

- A: A1(-1, -1, 0), A2(1, -1, 0), A3(0, 2, 0)
 B: B1(6, 4, 5), B2(6, 6, 5), B3(3, 5, 6)

Translation:

$$CA = \left(\frac{-1+1+0}{3}, \frac{-1-1+2}{3}, \frac{0+0+0}{3} \right) = (0, 0, 0)$$

Centroids

$$CB = \left(\frac{6+6+3}{3}, \frac{4+6+5}{3}, \frac{5+5+6}{3} \right) = (5, 5, 16/3)$$

Translated coord.:

$$A_1' = A_1 - x = (-1, -1, 0)$$

$$A_2' = A_2 - x = (1, -1, 0)$$

$$A_3' = A_3 - x = (0, 2, 0)$$

$$B_1' = B_1 - x = (1, -1, -1/3)$$

$$B_2' = B_2 - x = (1, 1, -1/3)$$

$$B_3' = B_3 - x = (-2, 0, 2/3)$$

translation operator of syst. A:
 (0, 0, 0)

translation operator of syst. B:
 (-5, -5, -16/3)

$x + P = 0$
 $P = -x$
 translation operator

both syst.
are at the
origin

→ translation
issue
solved

preserves vector format
(column)

$$A' = \begin{bmatrix} -1 & 1 & 0 \\ -1 & -1 & 2 \\ 0 & 0 & 0 \end{bmatrix}$$

$$B' = \begin{bmatrix} 1 & 1 & -2 \\ -1 & 1 & 0 \\ -1/3 & -1/3 & 2/3 \end{bmatrix}$$

Cov

$$C = A'B'^T = \begin{bmatrix} -1 & 1 & 0 \\ -1 & -1 & 2 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} 1 & -1 & -1/3 \\ 1 & 1 & -1/3 \\ -2 & 0 & 2/3 \end{bmatrix} = \begin{bmatrix} 0 & 2 & 0 \\ -6 & 0 & 2 \\ 0 & 0 & 0 \end{bmatrix}$$

covariance matrix

$$(C - \lambda I) \cdot V = 0 \rightarrow \det(C - \lambda I) = 0$$

$$\det \begin{bmatrix} 1 & 1 & 0 \\ -6 & -1 & 2 \\ 0 & 0 & -\lambda \end{bmatrix} = (-\lambda) \cdot (\lambda^2 - 2 \cdot (6\lambda)) = 0$$

$$= -\lambda(\lambda^2 + 12) = 0$$

$$(C - \lambda I) \quad \lambda_1 = 0 \quad \lambda_2 = 2i\sqrt{3} \quad \lambda_3 = -2i\sqrt{3}$$

complex numbers

$$(C - \lambda I) \cdot V = 0$$

$$\lambda_1 = 0 \rightarrow \begin{bmatrix} 0 & 2 & 0 \\ -6 & 0 & 2 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} \quad V_1 = \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix}, \quad V_1 = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

$$2y = 0 \rightarrow y = 0$$

$$-6x + 2z = 0$$

$$3 \rightarrow z = 3x \leftarrow 1$$

$$\lambda_2 = 2i\sqrt{3} \rightarrow \begin{bmatrix} -2i\sqrt{3} & 2 & 0 \\ -6 & -2i\sqrt{3} & 2 \\ 0 & 0 & -2i\sqrt{3} \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} \quad V_2 = \begin{bmatrix} 1 \\ i\sqrt{3} \\ 0 \end{bmatrix} \rightarrow \text{not a real number}$$

$$\begin{aligned} -2i\sqrt{3}x + 2y &= 0 \\ -6x - 2i\sqrt{3}y + 2z &= 0 \quad \uparrow \quad \uparrow \\ -2i\sqrt{3}z &= 0 \Rightarrow z = i\sqrt{3} \end{aligned}$$

$$\lambda_3 = -2i\sqrt{3} \rightarrow V_3 = \begin{bmatrix} 1 \\ -i\sqrt{3} \\ 0 \end{bmatrix} \rightarrow \text{not a real number}$$

There is no real soln.,
roots, therefore, physical
relevance using eigen-
decomposition from C.

↓
complex numbers

→ USE SVD (Singular Value Decomposition)

* Eigendecomposition DID NOT WORK!
3D ROTATION MATRIX MUST BE REAL!

* Find U, V real, orthogonal rotation matrices.

→ Find eigenvectors of two different, real, symmetric* matrices.

* Multiplying any matrix with its transpose *always creates a symmetric matrix.

$V = C^T C$
 $U = C C^T$

2 ways
of creating
symmetric
matrices

$$V = \begin{bmatrix} 0 & -6 & 0 \\ 2 & 0 & 0 \\ 0 & 2 & 0 \end{bmatrix} \begin{bmatrix} 0 & 2 & 0 \\ -6 & 0 & 2 \\ 0 & 0 & 0 \end{bmatrix} = \begin{bmatrix} 36 & 0 & -12 \\ 0 & 4 & 0 \\ -12 & 0 & 4 \end{bmatrix}$$

eigenvalues are
always real

$$\det(C - \lambda I) = 0$$

$$C = \begin{bmatrix} 0 & 2 & 0 \\ -6 & 0 & 2 \\ 0 & 0 & 0 \end{bmatrix}$$

$$\det \begin{bmatrix} 36-\lambda & 0 & -12 \\ 0 & 4-\lambda & 0 \\ -12 & 0 & 4-\lambda \end{bmatrix} = ((36-\lambda)(4-\lambda))^2 + (-12)(12)(4-\lambda) = 0$$

$$= (4-\lambda)((36-\lambda)(4-\lambda) - 144) = 0$$

$$(4-\lambda)(\lambda^2 - 40\lambda) = 0$$

$$\lambda = 4 \quad \lambda(\lambda - 40) = 0$$

$$\lambda_2 = \lambda_3 = 40$$

$$\lambda_1 = 4: (C - \lambda I) \cdot v = 0$$

$$\begin{bmatrix} 32 & 0 & -12 \\ 0 & 0 & 0 \\ -12 & 0 & 0 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

$32x - 12z = 0$
 $-12z = 0 \rightarrow z = 0$
 $y \rightarrow \text{anything}$

$$\lambda_2 = 0: \begin{bmatrix} 36 & 0 & -12 \\ 0 & 4 & 0 \\ -12 & 0 & 4 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

$36x - 12z = 0$
 $4y = 0 \rightarrow y = 0$
 $-12x + 4z = 0$

$$\lambda_3 = 40: \begin{bmatrix} 4 & 0 & -12 \\ 0 & -36 & 0 \\ -12 & 0 & -36 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

$-4x - 12z = 0 \rightarrow x = 3z$
 $-36y = 0 \rightarrow y = 0$
 $-12x - 36z = 0$

$$V = \begin{bmatrix} -3/\sqrt{10} & 0 & 1/\sqrt{10} \\ 0 & 1 & 0 \\ 1/\sqrt{10} & 0 & 3/\sqrt{10} \end{bmatrix}$$

Eigenvalue rank: $\lambda_3 = 40 > \lambda_1 = 4 > \lambda_2 = 0$

$$U = C C^T = \begin{bmatrix} 0 & 2 & 0 \\ -6 & 0 & 2 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} 0 & -6 & 0 \\ 2 & 0 & 0 \\ 0 & 2 & 0 \end{bmatrix} = \begin{bmatrix} 4 & 0 & 0 \\ 0 & 40 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$\lambda_1 = 4: \begin{bmatrix} 0 & 0 & 0 \\ 0 & 36 & 0 \\ 0 & 0 & -4 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

$36y = 0 \rightarrow y = 0$
 $-4z = 0 \rightarrow z = 0$
 $x?$

$$\lambda_2 = 0: \begin{bmatrix} 36 & 0 & 0 \\ 0 & 0 & 2 \\ 0 & 0 & -40 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

$-36x = 0 \rightarrow x = 0$
 $-40z = 0 \rightarrow z = 0$
 $y?$

$$\lambda_3 = 0: \begin{bmatrix} 4 & 0 & 0 \\ 0 & 40 & 0 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

