

# **Protein Structure Prediction & Ligand Docking** 실습

김유빈, 정우엽

# 실습에 들어 가기 전에

# Download Chimera

- Go to <https://www.cgl.ucsf.edu/chimera/download.html>

## Current Production Releases

- See the [release notes](#) for a list of new features and other information.
- For [more recent changes](#), use the [snapshot](#) and [daily](#) builds; they are less tested but usually reliable.
- **64-bit Releases:**

Platform	Installer, Size, and Checksum	Date	Notes
Microsoft Windows 64-bit	<a href="#">chimera-1.16-win64.exe</a> Size: 152332561 bytes MD5: 9672aa27cc7ea1d6cfe9c8680516c741	Dec 17, 2021	<a href="#">Instructions</a> <a href="#">Documentation</a> Runs on Windows 7 or later.
Mac OS X 64-bit	<a href="#">chimera-1.16-mac64.dmg</a> Size: 192170325 bytes MD5: 02cef4e3bf4e2ad5aae44c7104328ade	Dec 17, 2021	<a href="#">Instructions</a> <a href="#">Documentation</a> Runs on Mac OS X 10.12 or later.
Linux 64-bit	<a href="#">chimera-1.16-linux_x86_64.bin</a> Size: 154080130 bytes MD5: 0167c57d7e24c9b69e04fd0dabc5ce87	Dec 17, 2021	<a href="#">Instructions</a> <a href="#">Documentation</a> Compiled on CentOS 5.11.

- **32-bit releases are no longer supported.**

# Input & Result File Download

- Go to [https://github.com/seoklab/Public-practice/tree/main/AI-Bio\\_2023](https://github.com/seoklab/Public-practice/tree/main/AI-Bio_2023)

The screenshot shows a GitHub repository named 'Public Practice'. The repository contains a single file, 'README.md'. The content of 'README.md' includes:

- Introduction**: A brief description stating it's a repository for public files used in lectures, presentations, etc.
- Notice**: Guidelines for use, mentioning permission from the lecturer/presenter or group members.
- Download**: A section with a note about using DownGit and a link to 'Minhas Kamal'. A red box highlights the 'DownGit' link, and a red circle labeled '①' is placed above it.
- Licensing**: A Creative Commons Attribution-ShareAlike 4.0 International License logo.
- Copyright**: Copyright © 2022- Seoul National University Lab of Computational Biology and Biomolecular Engineering.

The screenshot shows a GitHub browser interface. The address bar is highlighted with a red box and labeled '②'. The main area displays a file upload history for the 'AI-Bio' folder. The history shows two uploads:

File	Type	Time
AF_monomer	AI-Bio file upload	1 hour ago
GalaxyTongDock	AI-Bio file upload	1 hour ago

The screenshot shows the DownGit website, which allows users to generate download links for GitHub repositories. The interface includes:

- A large red box highlighting the input field for 'GitHub File or Directory Link'.
- A red circle labeled '③' placed next to the input field.
- Two buttons at the bottom: 'Create Download Link' and 'Download'.
- The title 'DownGit' and subtitle 'Create GitHub Resource Download Link'.

# Modeling Target



# Model Protein - 5xra

## 5XRA

Crystal structure of the human CB1 in complex with agonist AM11542

PDB DOI: <https://doi.org/10.2210/pdb5XRA/pdb>

Classification: SIGNALING PROTEIN

Organism(s): Homo sapiens, *Desulfovibrio vulgaris* str. Hildenborough

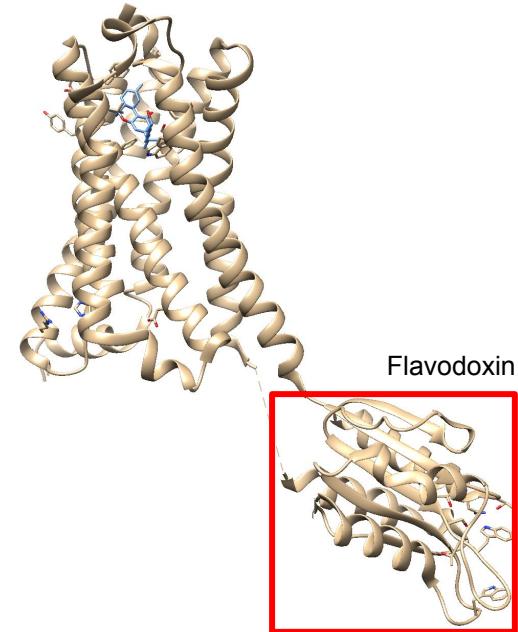
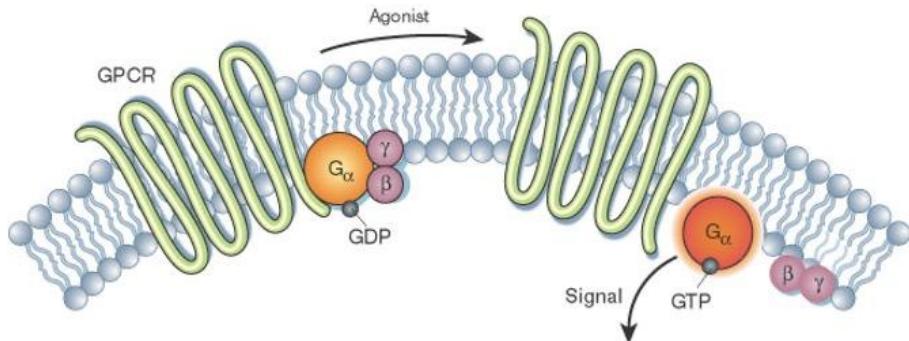
Expression System: Homo sapiens

Mutation(s): Yes ⓘ

Membrane Protein: Yes ⓘ OPM PDBTM MemProtMD mpstruc

Deposited: 2017-06-08 Released: 2017-07-12

Deposition Author(s): Hua, T., Vemuri, K., Nikas, P.S., Laprairie, R.B., Wu, Y., Qu, L., Pu, M., Korde, A., Shan, J., Ho, J.H., Han, G.W., Ding, K., Li, X., Liu, H., Hanson, M.A., Zhao, S., Bohn, L.M., Makriyannis, A., Stevens, R.C., Liu, Z.J.

