}$$

$$\boxed{\theta = \cos^{-1}\left[\frac{a_1b_1 + a_2b_2 + a_3b_3}{\sqrt{a_1^2 + a_2^2 + a_3^2} \cdot \sqrt{b_1^2 + b_2^2 + b_3^2}}\right]}$$

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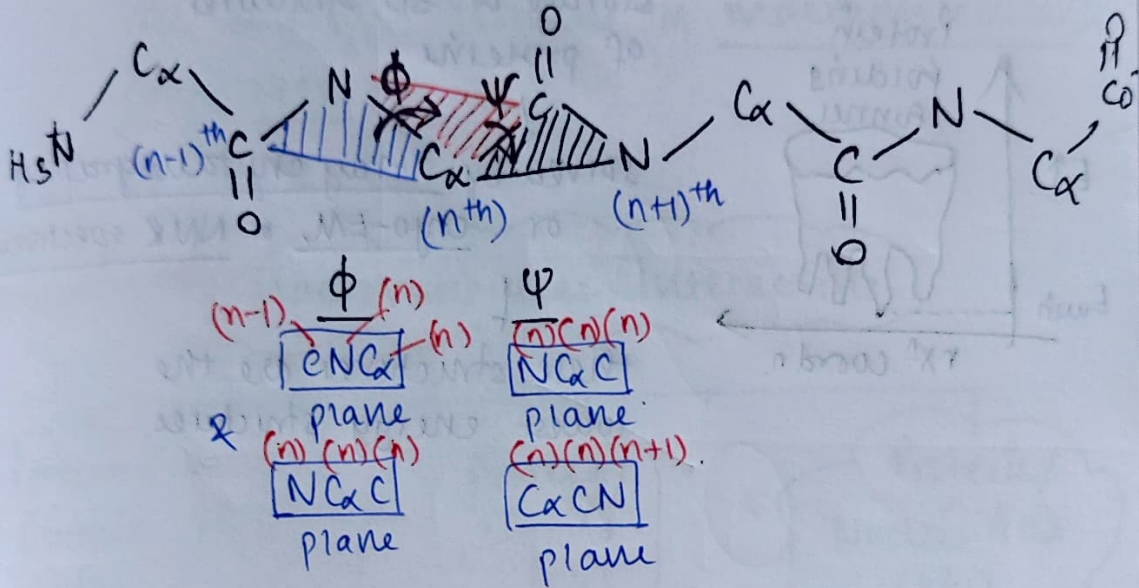


ϕ $(n-1)$ (n) (n) — CNC_α — (n) — plane

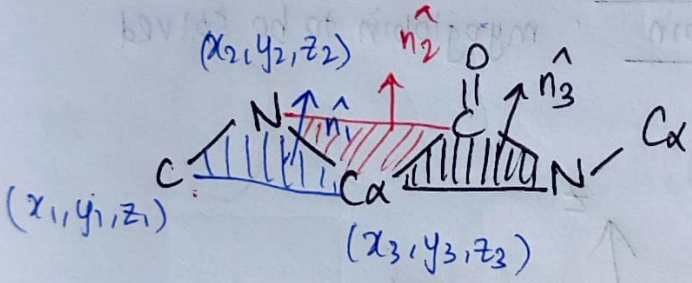
ψ (n) (n) (n) — $NC_\alpha C$ — plane

&

(n) (n) (n) — $NC_\alpha C$ — plane

(n) (n) $(n+1)$ — $C_\alpha CN$ — plane

coordinates from PDB.



$$\vec{CN} = (x_2 - x_1)\hat{i} + (y_2 - y_1)\hat{j} + (z_2 - z_1)\hat{k}$$

$$\vec{NC_\alpha} = (x_3 - x_2)\hat{i} + (y_3 - y_2)\hat{j} + (z_3 - z_2)\hat{k}$$

$$\vec{n_1} = \vec{CN} \times \vec{NC_\alpha} = a_1\hat{i} + a_2\hat{j} + a_3\hat{k}$$

$$\text{III}^{ly},\ \vec{n_2} = \vec{NC_\alpha} \times \vec{C_\alpha C} = b_1\hat{i} + b_2\hat{j} + b_3\hat{k}$$

$$\vec{n_1} \cdot \vec{n_2} = |\vec{n_1}|\,|\vec{n_2}| \cos\theta.$$

$$a_1b_1 + a_2b_2 + a_3b_3 = \sqrt{a_1^2 + a_2^2 + a_3^2} \cdot \sqrt{b_1^2 + b_2^2 + b_3^2} \cos\theta$$

$$\theta = \cos^{-1}\left[\frac{a_1b_1 + a_2b_2 + a_3b_3}{\sqrt{a_1^2 + a_2^2 + a_3^2}\sqrt{b_1^2 + b_2^2 + b_3^2}}\right].$$