$4x = 0 \rightarrow x = 0$
 $40y = 0 \rightarrow y = 0$
 $z?$

$$U = \begin{bmatrix} 0 & 1 & 0 \\ 1 & 0 & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

$$Q = V U^T = \underbrace{\begin{bmatrix} -3/\sqrt{10} & 0 & 1/\sqrt{10} \\ 0 & 1 & 0 \\ 1/\sqrt{10} & 0 & 3/\sqrt{10} \end{bmatrix}}_V \underbrace{\begin{bmatrix} 0 & 1 & 0 \\ 1 & 0 & 0 \\ 0 & 0 & 1 \end{bmatrix}}_{U^T} = \begin{bmatrix} 0 & -3/\sqrt{10} & 1/\sqrt{10} \\ 1 & 0 & 0 \\ 0 & 1/\sqrt{10} & 3/\sqrt{10} \end{bmatrix}$$

rotation matrix

check for reflection:

$$\det(Q) = (-(-3/\sqrt{10}, 1/\sqrt{10})) + (1/\sqrt{10}, 1/\sqrt{10}) = \frac{9}{10} + \frac{1}{10} = \frac{10}{10} = 1 \rightarrow \text{this is a proper rotation} \checkmark$$

$$Q \cdot A' = \begin{bmatrix} 0 & -3/\sqrt{10} & 1/\sqrt{10} \\ 1 & 0 & 0 \\ 0 & 1/\sqrt{10} & 3/\sqrt{10} \end{bmatrix} \begin{bmatrix} 1 & 1 & 0 \\ -1 & -1 & 2 \\ 0 & 0 & 0 \end{bmatrix} = A'^{\text{rot}} = \begin{bmatrix} 3/\sqrt{10} & 3/\sqrt{10} & -6/\sqrt{10} \\ -1 & 1 & 0 \\ -1/\sqrt{10} & -1/\sqrt{10} & 2/\sqrt{10} \end{bmatrix}$$

if $\det(Q) = -1 \Rightarrow$ reflection
+ normalised
for bro...
systems

RMSD: $(A'^{\text{rot}} - B')$

$$(1-1)^2 = (0.948 - 1.000)^2 + (-1 - (-1))^2 + (-0.316 - (-0.333))^2 \approx 0.0029$$

$$(2-2)^2 = (0.948 - 1.000)^2 + (1-1)^2 + (-0.316 - (-0.333))^2 \approx 0.0018$$

$$(3-3)^2 = (1.897 - (-2.000))^2 + (0-0)^2 + (0.632 - 0.667)^2 \approx 0.0118$$

$$A'^{\text{rot}} \approx \begin{bmatrix} 0.948 & 0.949 & -1.897 \\ -1 & 1 & 0 \\ -0.316 & -0.316 & 0.632 \end{bmatrix} / \sqrt{10} = \begin{bmatrix} 1.000 & 1.000 & -2.000 \\ -1.000 & 1.000 & 0.000 \\ -0.333 & -0.333 & 0.667 \end{bmatrix}$$

$\rightarrow (0.0029 + 0.0029 + 0.0118) = 0.0176$

$0.0176/3 \approx 0.00587$

$\text{RMSD} = (0.00587)^{1/2} \approx 0.077 \text{ A}$

→ 2 different systems as A, B and these systems define triangles. → 3 atoms
 Below are the coordinates of the systems.

A: A1(0,0,0), A2(1,0,0), A3(0,1,0) Calculate the (root-mean-square deviation)

B: B1(0.1,0,0), B2(1.1,0,0), B3(0.1,1,0) RMSD of the best-fit. → superposition

1-RMSD calculation without structural alignment:

$$\text{RMSD} = \left(\frac{1}{N} \sum_{C=1}^N |r_C - s_C|^2 \right)^{1/2}, \quad N = 3$$

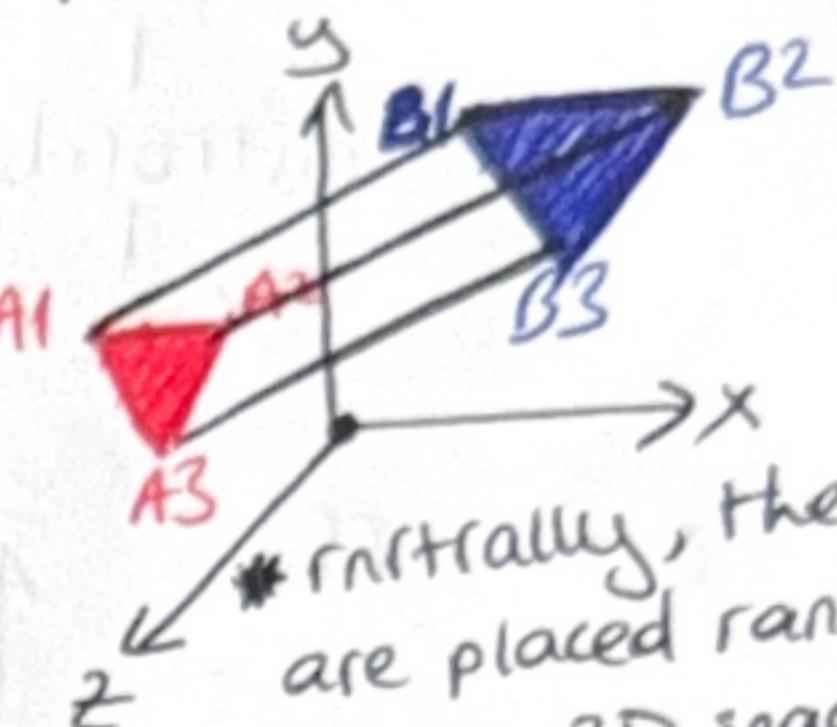
$$= \left(\frac{1}{N} ((A_1 - B_1)^2 + (A_2 - B_2)^2 + (A_3 - B_3)^2) \right)^{1/2}$$

$$= \left(\frac{1}{3} ((0.01) + (0.01) + (0.01)) \right)^{1/2} = \left(\frac{0.03}{3} \right)^{1/2} = 0.1 \text{ \AA}$$

(globally on average, two triangles differ by 0.1 \AA from each other)

* Superposition: vectorial summation in physics
 $\vec{F}_{\text{tot}} = \vec{F}_1 + \vec{F}_2 + \dots$

(structural alignment,
 place one thing on
 top of another)



* Initially, they are placed randomly in 3D space.

* Above, we calculated RMSD of two triangles, randomly distributed in 3D space. In other words, we have made an assumption such that following atoms match: A1-B1, A2-B2, A3-B3. We did not perform any structural alignments for this calculation. How to make sure that the structural matching that we have used was the best-fit? → WE CANNOT SO FAR.

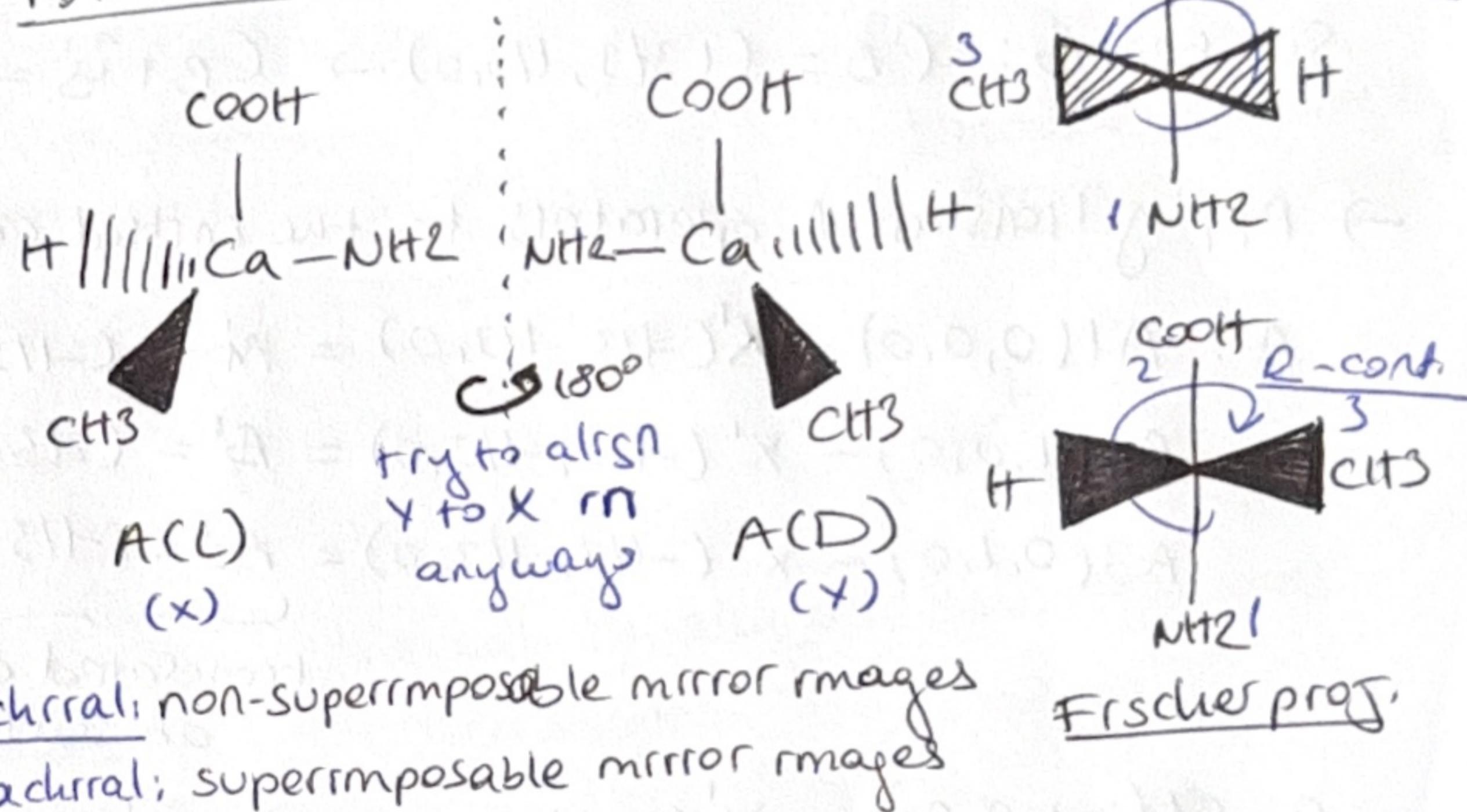
To find the best-fit:

Symmetry operations in nature

- Translation
- Rotation) considerations
- Reflection

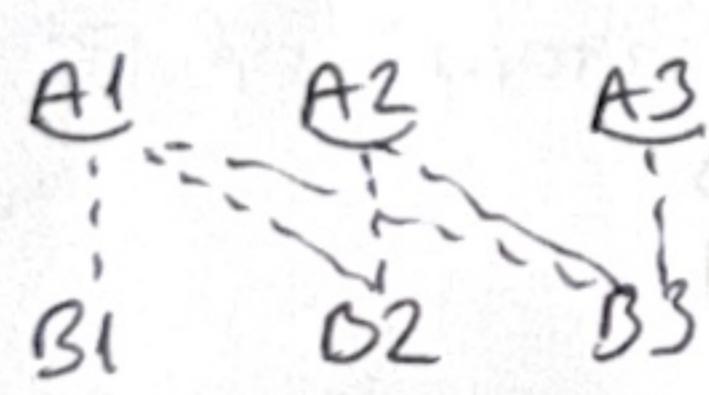
Recall from the 1st week that reflection operation cannot be used in most biomolecules due to the factor of chirality.

For reflection:



* chiral: non-superrimposable mirror images
 * achiral: superrimposable mirror images

→ RMSD possibilities:



$$(3) \cdot (2) \cdot (1) = 6 \text{ possibilities}$$

Let's see if a better atom matching is possible with aligning these two triangles. ↓

superposition

one of the possible matchings → RMSD = 0.1 \AA

All six of these RMSD calculations are done using exact coordinates of atoms, without translating or rotating triangles in 3D space. Among these A1-B1, A2-B2, A3-B3 matching gives the lowest RMSD value, indicating the highest structural similarity.

Let's see other RMSDs as well:

A1 A2 A3
 B1 B3 B2 N2.01 \AA

A1 A2 A3 or A1 A2 A3
 B2 B1 B3 B2 B3 B1
 N1.42 \AA N2.03 \AA

A1 A2 A3
 B3 B1 B2 B3 B2 B1
 N2.01 \AA N1.42 \AA

2- RMSD calculation with structural alignment: \rightarrow superimposition

* Align/superimpose system B onto system A and then calculate RMSD.
Resolve issue about translation:

Assumption:
center of mass (COM)
if all the atoms have
the same mass.

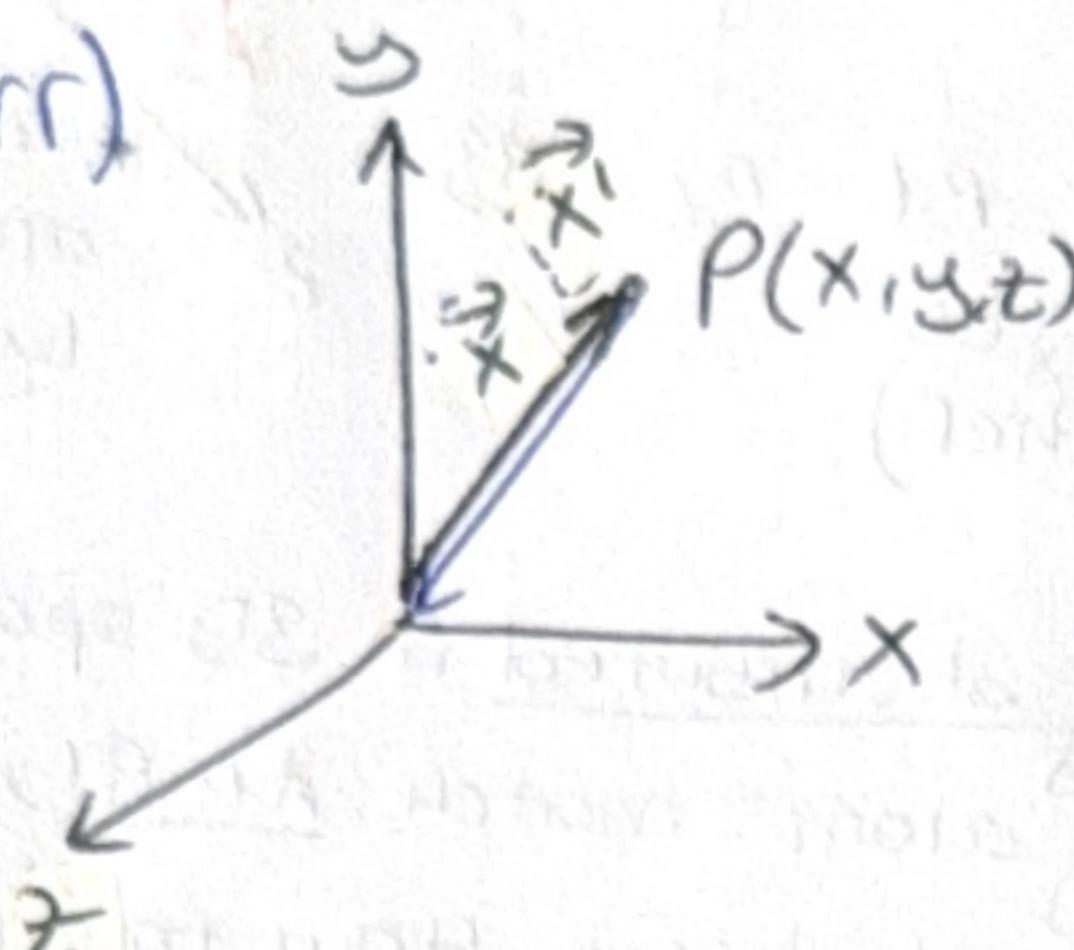
- Find the centroids (geometric centers) of the systems.
- Translate centroids to the origin \rightarrow same reference point for the systems to be compared.

soln. I) $C_A = \left(\frac{x_0 + x_1 + x_2}{3}, \frac{y_0 + y_1 + y_2}{3}, \frac{z_0 + z_1 + z_2}{3} \right) = (1/3, 1/3, 0)$

centroids

$C_B = \left(\frac{x_0 + x_1 + x_2}{3}, \frac{y_0 + y_1 + y_2}{3}, \frac{z_0 + z_1 + z_2}{3} \right) = (1.3/3, 1/3, 0)$

soln. II)



$$\vec{r} = x\hat{i} + y\hat{j} + z\hat{k}$$

$$\vec{x}' = -x\hat{i} - y\hat{j} - z\hat{k}$$

$$\vec{x} + \vec{x}' = \vec{0} \rightarrow \vec{x}' = -\vec{x}$$

$$(x\hat{i} + y\hat{j} + z\hat{k}) + (-x\hat{i} - y\hat{j} - z\hat{k}) = \vec{0}$$

translation operator for the system:

$$\vec{x}' = -x\hat{i} - y\hat{j} - z\hat{k}$$

translation operator
of the system A:

System A: $C_A = (1/3, 1/3, 0) \rightarrow C_A + \vec{x}' = \vec{0} \rightarrow \vec{x}' = -C_A = (-1/3, -1/3, 0)$

System B: $C_B = (1.3/3, 1/3, 0) \rightarrow C_B + \vec{x}' = \vec{0} \rightarrow \vec{x}' = -C_B = (-1.3/3, -1/3, 0)$

translation operator
of the system B:

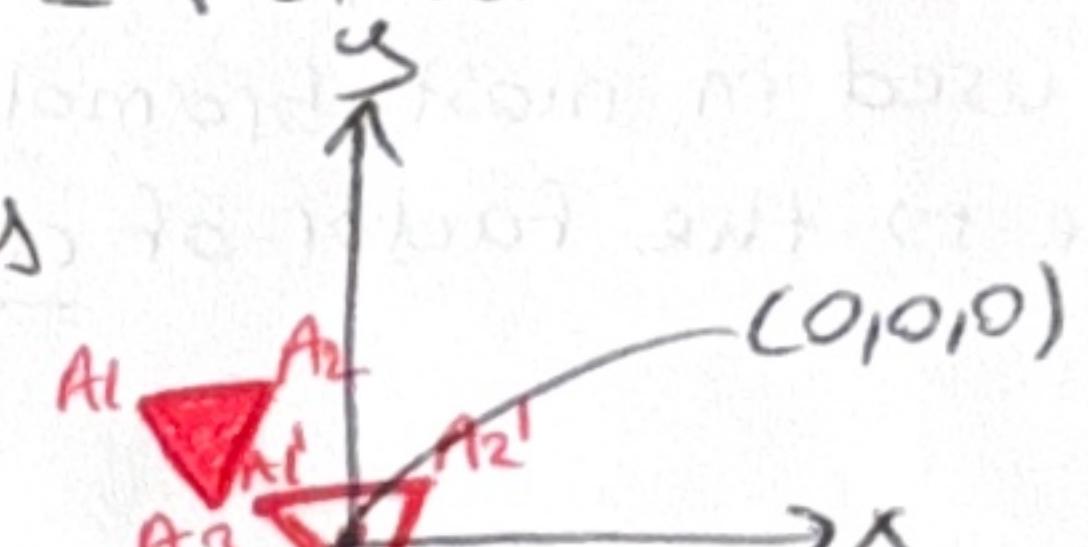
\rightarrow Apply translation operators to the central coordinates as well.

A: $A_1(0,0,0) - \vec{x}'(-1/3, -1/3, 0) = A'_1 = (-1/3, -1/3, 0)$ - for atom 1 of A

$A_2(1,0,0) - \vec{x}'(-1/3, -1/3, 0) = A'_2 = (2/3, -1/3, 0)$ - for atom 2 of A

$A_3(0,1,0) - \vec{x}'(-1/3, -1/3, 0) = A'_3 = (-1/3, 2/3, 0)$ - for atom 3 of A

translated coordinates
of system A

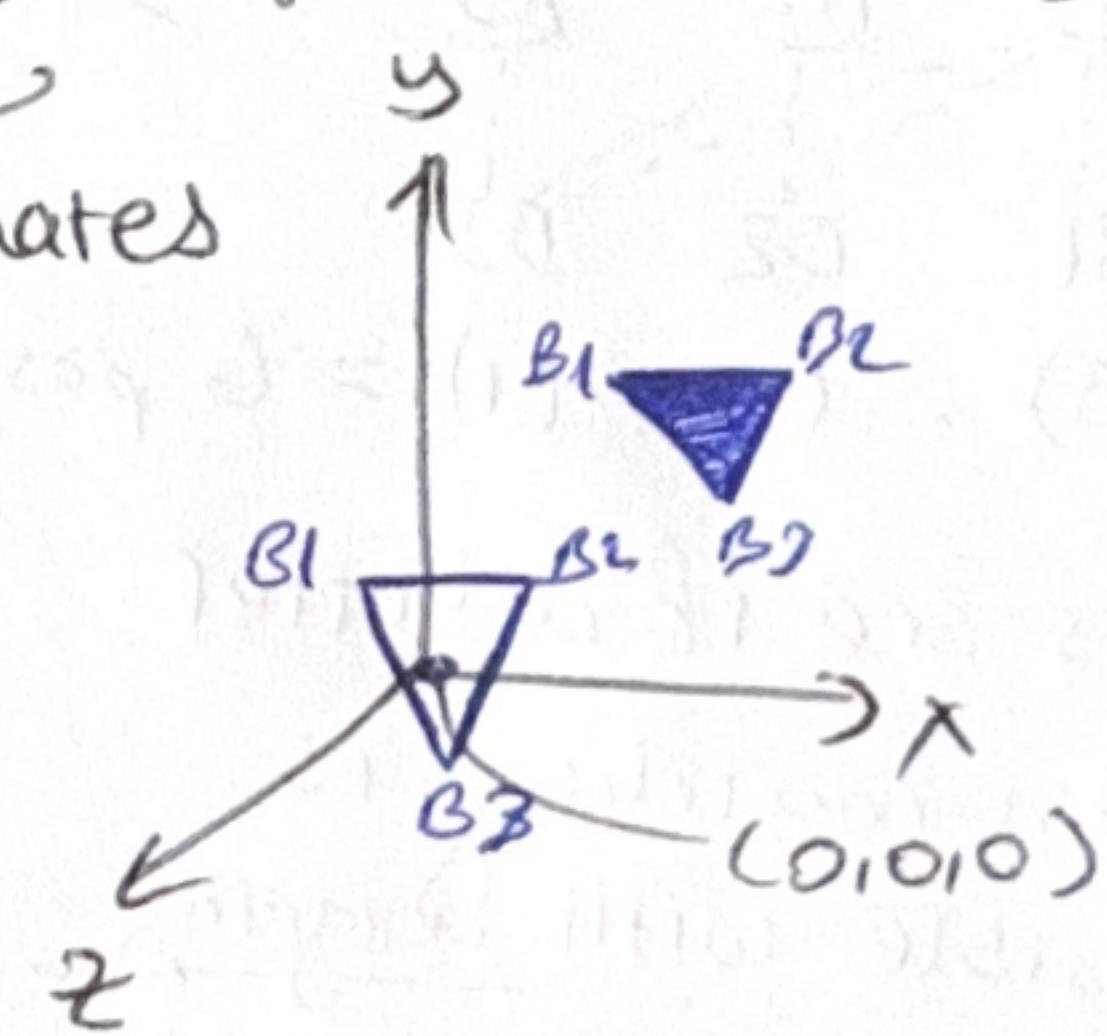


B: $B_1(0.1, 0, 0) - \vec{x}'(-1.3/3, -1/3, 0) = B'_1 = (-1/3, -1/3, 0)$

$B_2(1.1, 0, 0) - \vec{x}'(-1.3/3, -1/3, 0) = B'_2 = (2/3, -1/3, 0)$

$B_3(0.1, 1, 0) - \vec{x}'(-1.3/3, -1/3, 0) = B'_3 = (-1/3, 2/3, 0)$ - for atom 3 of B

translated coordinates
of system B



\rightarrow Just by looking to the translated coordinates $A'_1(-1/3, -1/3, 0) = B'_1(0.1, 0, 0)$, of system B

$A_2(1,0,0) = B_2(1.1, 0, 0)$, $A_3(0,1,0) =$

$B_3(0.1, 1, 0)$, we can say that the trans-

lated coordinates of the systems A and

B match. For this specific example,

only translation operation solved our

problem and matched two systems.