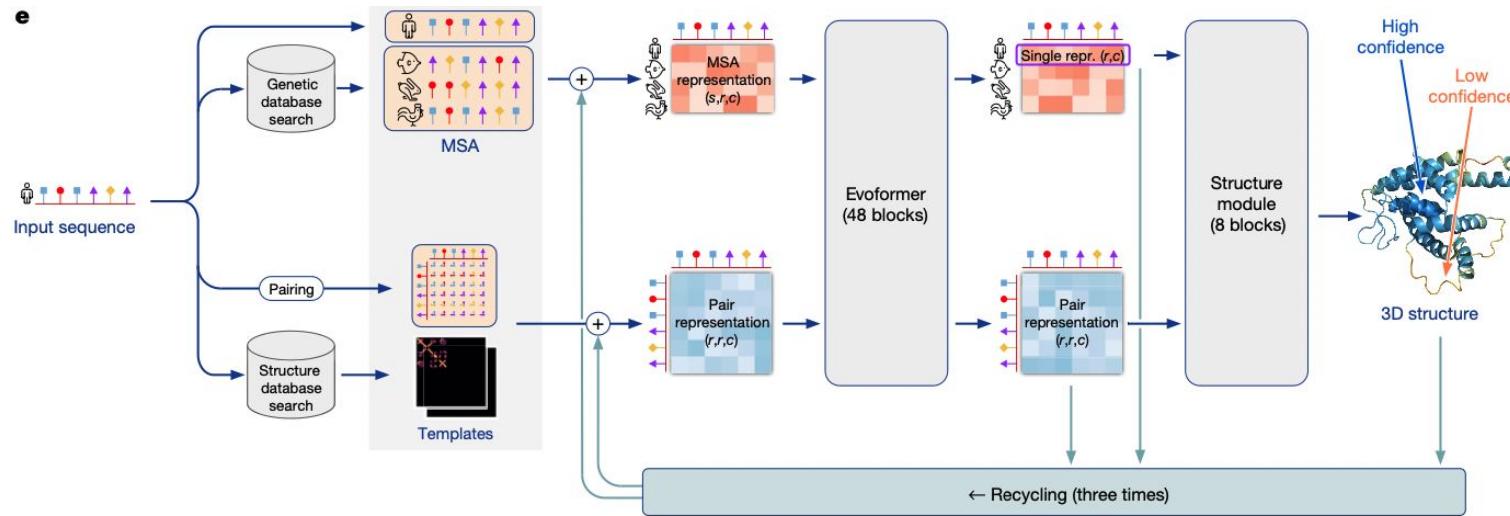


GPCR CB1  
+ Agonist AM11542

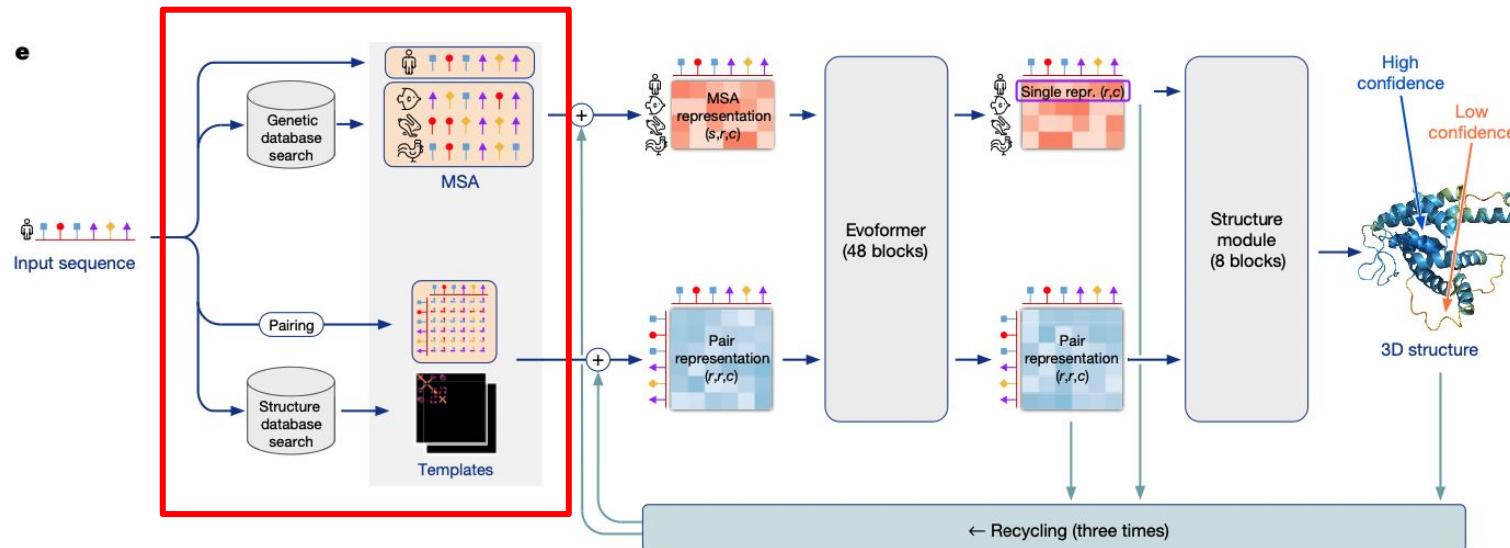
# **AF2, AF-multimer**

- GPCR and its structure prediction

# What is AlphaFold2, AlphaFold-Multimer?



# What is AlphaFold2, AlphaFold-Multimer?

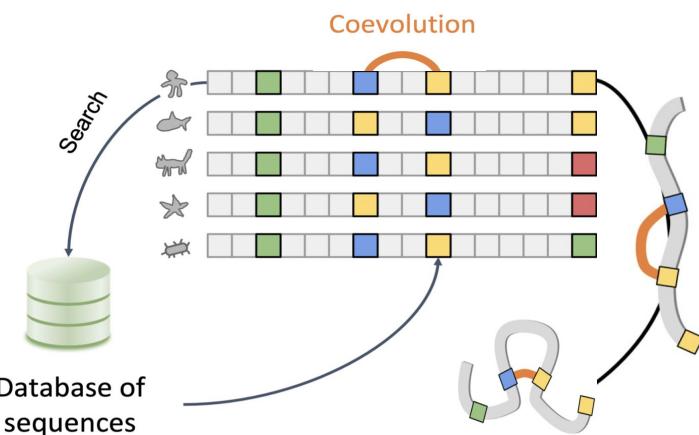


## 1. Build MSA & Get template information (HHblits, HMMer)

# What is AlphaFold2, AlphaFold-Multimer?

## 1. Build MSA & Get template information (HHblits, HMMer)

### Monomer



### Multimer - Paired MSA

#### UniRef30 paired

MQQDDDEQNFWATLSCPDLDLGGIIGGPRIVLTVALDHDIESKIIISLLIIDYGL  
MSENNNSFENFTVILLESWSLQSCISCSKIKLTLNFALENVELEEMWSSILINYSIT  
MGSUSDHEFDWAVILESWSLQSGISGSHPPLXLIIDIAVNNGENLALISFVIQYSIE  
MTG--HEDEFWAVILESWSLQSGISGSHPPLXLIIDIAVNNGENLALISFVIQYSIE  
---DHQNFWATLSCPDLDLGGIIGGPRIVLTVALDHDIESKIIISLLIIDYGL

Paired by species

#### Unpaired

FF--TIPSTLPGI--PGUSCGSDTYY  
EHDQSFWAVILESWSLQSGISGSHPPL  
---GTIQGFVITLESSPEELMGIGACRIV  
IAEFDTATLTELTLWACVSCSLLKK  
MSGISSHDQFVITLESSPEELMGIGACRIV  
MSETEAFQDFWVITLESSPEELMGIGACRIV  
MSAVDQFESTILWISTLIA--PGUSCGSDTYY

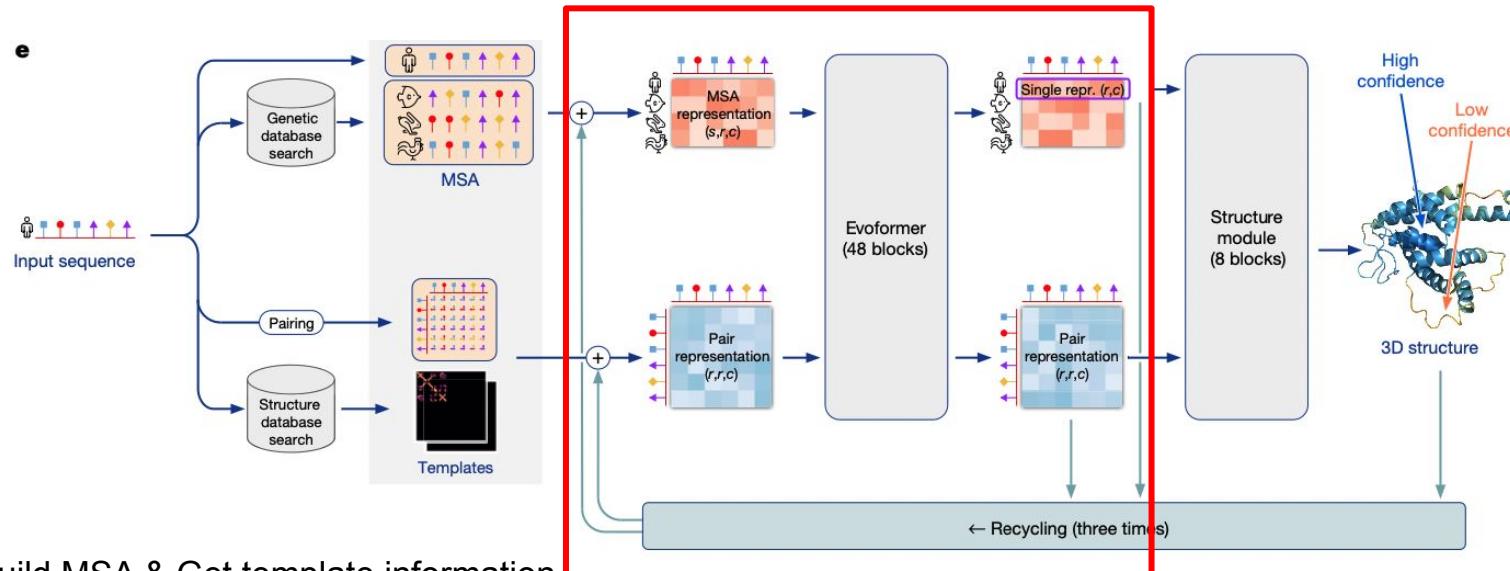
+

LVEISLTDIDYKESVIAALYSSCKA  
LIEIAISNVSDANIIIQILYSNCKA  
LTDIAVWENNEPFLISTLYSCKA  
LTTIAUWNVSRSSTVUDALYASCKA  
LSTLIASTIDYKESVIAALYSSCKA  
MTSICVENVQYEGSVLICQLPFTIKA

Nat Methods 19, 679–682 (2022).

Nature 596, 583–589 (2021)

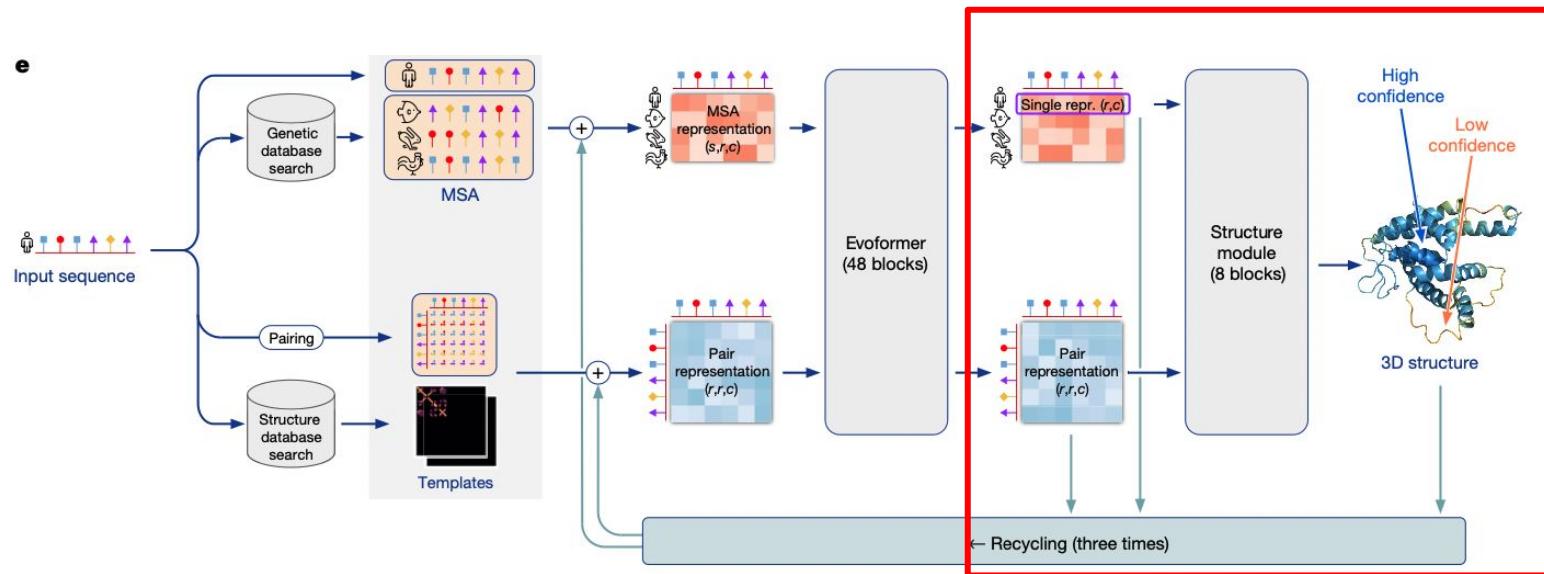
# What is AlphaFold2, AlphaFold-Multimer?