PDB protein data bank

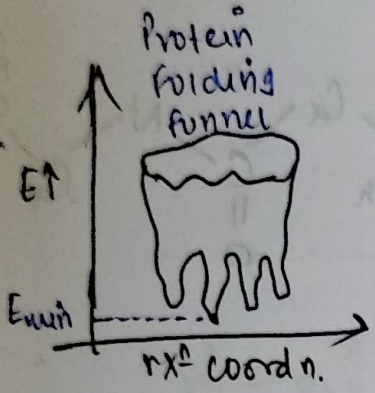
↳ storage of 3D structures of proteins

↓

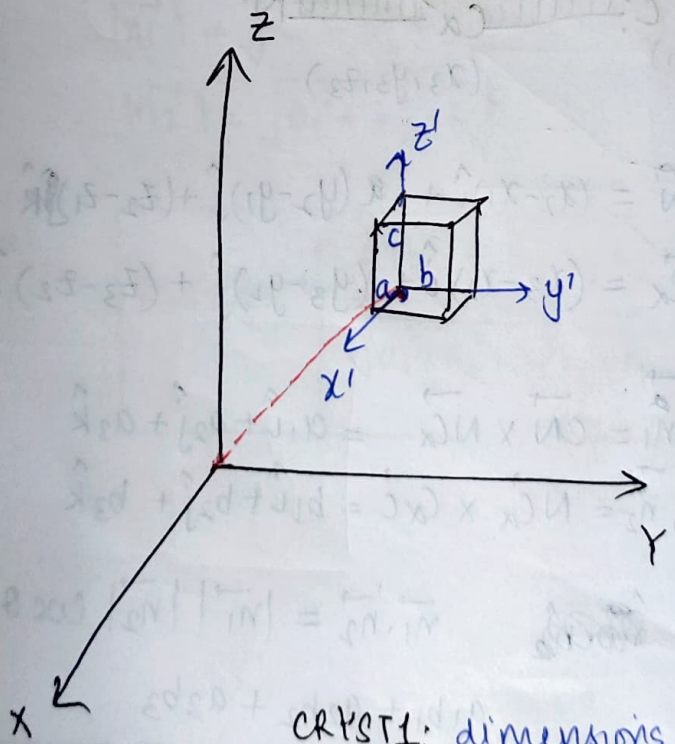
solved by X-ray crystallography or cryo-EM or NMR spectroscopy

↓

these structures are the lowest energy structures.



Sperm Whale Myoglobin: first structure of myoglobin to be solved



CRYST1: dimensions of unit cell (in Å)

IASY — amino-acyl t-RNA synthetase → (RNA + protein)

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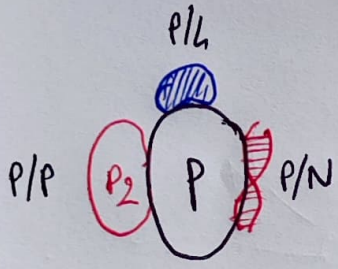
Assignment 2

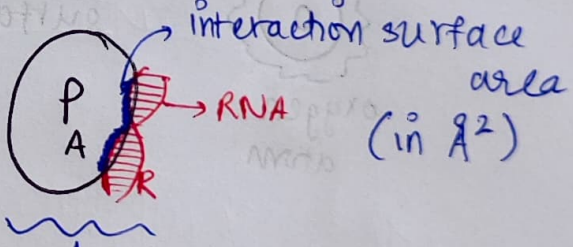
Calculate the interface area & identify the interface residues in macromolecular complexes

affinity chromatography

Macromolecular Interactions

- Protein / Protein (P/P)
- Protein / Ligand (P/L)
- Protein / Nucleic Acid (P/N)