\rightarrow Translation = vector addition (vector summation or vector subtraction)

$$\vec{V} = \vec{V}_1 + \vec{V}_2$$

$$\vec{V} = \vec{V}_1 - \vec{V}_2$$

translated system A : $A' = \begin{bmatrix} \vec{A}_1' & \vec{A}_2' & \vec{A}_3' \\ x_1 & -1/3 & 2/3 & -1/3 \\ y_1 & -1/3 & -1/3 & 2/3 \\ z_1 & 0 & 0 & 0 \end{bmatrix}$

each column is atom's coord. vector

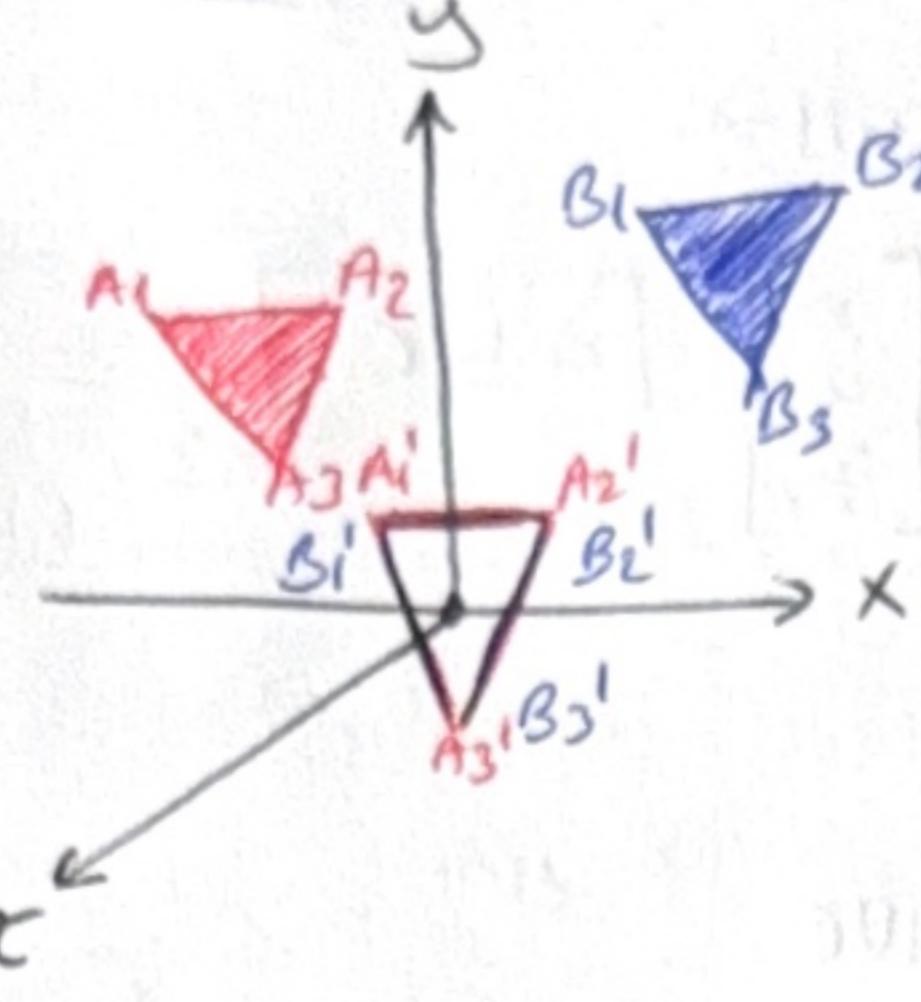
translated system B : $B' = \begin{bmatrix} \vec{B}_1' & \vec{B}_2' & \vec{B}_3' \\ x_1 & -1/3 & 2/3 & -1/3 \\ y_1 & -1/3 & -1/3 & 2/3 \\ z_1 & 0 & 0 & 0 \end{bmatrix}$

$\rightarrow A' = B'$

column = atomic coord. vector

* We have already seen that the translated coordinates of A and B are identical. This tells us the structures have the same orientation and only differed by translation in 3D space.

Visual representation:



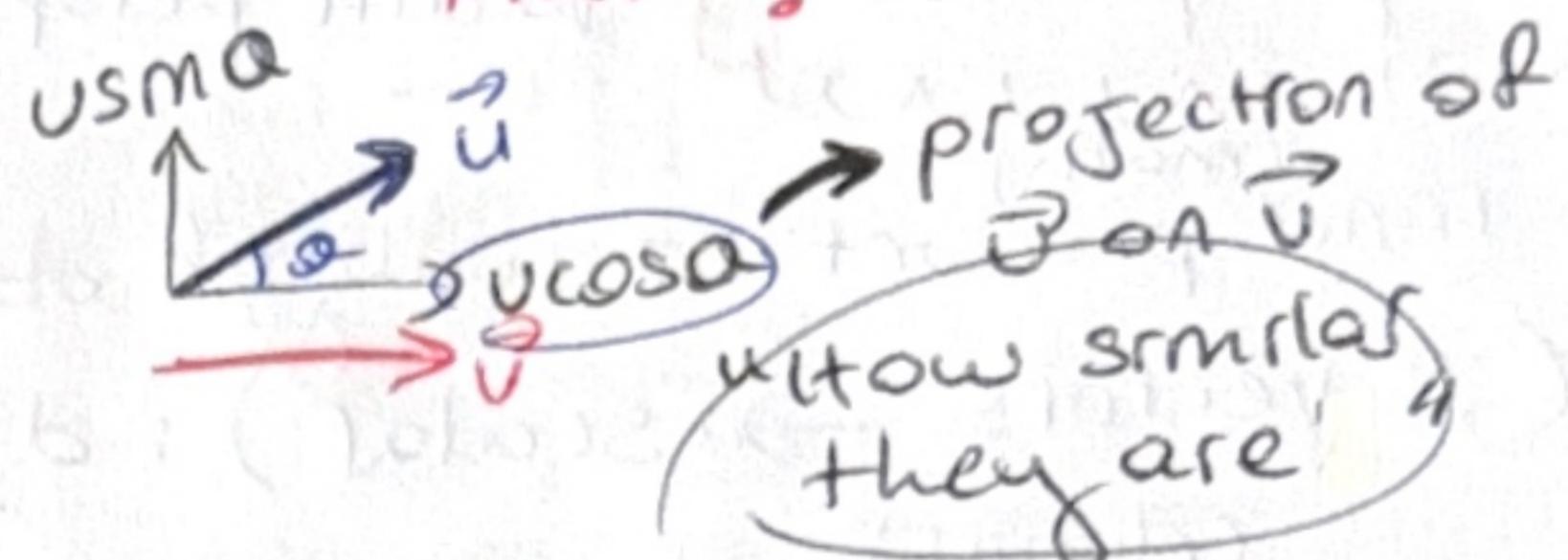
→ However, let's also solve the issue of rotation to prove that only translation gives the best-fit in this case.

Proofs are important in math!

Physical perspective:

Recall: * Dot product: $\vec{U} \cdot \vec{V} = |\vec{U}| \cdot |\vec{V}| \cos\theta$