1. Build MSA & Get template information

2. Obtain MSA representation  
& Pair representation through Evoformer

# What is AlphaFold2, AlphaFold-Multimer?

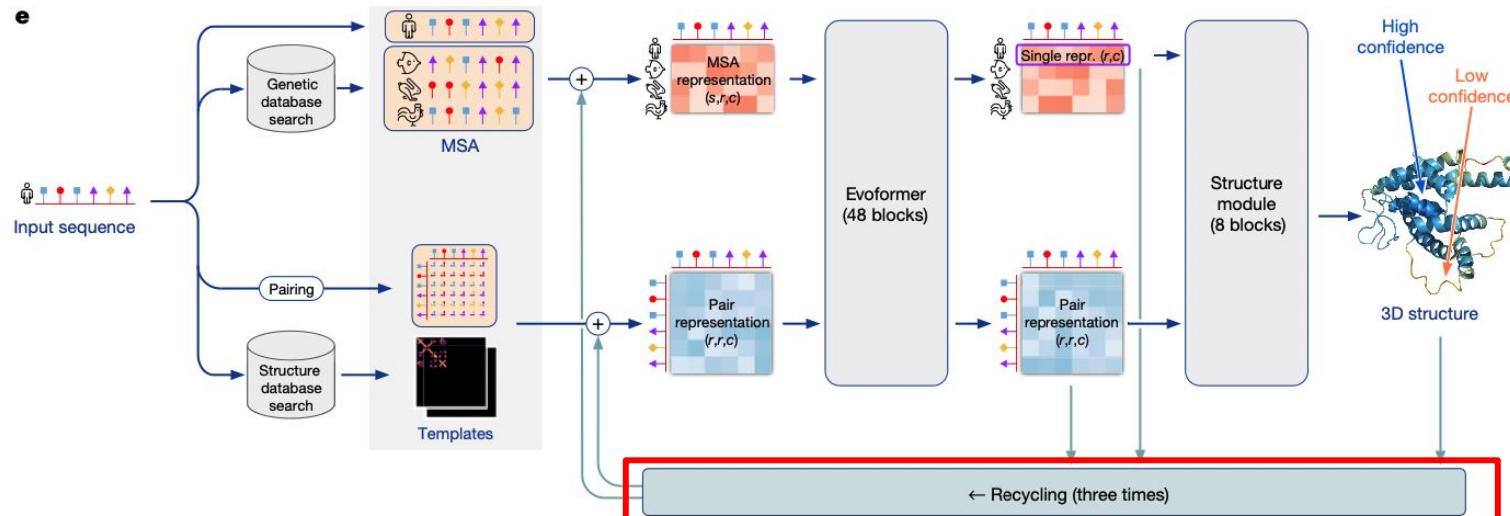


1. Build MSA & Get template information (HHblits, HMMer)

2. Obtain MSA representation & Pair representation through Evoformer

3. Predict structure using Structure module

# What is AlphaFold2, AlphaFold-Multimer?



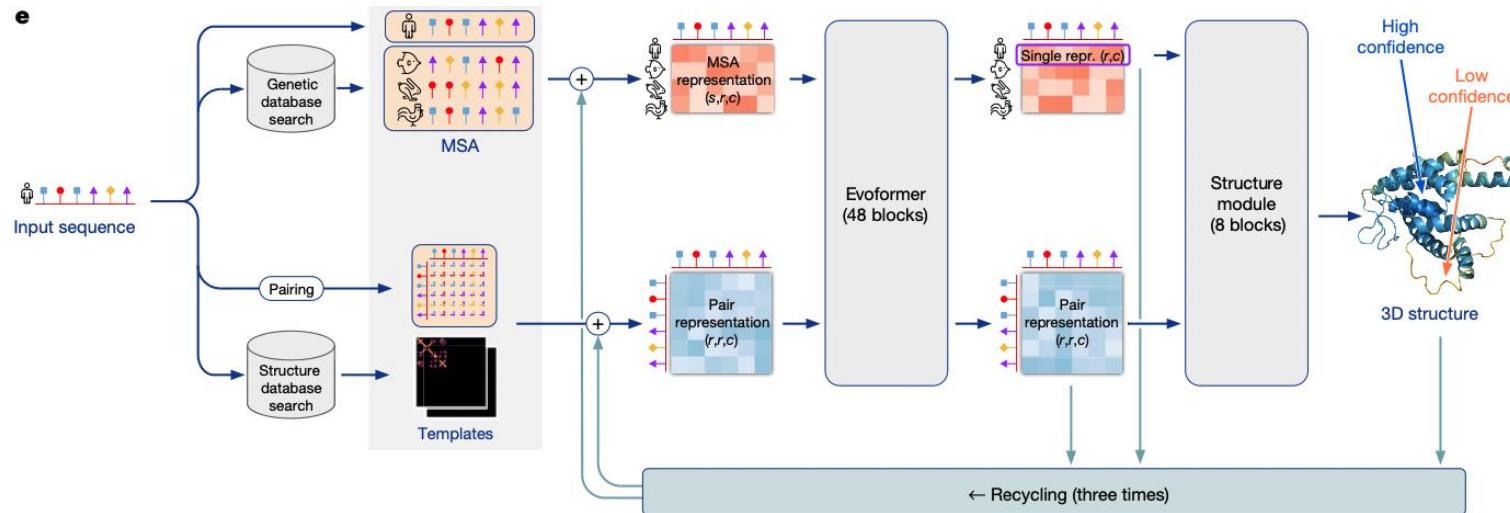
1. Build MSA & Get template information (HHblits, HMMer)

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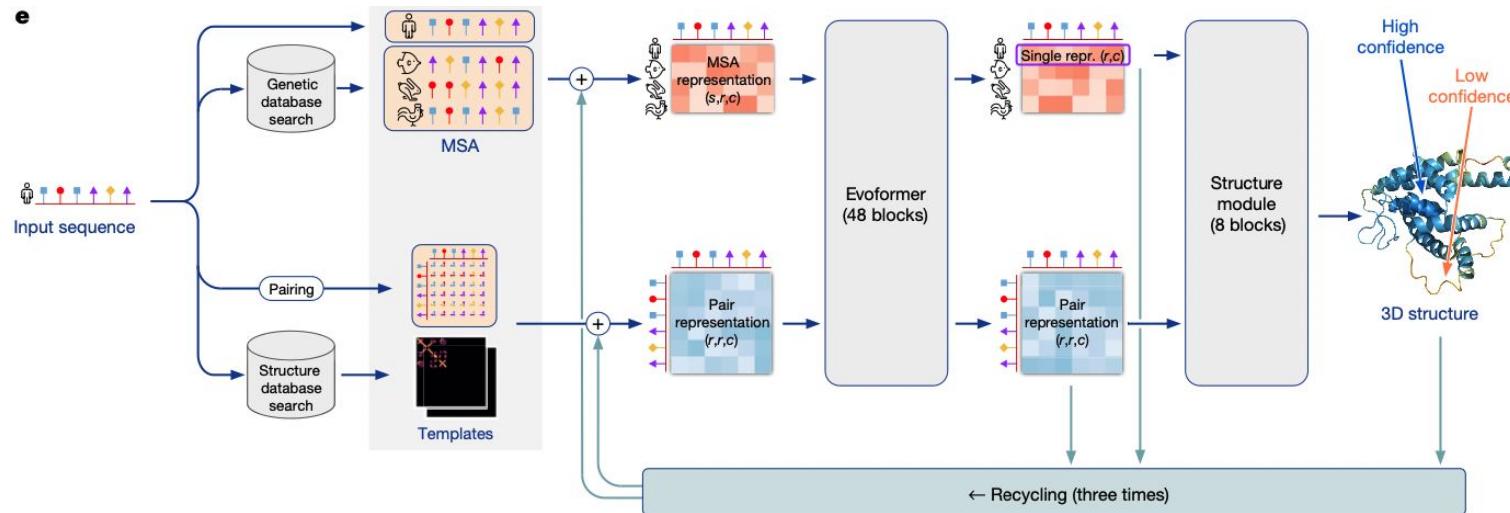
4. Iterative Refinement through recycling