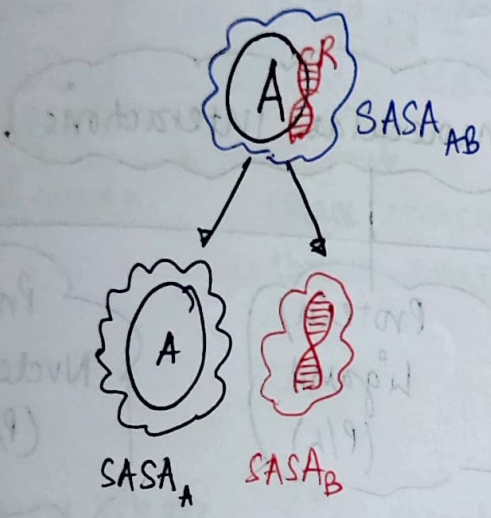


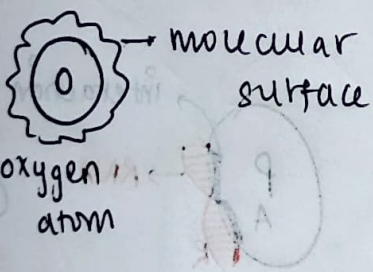
coordinates of both from PDB.

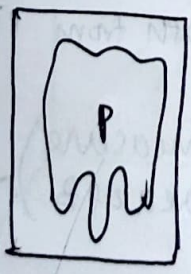
Buried surface Area (BSA) / Interface area (IA) = (measure area of A) + (measure area of B) − (area of AB)

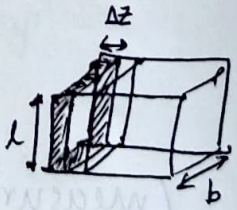
$$BSA(IA) = SASA_A + SASA_B - SASA_{AB}$$

Solvent Accessible Surface Area









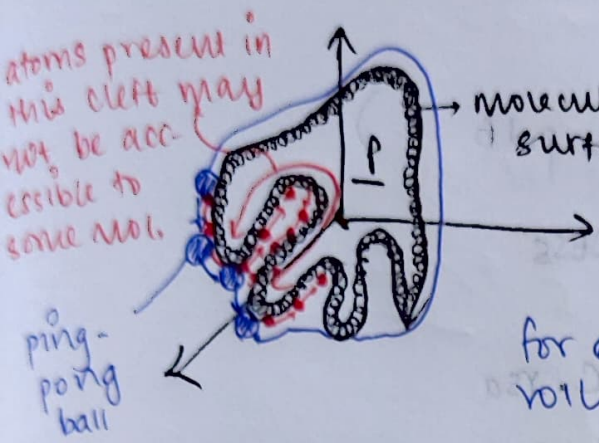
$\Delta z \to 0$

↓

calculate area = $l \times b$

↓

then integrate along ∫ wrt Δz.



→ absolute term

(●)

for eg, we have a ping-pong ball rolling on the surface

↓

when it comes to the cleft, it is not able to enter

↓

but if we take a smaller (•) ball, it is able to access

↓

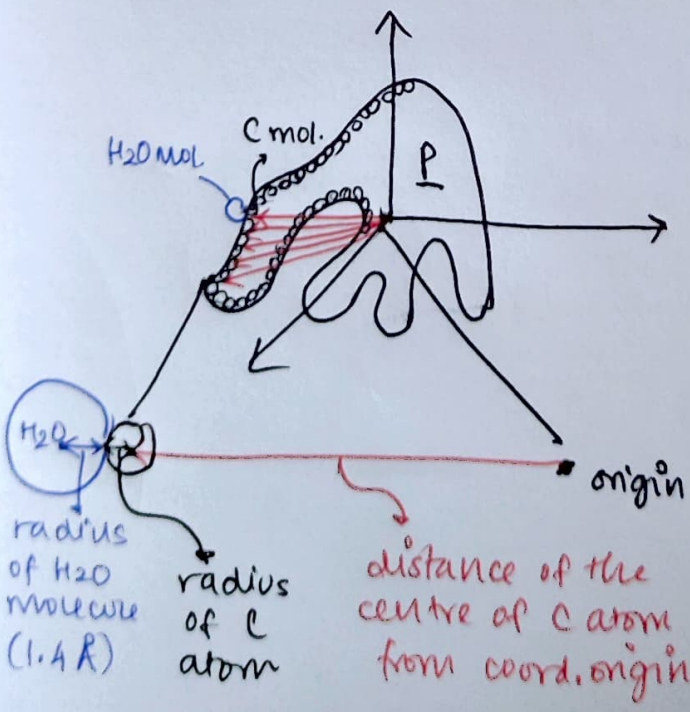
concept of Accessible Surface Area.

→ molecular surface area

→ $SASA_{water}$

solvent molecules → probe → to calculate the SASA.

↳ eg: water : 1.4 Å radius



NACCESS

program (1ASY_C.pdb)

Lee & Richard Algorithm

NACCESS

o/p { 1ASY_C.rsa
1ASY_C.asa