EXPERIMENT 5: STRUCTURE COMPARISON

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SUSTC

Structural superposition/alignment

RMSD (Root-Mean-Square Deviation)

- The way to evaluate the structural similarity by measuring the average distance between the atoms of superimposed proteins

$$\mathrm{RMSD} = \sqrt{\frac{1}{N}\sum_{i=1}^{N}\delta_i^2}$$

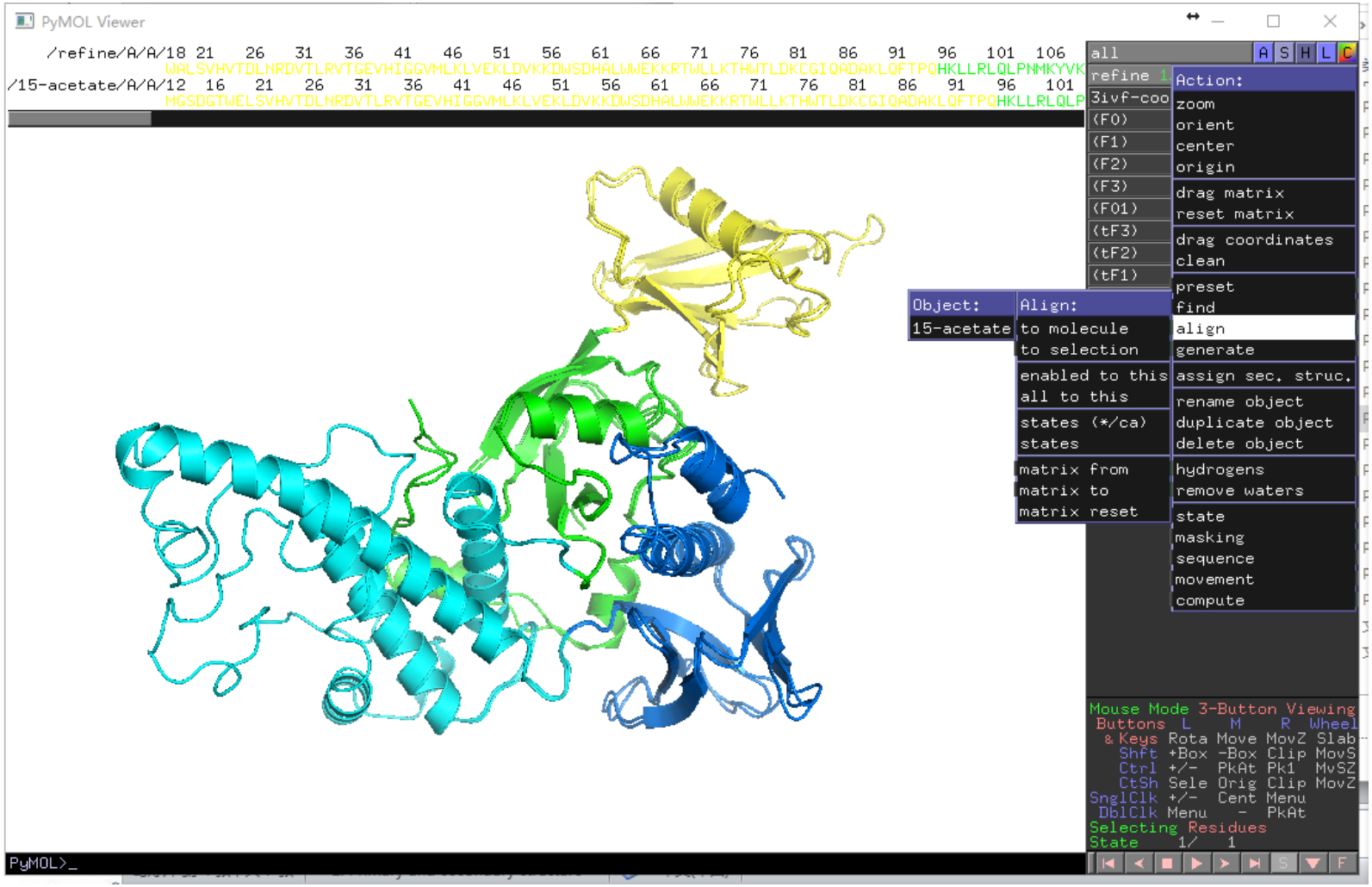
where δ is the distance between N pairs of equivalent atoms (usually the backbone atoms)

- Indication of RMSD
  - <1Å, near identical
  - 1-2Å, highly similar
  - 2-4Å, similar
  - >4Å, usually no similarity