# What is AlphaFold2, AlphaFold-Multimer?



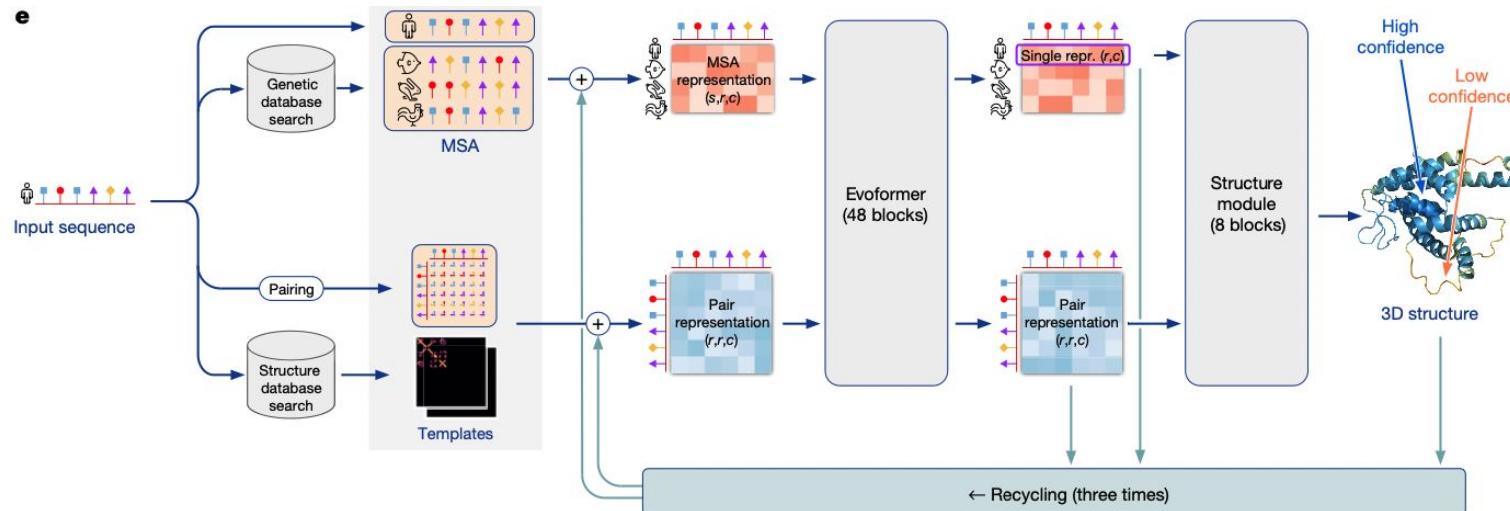
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# What is AlphaFold2, AlphaFold-Multimer?



1. Build MSA & Get template information (HHblits, HMMer) - **several hours, need ~2TB for database**
2. Obtain MSA representation & Pair representation through Evoformer
3. Predict structure using Structure module
4. Iterative Refinement through recycling

# What is AlphaFold2, AlphaFold-Multimer?



1. Build MSA & Get template information (HHblits, HMMer)
  2. Obtain MSA representation & Pair representation through Evoformer
  3. Predict structure using Structure module
  4. Iterative Refinement through recycling
- Need GPUs  
with a large amount of RAM**

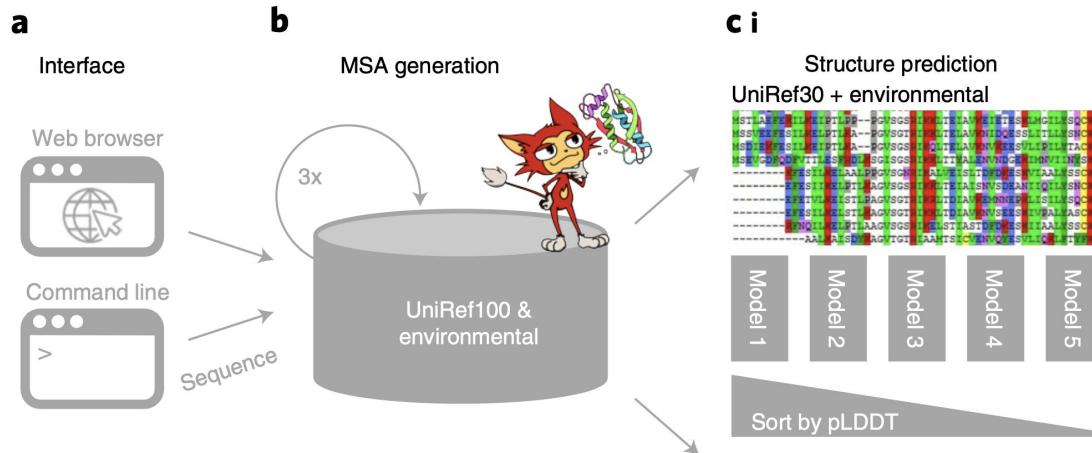
# AF2, AF-multimer 실습

- GPCR and its complex prediction w/ ColabFold

# ColabFold



- <https://colab.research.google.com/github/sokrypton/ColabFold/blob/main/AlphaFold2.ipynb>
- Build MSA by MMseqs2 (40-60 folds Faster)
- Speed up structure predictions by avoiding recompilation and adding an early stop criterion (~90 folds faster)



# Model Protein - 5xra

## 5XRA

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Expression System: Homo sapiens

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Modeling GPCR in CB1 5XRA  
with ColabFold!



GPCR CB1 + Agonist  
AM11542

# Input Protein sequence

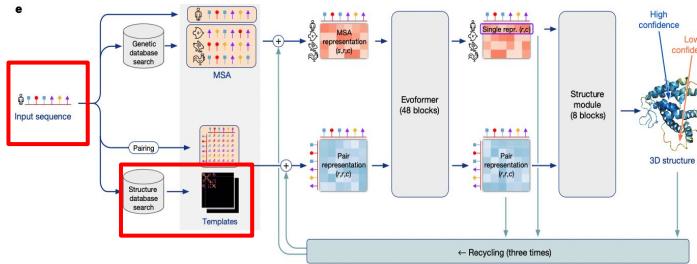
- **Input Files : /Public-practice/AI-Bio\_2023/AF\_monomer/CB1.fa**
  - **Fasta File of CB1 (Protein sequence file)**
  - **RCSB Database for proteins (<https://www.rcsb.org/>) (Protein crystal structure file)**

[https://github.com/seoklab/Public-practice/tree/main/AI-Bio\\_2023/AF\\_monomer](https://github.com/seoklab/Public-practice/tree/main/AI-Bio_2023/AF_monomer)



```
# CB1.fa
> chain_A
GENFMDIECFMVLNPSQLAIAVSLTGTFTVLENLLVLCVILHSRSLRCRPSYHFIGSLAVADLLGSVIFVYSFIDFH
VFHRKDSRNVFLFKLGGVTASFTASVGSLFLAAIDRYISIHRPLAYKRIVTRPKAVVAFCLMWIAVIAVLPLLGWNC
EKLQSVCSIDFPHIDKTYLMFWIGVVSVLLLFIYAYMYILWKAHSHAVMDIELAKTLVLILVVLIIICWGPLLAIMVYDVF
GKMNKLIKTVFAFCMSLCLLNSTVNPIIYALRSKDLRHAFRSMFPS
```

# Input Protein sequence



Input protein sequence(s), then hit Runtime -> Run all

query\_sequence: "ENFMIDECFMVLNPSQLAIAVSLTGTFTVLENLLVLCVILHSRSLRCRPSYHFIGSLAVADLLGSVIFVYSFIDFHVFHRKDSRNVFLFKLGGVTASFTAVGSLFLAAIDRYISI"

- Use : to specify inter-protein chainbreaks for **modeling complexes** (supports homo- and hetro-oligomers). For example PI...SK:PI...SK for a homodimer

jobname: "CB1"

num\_relax: 5

- specify how many of the top ranked structures to relax using amber

template\_mode: pdb100

- none = no template information is used. pdb100 = detect templates in pdb100 (see [notes](#)). custom - upload and search own templates (PDB or mmCIF format, see [notes](#))

코드 표시

Chain이 여러 개인 경우  
각 chain 사이를 :로  
구분  
**jobname (ex. CB1)**

Constrained relaxation of  
structures using Amber force  
field  
(stereochemical violation 제거)

Template\_mode:

i) **None** - no template information is used

ii) **pdb100** - detect templates in pdb100 (representative structure database based on the pairwise structure similarity by FoldSeek)

iii) **custom** - upload & search own templates

# MSA options

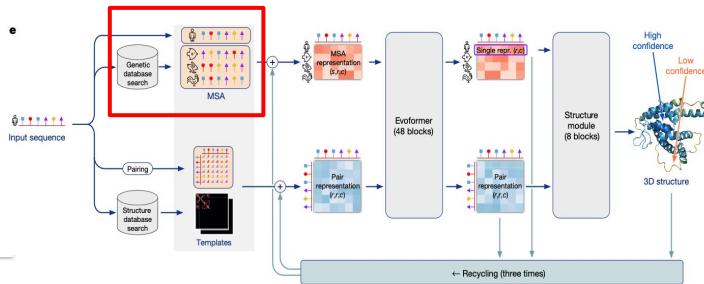
MSA options (custom MSA upload, single sequence, pairing mode)

msa\_mode: mmseqs2\_uniref\_env

pair\_mode: unpaired\_paired

- "unpaired\_paired" = pair sequences from same species + unpaired MSA, "unpaired" = separate MSA for each chain, "paired" - only use paired sequences.