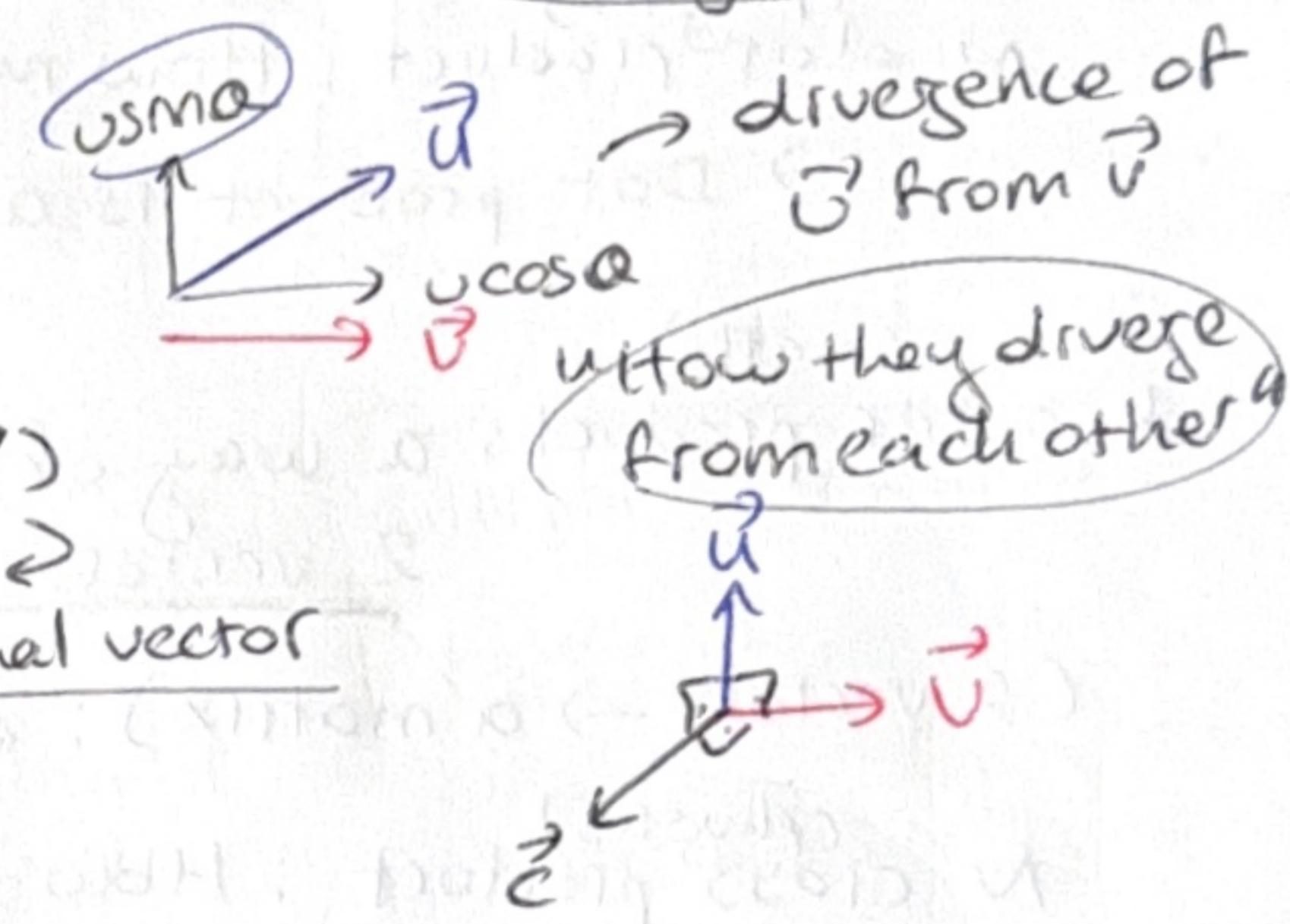
- from week 1
- gives a scalar indicating that how well 2 vectors are aligned.
 - scalar operation.



* Cross product: $\vec{U} \times \vec{V} = |\vec{U}| \cdot |\vec{V}| \sin\theta$

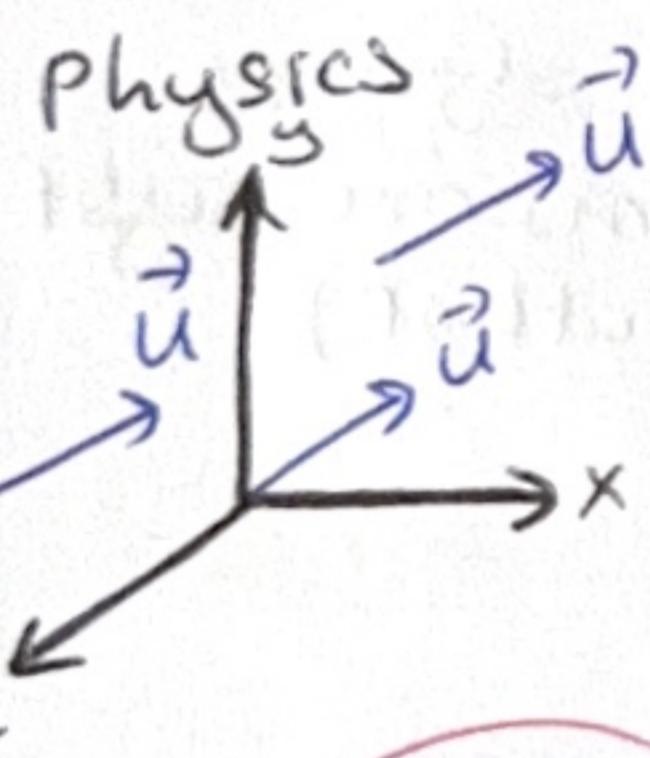
- gives a vector that is perpendicular orthogonal to both vectors. ($\vec{C} = \vec{U} \times \vec{V}$)

- vectorial operation → output is a normal vector



3 approaches

vectors



* vector = arrow (w. a direction + a length)

* can be freely translated in space (still same vector)

* combined persp. (physics + CS)

* a vector can be anything

* cannot be freely translated in space

! (there is one exception)

* We usually use column vectors in physics.

$$\text{Ex: } A = \begin{bmatrix} x \\ y \\ z \end{bmatrix} \quad \begin{cases} \text{coord.} \\ \text{in 3D space} \end{cases}$$

* We also use row vectors in some specific cases such as solving systems of equation (Gaussian elimination)

$$\begin{array}{c|cc|c} x & 2 & 3 & 8 \\ \hline 2 & 3 & & \\ 4 & 1 & 6 & \end{array} \rightarrow (2x+3y=8) \quad 2$$

$$\begin{array}{c|cc|c} & & & \\ \hline & & & \\ & & & \end{array} \rightarrow 4x+y=6$$

$$-5y = -10$$

of rows

3×1 # of columns

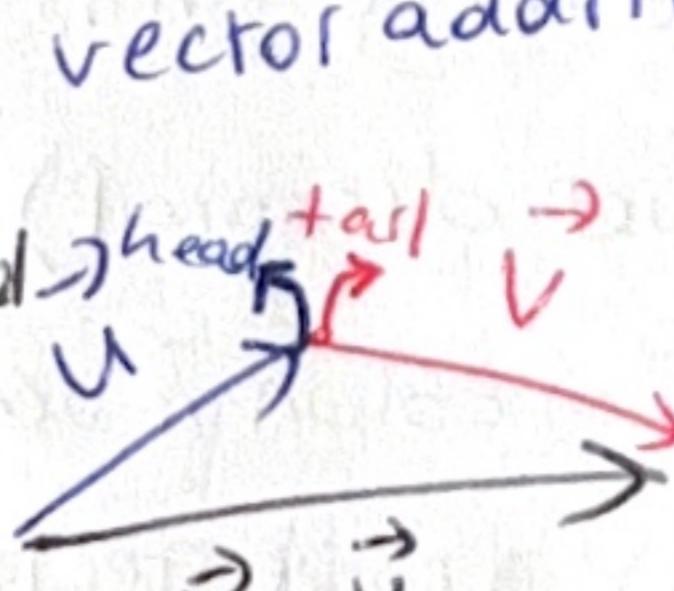
$$\begin{cases} y=2 \\ x=1 \end{cases} \rightarrow \text{roots}$$

Vector dimensions:

$$2 \rightarrow \begin{bmatrix} a & b & e \\ c & d & f \end{bmatrix} \quad (2 \times 3) - \text{dimensions}$$

$$3 \rightarrow \begin{bmatrix} a & b & c \\ d & e & f \\ g & h & i \end{bmatrix} \quad 3 \times 3 \rightarrow \begin{bmatrix} x \\ y \\ z \end{bmatrix} \quad 3 \times 1$$

to add 2 vectors, put one's tail to the head of the other's



$\vec{U} + \vec{V}$

vector dimensions in addition:

$$\begin{bmatrix} x \\ y \\ z \end{bmatrix}_{3 \times 1} + \begin{bmatrix} a \\ b \\ c \end{bmatrix}_{3 \times 1} = \begin{bmatrix} x+a \\ y+b \\ z+c \end{bmatrix}_{3 \times 1}$$

dimensions do not change

vector dimensions in scalar multiplication:

$$3 \cdot \begin{bmatrix} x \\ y \\ z \end{bmatrix}_{3 \times 1} = \begin{bmatrix} 3x \\ 3y \\ 3z \end{bmatrix}_{3 \times 1}$$

dimension is conserved

vector dimensions in vectorial multiplication:

$$(3 \times 1) \cdot (1 \times 3) = (3 \times 3)$$

inner dimension should match

$$\begin{bmatrix} x \\ y \\ z \end{bmatrix}_{3 \times 1} \cdot \begin{bmatrix} a & b & c \end{bmatrix}_{1 \times 3} = \begin{bmatrix} xa & xb & xc \\ ya & yb & yc \\ za & zb & zc \end{bmatrix}_{3 \times 3}$$

new dimensions

New perspective: math perspective

- * inner product: a way of obtaining a scalar multiplying 2 vectors (2 vectors → scalar); dimensions collapsed → inner product (physics)
→ Dot product is an example of inner product.
- * outer product: a way of creating a matrix multiplying 2 vectors.
(math) → outer product → dot product

(2 vectors → a matrix); dimensions expanded → outer

N cross product: itow 2 vectors diverge from each other.