Methods

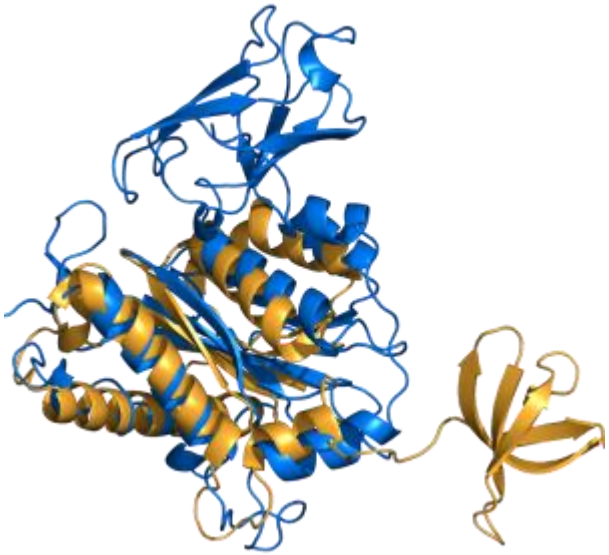
- **Least-square fitting (LSQ)**
- DALI
  - Distance alignment matrix
    - Break the input structures into hexa-peptide fragments
    - Calculate a distance matrix by evaluating the contact patterns between successive fragments
- **Combinatorial extension (CE)**
  - Similar to DALI
- Sequential Structure Alignment Program (SSAP)
  - Double dynamic programming
    - Produce a structural alignment based on atom-to-atom vectors in structure space

Simple alignment in PyMOL

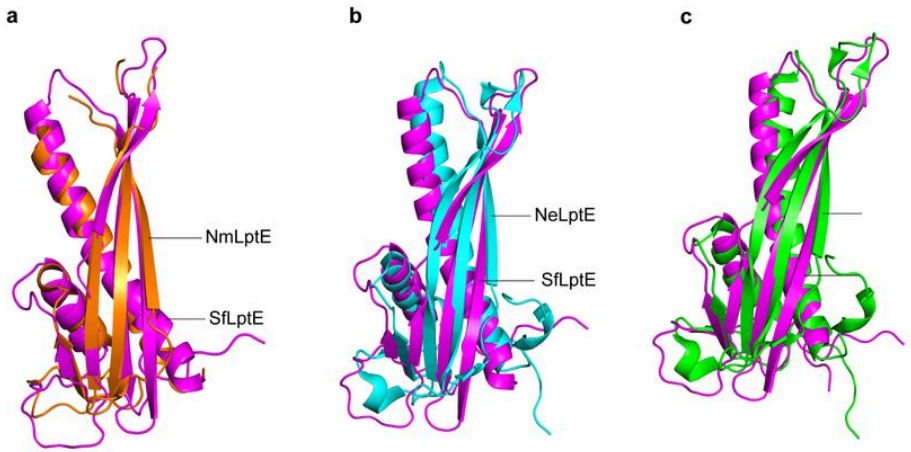


Cealign plugin in PyMOL

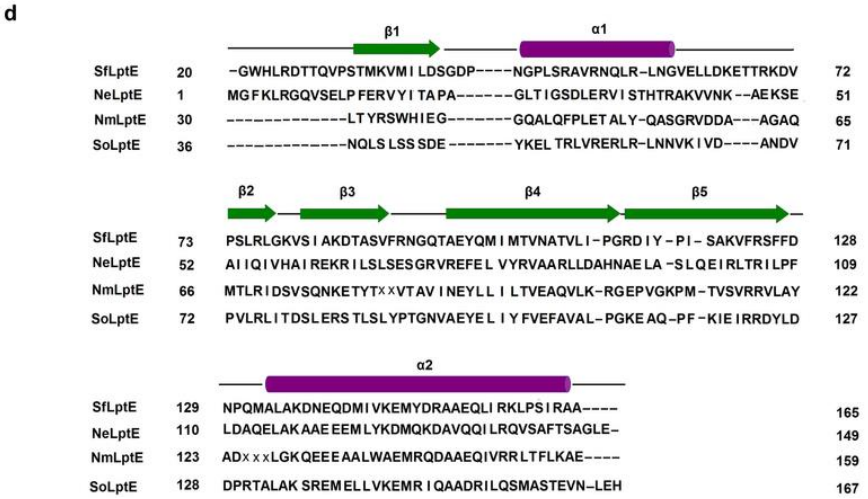
- Used for accurate structural alignment
- Better results for structures with low sequence similarity



Structure-based sequence alignment



Much more accurate!



Tasks

1. Open human hemoglobin structure (PDB id: 4HHB) in PyMOL
   - PDB Loader in Plugins
2. Create new objects containing either alpha-subunit or beta-subunit
   - You can use different sequence mode to make selection
3. Align beta-subunit to alpha-subunit
   - RMSD value and indication?

structure

4. Analyze the pairwise sequence alignment
   - Which region cannot be aligned? Your explaination?
5. Load human neuroglobin (PDB id: 4MPM) and a globin-like protein (PDB id: 4BJA), and align them to alpha-globin, respectively
   - Evaluate your results
6. Use Cealign to realign the globin-like protein to alpha-globin
   - Compared with the simple align, which one give a better alignment?
7. Compare the structure-based alignment and simple sequence alignment of the three globins (this part you can finish at home)
   - Which one give you a better alignment? Why?

Lab report format

- Title
- Your name and student No.
- Introduction
- Methods
- Results
- Conclusions