코드 표시

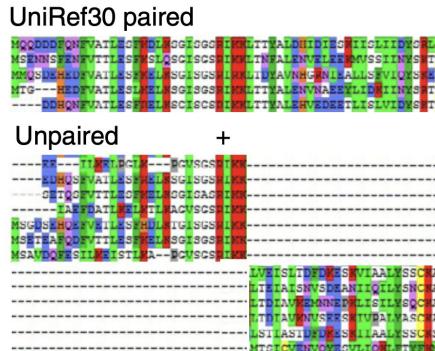


## MSA mode:

- MMseqs2 (UniRef + Environmental) - use UniRef sequences + Environmental sequences
- MMseqs2 (UniRef) - only use UniRef sequences
- single\_sequence - only use single sequence
- custom - upload own MSA

## Pair mode:

- unpaired + paired - pair sequences from same species + unpaired MSA
- unpaired - separate MSA for each chain
- paired - only use paired sequences



# Advanced Settings

## Advanced settings

`model_type: auto`

### Model type : AlphaFold2 or AlphaFold-Multimer

- if `auto` selected, will use `alphafold2_ptm` for monomer prediction and `alphafold2_multimer_v3` for complex prediction. Any of the mode\_types can be used (regardless if input is monomer or complex).

`num_recycles: 3`

- if `auto` selected, will use `num_recycles=20` if `model_type=alphaFold2_multimer_v3`, else `num_recycles=3` .

`recycle_early_stop_tolerance: auto`

- if `auto` selected, will use `tol=0.5` if `model_type=alphaFold2_multimer_v3` else `tol=0.0`.

`pairing_strategy: greedy`

### Pairing strategy : MSA pairing strategy

- `greedy` = pair any taxonomically matching subsets, `complete` = all sequences have to match in one line.

## Sample settings

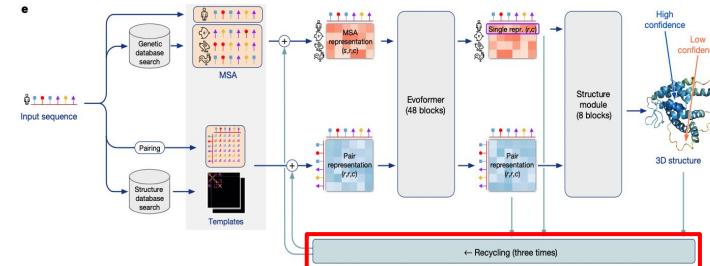
- enable dropouts and increase number of seeds to sample predictions from uncertainty of the model.
- decrease `max_msa` to increase uncertainty

`max_msa: auto`

### Sampling settings : When want to get more diverse structures

`num_seeds: 1`

`use_dropout:`



# Run prediction!

## Run Prediction

```
display_images: ✓  
코드 표시  
...  
2023-10-20 08:01:14.962 Downloading alphafold2 weights to : - 100% [██████████] 3.47G/3.47G [00:24:00:00, 150MB/s]  
2023-10-20 08:01:14.964 Unable to initialize backend 'room': NOT_FOUND: Could not find registered platform with name: "room". Available platform names are: '  
2023-10-20 08:01:20.883 2023-10-20 08:01:14.964 Unable to initialize backend 'tpu': INTERNAL: Failed to load open libtpu.so: libtpu.so: cannot open shared object file: No such file or d  
2023-10-20 08:01:21.091 2023-10-20 08:01:14.964 Found 8 citations for tools or databases  
2023-10-20 08:01:21.091 Query 1/1: CBL_9e17c (length 437)  
PENDING: 0% | 0/150 [elapsed: 00:00 remaining: 00:00] 2023-10-20 08:01:21.092 Sleeping for 10s. Reason: PENDING  
RUNNING: 1% | 1/150 [elapsed: 00:11 remaining: 02:49] 2023-10-20 08:01:21.093 Sleeping for 7s. Reason: RUNNING  
RUNNING: 11% | 17/150 [elapsed: 00:19 remaining: 02:29] 2023-10-20 08:01:21.094 Sleeping for 6s. Reason: RUNNING  
RUNNING: 15% | 23/150 [elapsed: 00:25 remaining: 02:22] 2023-10-20 08:01:21.095 Sleeping for 8s. Reason: RUNNING  
RUNNING: 21% | 31/150 [elapsed: 00:34 remaining: 02:11] 2023-10-20 08:01:21.096 Sleeping for 10s. Reason: RUNNING  
RUNNING: 27% | 41/150 [elapsed: 00:44 remaining: 01:59] 2023-10-20 08:01:21.097 Sleeping for 10s. Reason: RUNNING  
RUNNING: 34% | 51/150 [elapsed: 00:54 remaining: 01:49] 2023-10-20 08:01:21.098 Sleeping for 10s. Reason: RUNNING  
RUNNING: 41% | 61/150 [elapsed: 01:06 remaining: 01:35] 2023-10-20 08:01:21.099 Sleeping for 6s. Reason: RUNNING  
RUNNING: 45% | 67/150 [elapsed: 01:13 remaining: 01:30] 2023-10-20 08:01:21.100 Sleeping for 8s. Reason: RUNNING  
RUNNING: 50% | 75/150 [elapsed: 01:22 remaining: 01:21] 2023-10-20 08:01:21.101 Sleeping for 7s. Reason: RUNNING  
RUNNING: 55% | 82/150 [elapsed: 01:29 remaining: 01:14] 2023-10-20 08:01:21.102 Sleeping for 8s. Reason: RUNNING  
RUNNING: 60% | 90/150 [elapsed: 01:36 remaining: 01:07] 2023-10-20 08:01:21.103 Sleeping for 8s. Reason: RUNNING  
2023-10-20 08:03:19.357 Sequence 0 found templates. ['5tqz_A', '5x16_A', '5v3g_A', '5xra_A', '7ddz_A', '7k15_A', '6i11_A', '7fee_A', '5u09_A', '6kgi_A', '7w
```

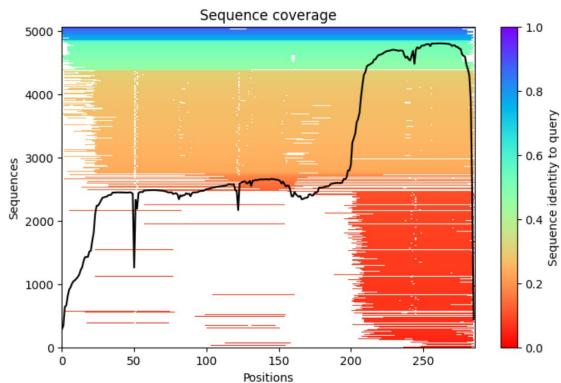
## Log : AlphFold running log

### - Template information

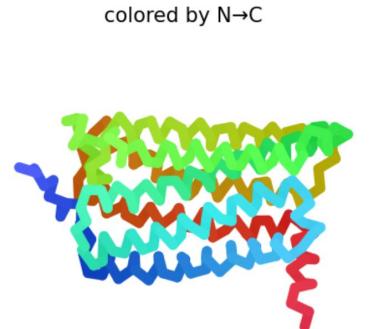
### - MSA setting information

### - Scoring information : pLDDT & pTM value

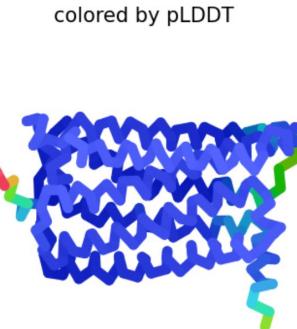
etc



Sequence coverage : MSA information visualization

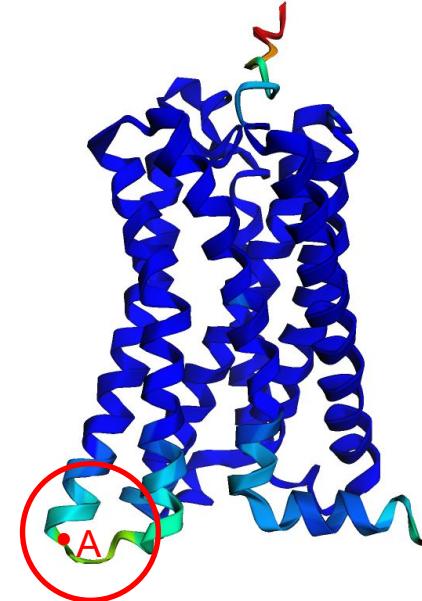


Colored structure : Visualization with reliability etc



# What is pLDDT, pTM ?

- **pLDDT** (predicted local distance difference test )
  - i. predict the per-residue IDDT-Ca score
  - ii. local error metric
  - iii. value from 0~100 (uncertain ~ certain)

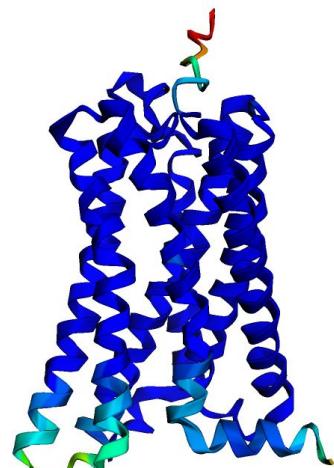


- **pTM** (predicted TM score)
  - i. whether the model is confident in overall domain packing
  - ii. Value from (0-1] (not matched ~perfectly matched)