- output: a vector that is perpendicular to both (normal vector)

* output = a vector (orthogonal) → operator Γ = a matrix (transformation)

→ Transformation matrix: a way to rotate, scale, shear or reflect objects using matrix multiplication. → transforms one syst. into another)

Ex: in 2D space $(x,y) \rightarrow$ 2D transformation matrix $\begin{bmatrix} a & b \\ c & d \end{bmatrix}_{2 \times 2}$

$$\begin{bmatrix} a & b \\ c & d \end{bmatrix}_{2 \times 2} \begin{bmatrix} x \\ y \end{bmatrix}_{2 \times 1} = \begin{bmatrix} x' \\ y' \end{bmatrix}_{2 \times 1}$$

transforms coordinates from one coordinate system into another

Some rules to mention before we move on:

1) Transpose matrix: $V \rightarrow V^T$ (flip over diagonal) $V = \begin{bmatrix} a & b \\ c & d \end{bmatrix}_{2 \times 2} \rightarrow V^T = \begin{bmatrix} a & c \\ b & d \end{bmatrix}_{2 \times 2}$ → row

2) Assume that $V = (n \times 1)$, $U = (1 \times n) \Rightarrow$ column vectors
 $V^T = (1 \times n)$, $U^T = (n \times 1) \Rightarrow$ row vectors

$$U^T V = [1 \dots n]_{1 \times n} \begin{bmatrix} 1 \\ \vdots \\ n \end{bmatrix}_{n \times 1} = \begin{bmatrix} x \\ \vdots \\ x \end{bmatrix}_{1 \times n}$$

$(1 \times n)(n \times 1) = (1 \times 1) \Rightarrow$ scalar
inner product
dot prod. (directionality does not matter)

$$U V^T = \begin{bmatrix} 1 \\ \vdots \\ n \end{bmatrix}_{n \times 1} \begin{bmatrix} 1 & \dots & n \end{bmatrix}_{1 \times n} = \begin{bmatrix} 1 & \dots & n \end{bmatrix}_{n \times n}$$

$UV^T \neq VU^T$
(directionality matters)

outer product
 n cross prod.
 $(n \times 1)(1 \times n) = (n \times n)$ matrix

$$U^T V^T = V^T U$$

3) Identity matrix: (I)

$$\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}_{3 \times 3}$$

$I \cdot A = A \cdot I$ (no directionality)

does not contribute

$$\begin{bmatrix} 1 & 2 \\ 3 & 4 \end{bmatrix}_{2 \times 2} \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}_{2 \times 2} = \begin{bmatrix} 1 & 2 \\ 3 & 4 \end{bmatrix}_{2 \times 2}$$

4) Matrix multiplication:

$$\begin{bmatrix} a & b \\ c & d \\ e & f \end{bmatrix}_{3 \times 2} \begin{bmatrix} x & y \\ z & t \end{bmatrix}_{2 \times 2} =$$

$$\begin{bmatrix} ax+bx & ay+bt \\ cx+dz & cy+dt \\ ex+ft \end{bmatrix}_{3 \times 2}$$

$$\text{Cov}(x,y) = \frac{\sum_{t=1}^n (y_t - \bar{y})}{n-1}$$

Resolve the issue about rotation:

rr) Calculate the covariance "C" matrix:

- Square matrix that shows how much each pair of variables in a dataset varies together \rightarrow general definition

* in the structural context: how atomic positions vary between the two systems.

1st way:
directly matrix
multiplication
 $A = C^T$

$$\begin{bmatrix} -1/3 & 2/3 & -1/3 \\ -1/3 & -1/3 & 2/3 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3}$$

(Let's call $A' = P$, $B' = Q$)

$$C = A'B'^T = \begin{bmatrix} -1/3 & 2/3 & -1/3 \\ -1/3 & -1/3 & 2/3 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3} \begin{bmatrix} -1/3 & -1/3 & 0 \\ 2/3 & -1/3 & 2/3 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3}$$

B'

* correlation:
standardize the
data by dividing
by the std. matrix
A scale-invariant

$$C = \begin{bmatrix} 1 & 0 & 0 \\ 2/3 & -1/3 & 0 \\ -1/3 & 2/3 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3}$$

actual distance
info is lost!
relationship
and relative
orientation
between
two points

A'

How the position
of atoms more
structure correlate
with the positions of
atoms in the other

sum of the
outer products =
(dear: 2 vectors)

$$C = p_1 q_1^T + p_2 q_2^T + p_3 q_3^T$$

outer
product

matrix

$$\begin{bmatrix} x \\ y \\ z \end{bmatrix}_{3 \times 1} \begin{bmatrix} a & b & c \end{bmatrix}_{1 \times 3} = \begin{bmatrix} ? \end{bmatrix}_{3 \times 0}$$

$$p_1 = q_1 = \begin{bmatrix} -1/3 \\ -1/3 \\ 0 \end{bmatrix}_{3 \times 1} \rightarrow p_1 q_1^T = \begin{bmatrix} -1/3 \\ -1/3 \\ 0 \end{bmatrix}_{3 \times 1} \begin{bmatrix} -1/3 & -1/3 & 0 \end{bmatrix}_{1 \times 3} = \begin{bmatrix} 1/9 & 1/9 & 0 \\ 1/9 & 1/9 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3}$$

$$p_2 = q_2 = \begin{bmatrix} 2/3 \\ -1/3 \\ 0 \end{bmatrix}_{3 \times 1} \rightarrow p_2 q_2^T = \begin{bmatrix} 2/3 \\ -1/3 \\ 0 \end{bmatrix}_{3 \times 1} \begin{bmatrix} 2/3 & -1/3 & 0 \end{bmatrix}_{1 \times 3} = \begin{bmatrix} 4/9 & -2/9 & 0 \\ -2/9 & 4/9 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3}$$

$$p_3 = q_3 = \begin{bmatrix} -1/3 \\ 2/3 \\ 0 \end{bmatrix}_{3 \times 1} \rightarrow p_3 q_3^T = \begin{bmatrix} -1/3 \\ 2/3 \\ 0 \end{bmatrix}_{3 \times 1} \begin{bmatrix} -1/3 & 2/3 & 0 \end{bmatrix}_{1 \times 3} = \begin{bmatrix} 1/9 & -2/9 & 0 \\ -2/9 & 1/9 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3}$$

Covariance = sum of the outer products $\Rightarrow C = PQ^T = \sum p_i q_i^T = p_1 q_1^T + p_2 q_2^T + p_3 q_3^T$

$$\underbrace{\begin{bmatrix} 1/9 & 1/9 & 0 \\ 1/9 & 1/9 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3}}_{p_1 q_1^T} + \underbrace{\begin{bmatrix} 4/9 & -2/9 & 0 \\ -2/9 & 4/9 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3}}_{p_2 q_2^T} + \underbrace{\begin{bmatrix} 1/9 & -2/9 & 0 \\ -2/9 & 1/9 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3}}_{p_3 q_3^T} = \begin{bmatrix} 2/3 & -1/3 & 0 \\ -1/3 & 2/3 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3} = C \Rightarrow \text{symmetric matrix}$$

sum of the
outer products

rv) Perform "Singular Value Decomposition" (SVD) on covariance matrix (C):
↳ to find the principle axes of rotation

→ Decompose C into its own rotational components \rightarrow to do that solve:

$$(C - \lambda I) \cdot v = 0$$

→ Spectral vectors (v) that do not change direction (for non-zero v)
when C acts on them, they may be stretched or compressed, but not rotated relative to their original orientation.