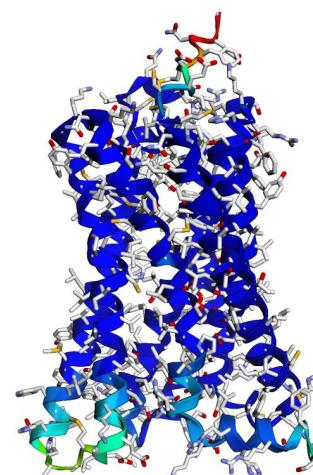
$$\text{TM-score} = \text{Max} \left[ \frac{1}{L_N} \sum_{i=1}^{L_T} \frac{1}{1 + \left( \frac{d_i}{d_0} \right)^2} \right]$$

# Visualization of predicted structures

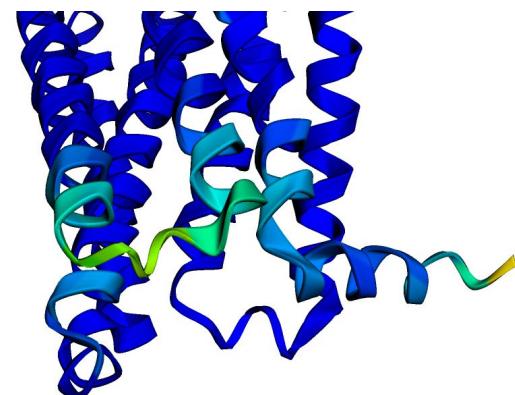
Show side chain X



Show side chain O



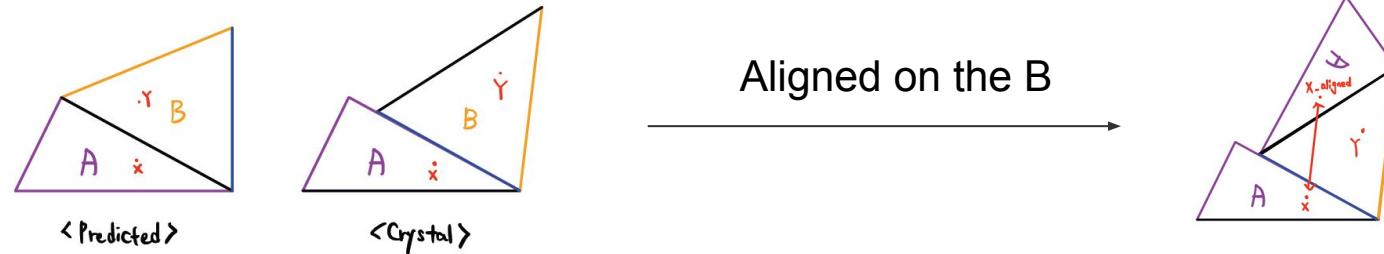
Focusing on the loop



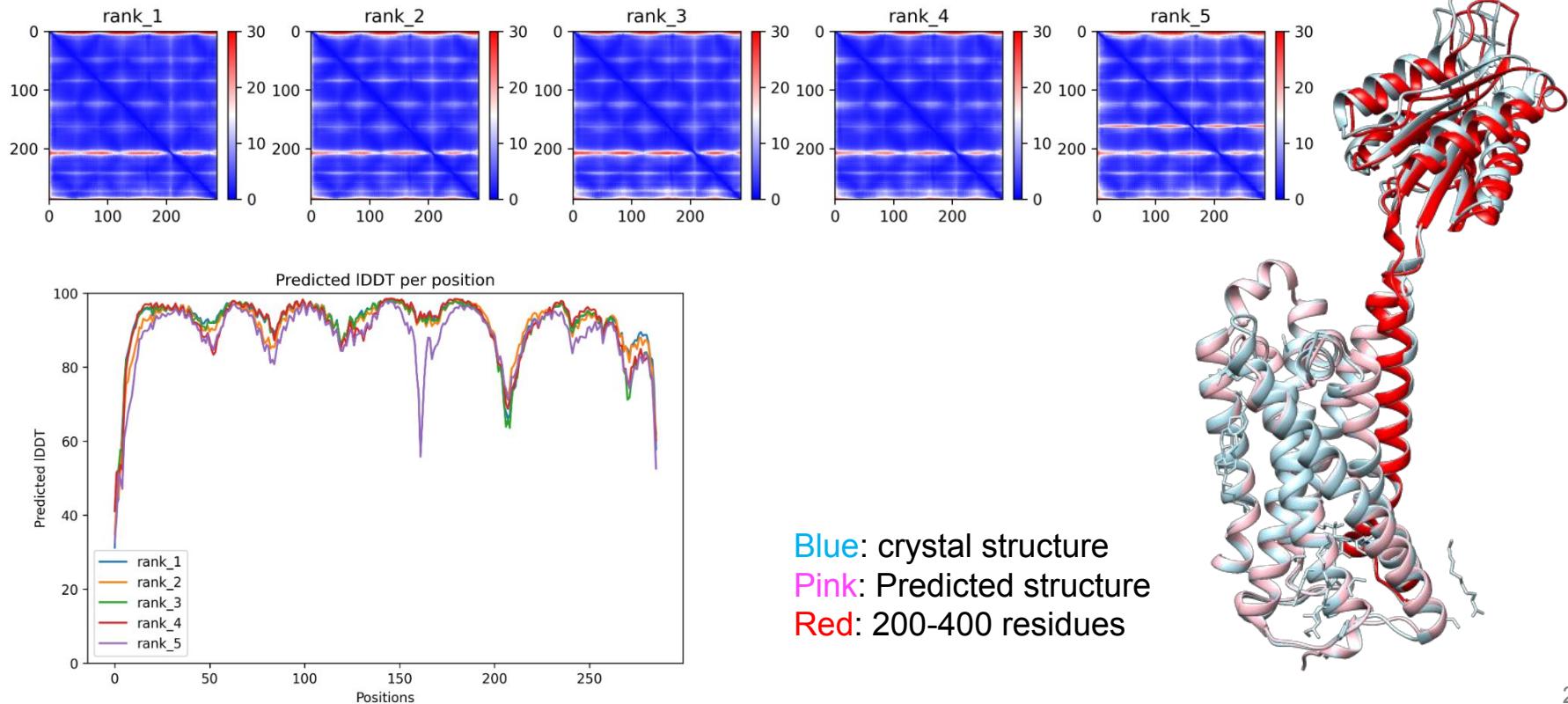
pIDDT:    ■ Very low (<50)    ■ Low (60)    ■ OK (70)    ■ Confident (80)    ■ Very high (>90)

# What is PAE ?

- **PAE** (predicted aligned error)
  - For every pair  $(x, y)$  of residues in the structure, PAE is calculated by AlphaFold's estimate of position error at residue  $x$ , while the predicted and true structures are aligned on residue  $y$ .
  - If the relative position of two domains is confidently predicted, the PAE values will be low (less than 5Å) for pairs of residues from each domain.



# Plots for predicted structures



# Multimer case - 6yx9

6YX9

Display Files Download Files

Cryogenic human adiponectin receptor 2 (ADIPOR2) at 2.4 Å resolution determined by Serial Crystallography (SSX) using CrystalDirect

PDB DOI: 10.2210/pdb6YX9/pdb

Classification: MEMBRANE PROTEIN

Organism(s): Homo sapiens

Expression System: Drosophila melanogaster

Mutation(s): No

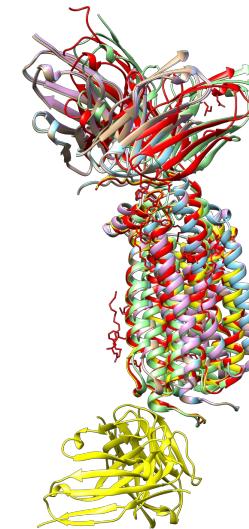
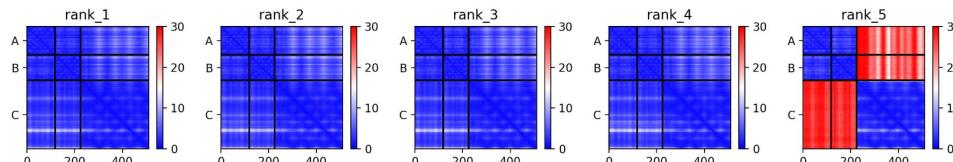
Membrane Protein: Yes

PDBTM

MemProtMD

mpstruc

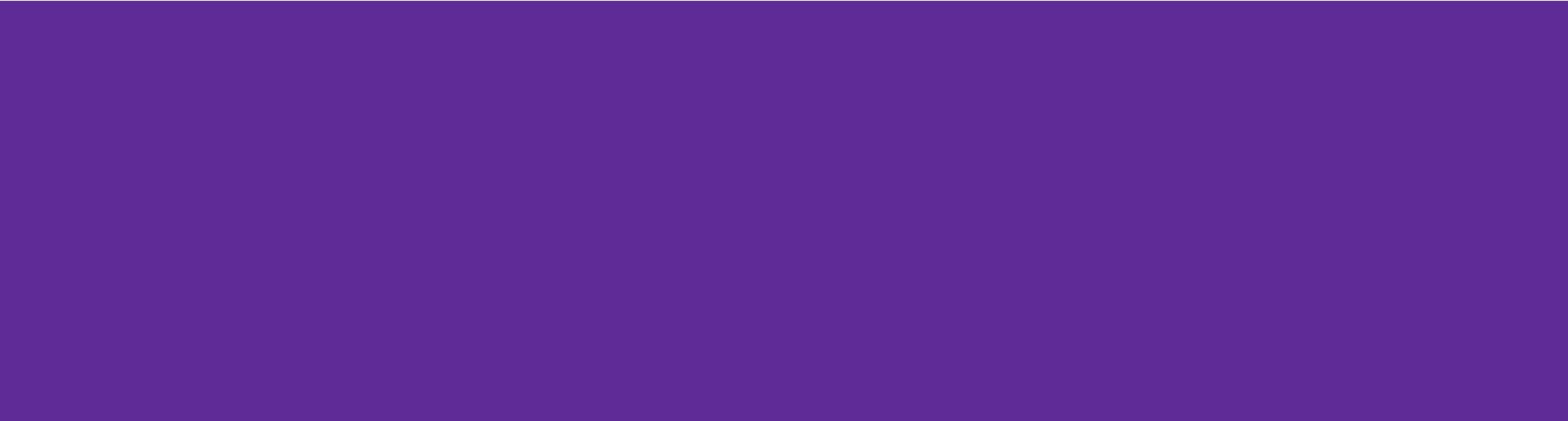
PAE score for 6yx9 - A: Heavy chain, B: Light chain, C: antigen



Crystal structure - red  
Ranked #5 structure - yellow

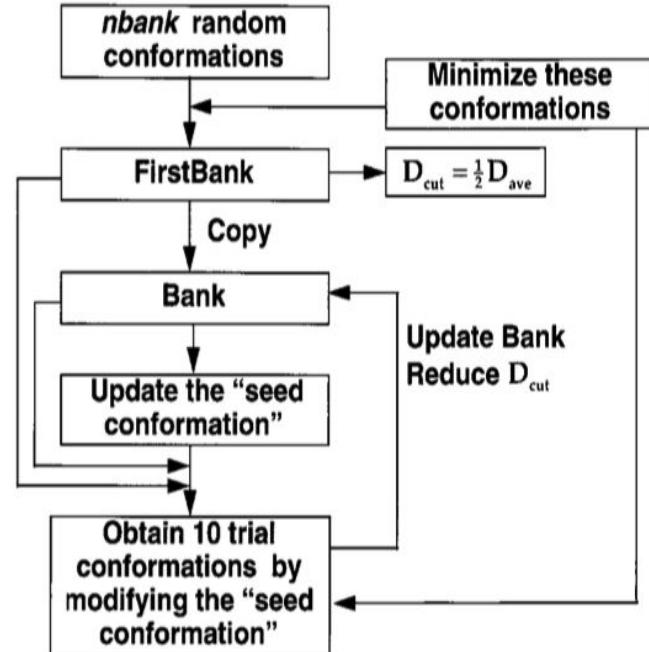
- PAE score can be a criterion of whether the binding geometry is well predicted !

# GalaxyDock 실습



# GalaxyDock : What it is

- Protein-Ligand Docking tool based on CSA
  - CSA : Genetic algorithm + Simulated Annealing
- Based on GalaxyDock BP2 Score
  - Hybrid of physics-based, empirical, knowledge-based
- 6+K Degrees of freedom of Ligand
  - Fixed Ring conformation, Rigid Receptor Protein
  - Degrees of freedom
    - Translation + Rotation + Torsion angle



# GalaxyDock : Preparing input

- Receptor : Crystal structure or Predicted structure by AF2 etc. → .pdb format
- Ligand
  - Prepare SMILES of the target molecule

```
# lig.smi  
c1(O)cc(cc2OC(C)(C)[C@H]3[C@H](c12)CC(=CC3)C)C(CCCCCCBr)(C)C
```

- Convert SMILES to .mol2 using Corina (<https://mn-am.com/products/corina/>) : 1D→3D

```
corina -i t=smiles lig.smi -o t=mol2 >> lig.mol2
```

- Preprocess mol2 file : attach hydrogen and assign partial charge with Chimera command

```
del H          # delete Hydrogen      addh          # attach Hydrogen  
addcharge all method gas           # assign partial charge
```

# GalaxyDock : Run & Analysis

- Let's Run!! with GalaxyWeb

<https://galaxy.seoklab.org/>

## Input file

/Public-practice/AI-Bio\_2023/GalaxyDock/ lig.mol2

/Public-practice/AI-Bio\_2023/GalaxyDock/CB1\_AF1.pdb

## binding site

79A, 95A, 181A, 231A, 255A

**GalaxyDockWEB**

Given a protein receptor structure and a set of ligand structures, protein-ligand complex structures are predicted by the GalaxyDock protein-ligand docking program.

**User Information**

Job name

E-mail address (Optional)

**Input protein and ligand structures**

PDB File  
(≤1000 AA)  파일 선택 선택한 파일 없음  
Protein Structure File (allowed file extensions: pdb, txt)

Ligand File  
(≤150 atoms per ligand, up to 500 ligands)  파일 선택 선택한 파일 없음  
Ligand Structure Files (allowed file extensions: mol2, pdb, xyz)  
Note: Ligand structure with stereochemically wrong topology might results in inaccurate docking. (e.g. 2D-projected structure of non-planar ligands)

**Binding pocket residues**

Binding pocket residues  
(≤10 res)   
Residue numbers should follow the input PDB file residue numbering with chain ID.  
Up to 10 residue numbers can be submitted in integers separated by commas  
(example: 51A,64C,78B).

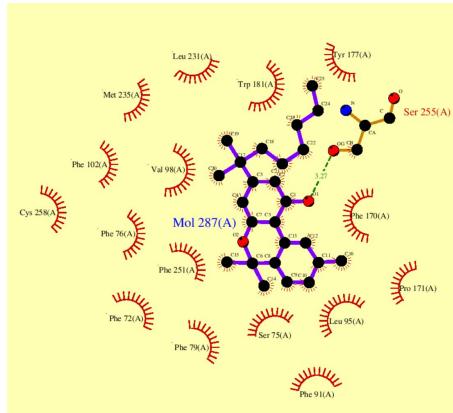
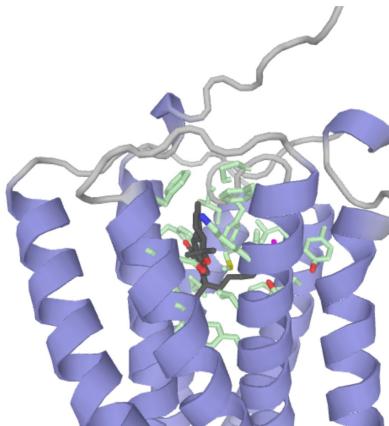
**Submit**

submit  reset

# GalaxyDock : Run & Analysis

- Result Page

<http://galaxy.seoklab.org/cgi-bin/report.Dock.cgi?key=6c8bd214d7543dc3ad2cfb12c063d9>



RES A	72	PHE
RES A	75	SER
RES A	76	PHE
RES A	79	PHE
RES A	91	PHE
RES A	95	LEU
RES A	98	VAL
RES A	99	THR
RES A	102	PHE
RES A	169	ILE
RES A	170	PHE
RES A	171	PRO
RES A	173	ILE
RES A	177	TYR
RES A	178	LEU
RES A	181	TRP
RES A	231	LEU
RES A	235	MET
RES A	251	PHE
RES A	255	SER
RES A	258	CYS