* V do not change direction but can be stretched or compressed.

$$CV = \lambda V \rightarrow \text{eigenvector}$$

↳ eigenvalue (scalar, stretching factor)

To find eigenvectors (rotation axes) solve: $(C - \lambda I) \cdot V = 0$

First find eigenvalues:

→ For a non-trivial solution (i.e. $V \neq 0$), the determinant of $(C - \lambda I)$ must be zero: $\det(C - \lambda I) = 0$

$$\begin{aligned} \det \begin{bmatrix} 2 & 1 & 0 \\ -1/3 & 2/3 - \lambda & 0 \\ 0 & 0 & -1 \end{bmatrix} &= (2 - \lambda) \cdot ((2/3 - \lambda) \cdot (-1)) - ((-1/3) \cdot ((-1/3) \cdot (-\lambda))) - 0 \cdot 0 + 0 \cdot \dots = 0 \\ &= (-\lambda) [(2/3 - \lambda)^2 - 1/9] = 0 \\ &= (-\lambda) \cdot (4/9 - 4\lambda/3 + \lambda^2 - 1/9) = 0 \\ &= (-\lambda) \cdot (3/9 - 4\lambda/3 + \lambda^2) = 0 \\ &= (-\lambda) \cdot (\lambda - 1/3) \cdot (\lambda + 1) = 0 \quad \begin{array}{l} \text{scalars} \\ \text{(eigenvalues)} \end{array} \\ \lambda_1 = 0 & \quad \lambda_2 = 1/3 \quad \lambda = -1 \quad \rightarrow \text{roots of the equation} \end{aligned}$$

Then find eigenvectors: use the equation $(C - \lambda I) \cdot V = 0$

$$(\lambda_1 = 0, \lambda_2 = 1/3, \lambda_3 = -1)$$

$$\lambda = 0: \begin{bmatrix} 2/3 & -1/3 & 0 \\ -1/3 & 2/3 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3} - 0 \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}_{3 \times 3} = \begin{bmatrix} 2/3 & -1/3 & 0 \\ -1/3 & 2/3 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3} \begin{bmatrix} x \\ y \\ z \end{bmatrix}_{3 \times 1} = 0 \quad \begin{array}{l} \text{---} \\ \frac{2x}{3} - \frac{y}{3} = 0 \\ \left(-\frac{x}{3} + \frac{2y}{3} \right) = 0 \\ \text{---} \\ 0x + 0y + 0z = 0 \end{array}$$

$$V_1 = \begin{bmatrix} 0 \\ 0 \\ 1 \end{bmatrix}_{3 \times 1} \quad \begin{array}{l} \text{---} \\ y = 0 \\ x = 0 \\ z = 1 \end{array}$$

$z \rightarrow$ can be anything
(not saying $z = 1$)

$$\lambda_2 = 1: \begin{bmatrix} 2/3 & -1/3 & 0 \\ -1/3 & 2/3 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3} - 1 \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}_{3 \times 3} = \begin{bmatrix} -1/3 & -1/3 & 0 \\ -1/3 & -1/3 & 0 \\ 0 & 0 & -1 \end{bmatrix}_{3 \times 3} \begin{bmatrix} x \\ y \\ z \end{bmatrix}_{3 \times 1} = 0 \quad \begin{array}{l} \text{---} \\ -\frac{x}{3} - \frac{y}{3} = 0 \\ -\frac{x}{3} - \frac{y}{3} = 0 \\ -z = 0 \rightarrow z = 0 \end{array}$$

$$V_2 = \begin{bmatrix} 1 \\ -1 \\ 0 \end{bmatrix}_{3 \times 1} \quad \begin{array}{l} \text{---} \\ x = -y \\ z = 0 \end{array}$$

$$\lambda_3 = 1/3: \begin{bmatrix} 2/3 & -1/3 & 0 \\ -1/3 & 2/3 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3} - 1/3 \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}_{3 \times 3} = \begin{bmatrix} 1/3 & -1/3 & 0 \\ -1/3 & 1/3 & 0 \\ 0 & 0 & -1/3 \end{bmatrix}_{3 \times 3} \begin{bmatrix} x \\ y \\ z \end{bmatrix}_{3 \times 1} = 0 \quad \begin{array}{l} \text{---} \\ \frac{x}{3} - \frac{y}{3} = 0 \\ -\frac{x}{3} + \frac{y}{3} = 0 \\ -z = 0 \rightarrow z = 0 \end{array}$$

$$V_3 = \begin{bmatrix} 1 \\ 1 \\ 0 \end{bmatrix}_{3 \times 1}$$

V_1, V_2, V_3 , respectively $\begin{bmatrix} 0 \\ 0 \\ 1 \end{bmatrix}, \begin{bmatrix} 1 \\ -1 \\ 0 \end{bmatrix}, \begin{bmatrix} 1 \\ 1 \\ 0 \end{bmatrix} \rightarrow$ eigenvectors

$$\lambda = 0 \quad \lambda = 1 \quad \lambda = 1/3 \rightarrow$$
 eigenvalues

$|d_3| \geq |d_2| \geq |d_1| \rightarrow$ general formula

Construct the eigenvector matrix:

$$X = \begin{bmatrix} 1/\sqrt{2} & 1/\sqrt{2} & 0 \\ -1/\sqrt{2} & 1/\sqrt{2} & 0 \\ 0 & 0 & 1 \end{bmatrix}_{3 \times 3} \rightarrow \begin{bmatrix} \hat{v}_2 & \hat{v}_3 & \hat{v}_1 \\ 1 & 1 & 1 \\ 1 & 1 & 1 \end{bmatrix}_{3 \times 3}$$

→ Normalize eigenvectors:
 $\hat{n} = \frac{\vec{n}}{|\vec{n}|}$ unit vector: in the direction of \vec{n} but length of 1.

$$\lambda_2 = 1 \rightarrow \hat{v}_2 = \begin{bmatrix} 1/\sqrt{2} \\ -1/\sqrt{2} \\ 0 \end{bmatrix}_{3 \times 1} \quad \lambda_3 = 1/3 \rightarrow \hat{v}_3 = \begin{bmatrix} 1/\sqrt{2} \\ 1/\sqrt{2} \\ 0 \end{bmatrix}_{3 \times 1}$$

$$\lambda_1 = 0 \rightarrow \hat{v}_1 = \begin{bmatrix} 0 \\ 0 \\ 1 \end{bmatrix}_{3 \times 1}$$

(normalized eigenvectors, unit vectors)

v) Compute the rotation matrix (U):

$$U = X X^T = \begin{bmatrix} 1/\sqrt{2} & -1/\sqrt{2} & 0 \\ 1/\sqrt{2} & 1/\sqrt{2} & 0 \\ 0 & 0 & 1 \end{bmatrix}_{3 \times 3} \begin{bmatrix} 1/\sqrt{2} & 1/\sqrt{2} & 0 \\ -1/\sqrt{2} & 1/\sqrt{2} & 0 \\ 0 & 0 & 1 \end{bmatrix}_{3 \times 3}^T = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}_{3 \times 3} = U \text{ (rotation matrix)}$$

(in this case:
 $U = I$ (identity matrix))

* the optimal rotation can be achieved by translation of 0° or \Rightarrow no rotation is needed!
 360° degrees.

(Recall that ref-
lection is not being
considered in bromole-
cular systems)

Proof for the systems only being diverged by translation. turn back to the beginning

vi) Check for reflection:

if $\det(A) = -1 \Rightarrow$ reflection

if $\det(A) = 1 \rightarrow$ rotation without reflection \Rightarrow this is what we want to preserve chirality of bromolecules

$$\det(U) = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}_{3 \times 3} = 1 \cdot (1 \cdot 1 - 0 \cdot 0) - 0 \cdot (\dots) + 0 \cdot (\dots) = 1 \rightarrow \text{preserves chirality} \checkmark \text{ (2nd proof)}$$

\rightarrow To make sure that we did not change the handedness (chirality) of the molecule.
 $[\det(A)=1]$

vii) Apply rotation matrix on translated coord.:

$$\begin{bmatrix} -1/3 & 2/3 & -1/3 \\ -1/3 & -1/3 & 2/3 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}_{3 \times 3} = \begin{bmatrix} -1/3 & 2/3 & 0 \\ -1/3 & -1/3 & 0 \\ 0 & 0 & 0 \end{bmatrix}_{3 \times 3} \rightarrow A' = B' = P = PI$$

perfectly matched after translation and rotation

viii) Calculate RMSD of the translated and rotated systems:

$$P1 - Q1: P1(-1/3, -1/3, 0) - Q1(-1/3, -1/3, 0) = (0, 0, 0)$$

$$P2 - Q2: P2(2/3, -1/3, 0) - Q2(2/3, -1/3, 0) = (0, 0, 0)$$

$$P3 - Q3: P3(-1/3, 2/3, 0) - Q3(-1/3, 2/3, 0) = (0, 0, 0)$$

$$\text{RMSD} = \left(\frac{1}{N} \sum_{i=1}^N (P_i - Q_i)^2 \right)^{1/2}$$

$$= 0.00 \text{ \AA}$$