# Chimera 실습



# Visualization of predicted structures with Chimera

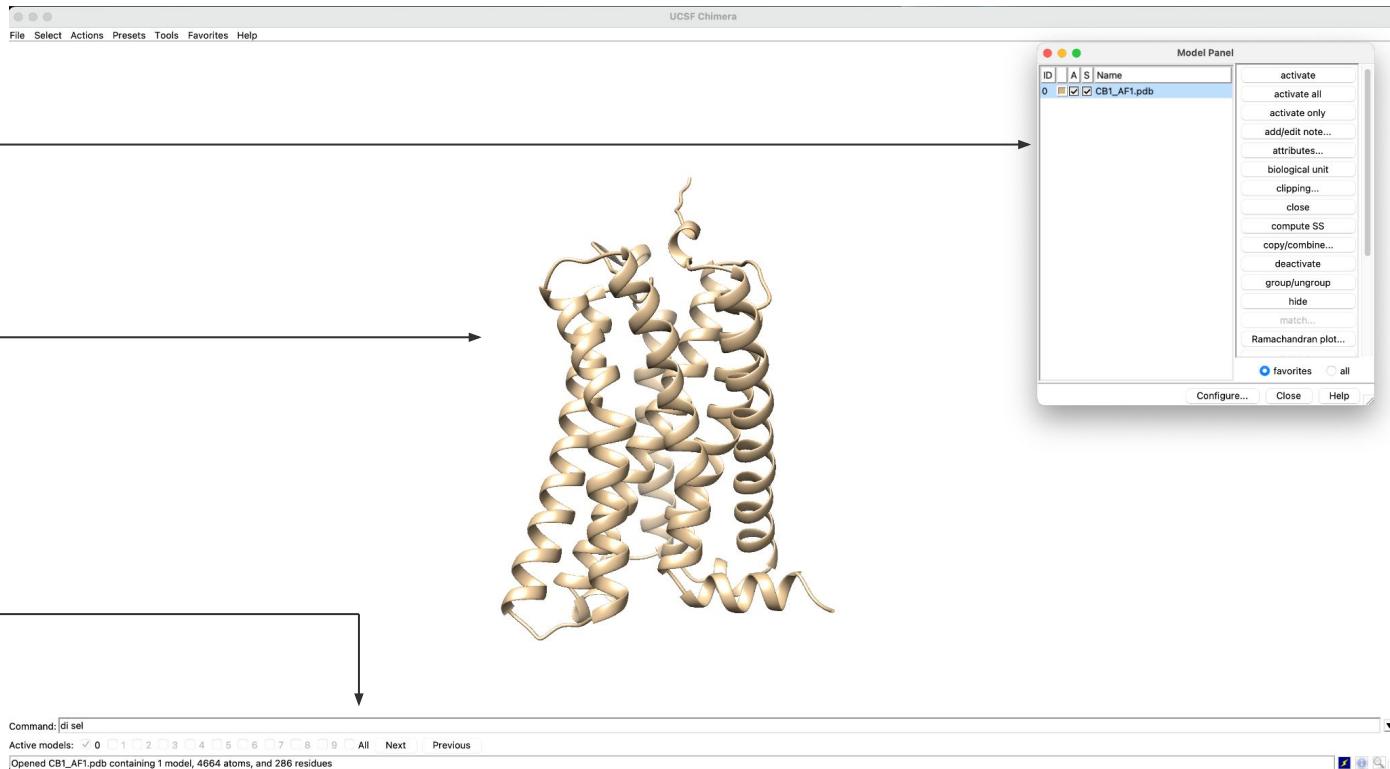
When open .pdb

Opened files  
show, active etc

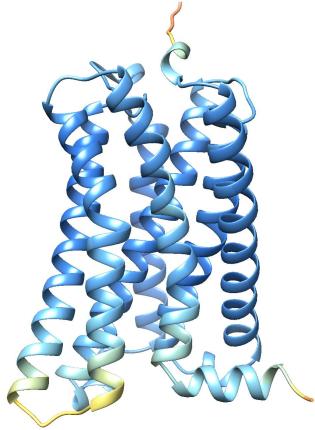
3D structure

회전, 병진 등 가능

Command line  
3D structure 조작



# Visualization of predicted structures with Chimera

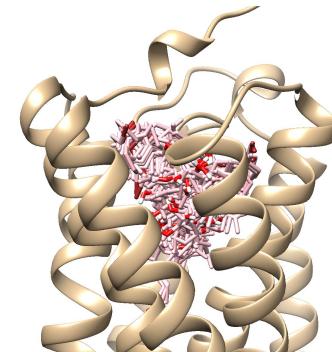


**Let's open the CB1\_AF1.pdb**

- /Public-practice/AI-Bio\_2023/GalaxyDock/CB1\_AF1.pdb

**When want to see pLDDT of AlphaFold model,**

“ range bfactor, 50 #F08253 70 #FADA4D 90 #7EC9EF 100 #1B57CE “



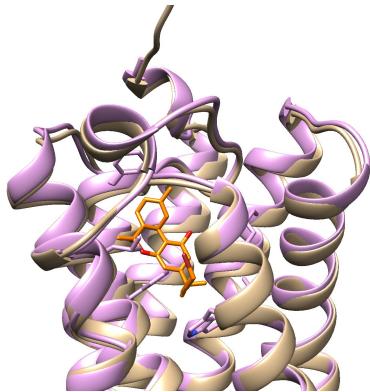
**Let's open the GD\_result.mol2**

- /Public-practice/AI-Bio\_2023/GalaxyDock/GD\_result.mol2

**Too much color, CB1 into basic color and ligand into pink, hetero atom into each color**

“ col tan #0 “ → “ col pink #1 “ → “ col byhet “ ( col [color] [target] # = model, :. = chain, : = residue )

# Visualization of predicted structures with Chimera



**Let's open original complex, complex.pdb**

- /Public-practice/AI-Bio\_2023/GalaxyDock/complex.pdb

**Let's align the complex to the model structure, color it**

“ mm #0 #2 alg sw “ ( mm [ref] [tar] alg sw )

→ “ sel #2:8D3 “ → “ col orange sel “ → ” col byhet “ → ” ~sel “

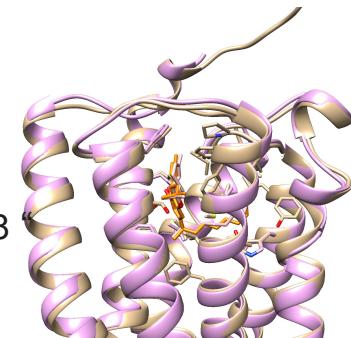
( sel [tar] / #N:R = Residue R in model N, :R.C = Residue in chain C / ~ : not )

**To compare the model and crystal, delete all docked ligand except top1  
and show side chain of contacting residues**

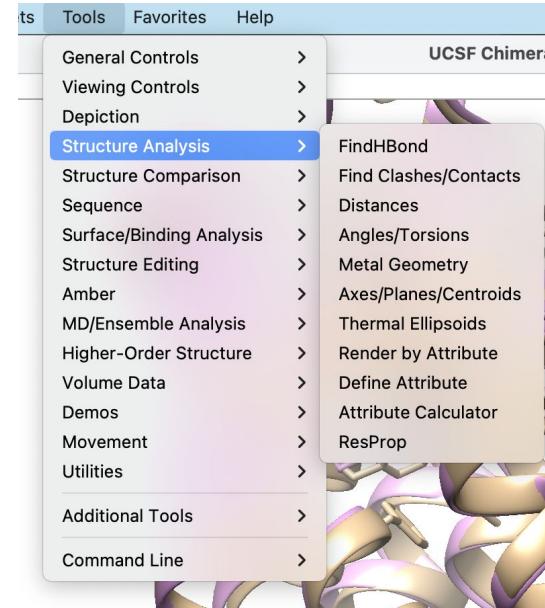
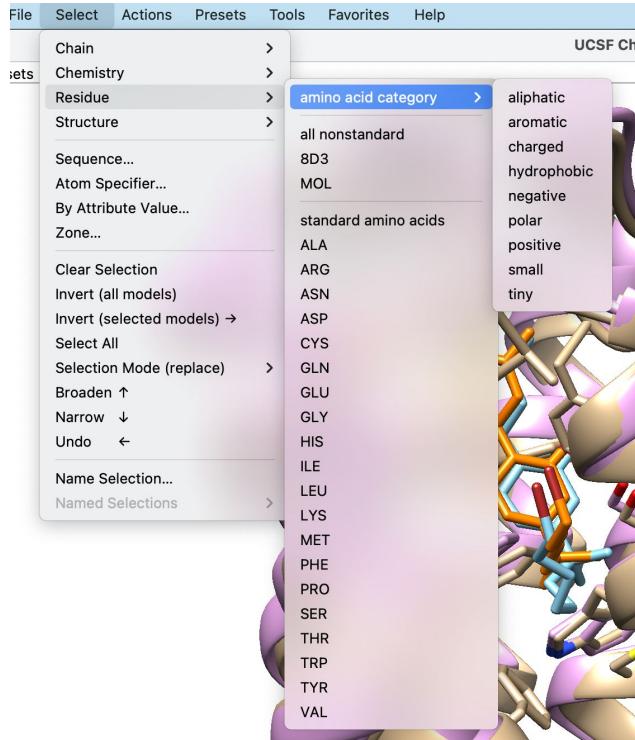
“ sel #1.2-50 ” → “ del sel “

→ “sel :72:75:76:79:91:95:98:99:102:169:170:171:173:177:178:181:231:235:251:255:258

→ “ ~sel #1 #2 “ → “ di sel “ → “ del H “ ( di [tar] / 연속 = 쉼표 등으로 구분 없이 )



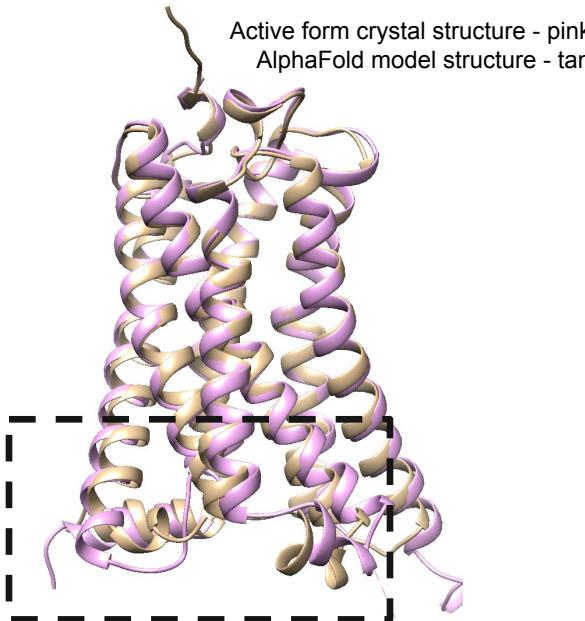
# Visualization of predicted structures with Chimera



Many other functions

<https://www.cgl.ucsf.edu/chimera/docindex.html>

# Limitation of AlphaFold



How to consider  
active, inactive form?

If we use only inactive form templates, then it could predict inactive form!

Input protein sequence(s), then hit Runtime > Run all

query\_sequence: `"PIAQIHLILEGRSDEQKETLIREVSEAIRSLDAPLTSVRVITEMAKGHFGIGGELASK"`

jobname: `"test"`

num\_relax: `0`

specify how many of the top ranked structures to relax using amber

template\_mode: `custom`

none = no template information is used. pdb100 = detect templates in pdb100 (see [notes](#)). custom - upload and search own templates (PDB or mmCIF format, see [notes](#))

코드 표시

파일 선택, 선택한 파일 없음 Cancel upload

#### Using custom templates

To predict the structure with a custom template (PDB or mmCIF formatted): (1) change the `template_mode` to "custom" in the execute cell and (2) wait for an upload box to appear at the end of the "Input Protein" box. Select and upload your templates (multiple choices are possible).

- Templates must follow the four letter PDB naming with lower case letters.
- Templates in mmCIF format must contain `_entity_poly_seq`. An error is thrown if this field is not present. The field `_pdbx_audit_revision_history.revision_date` is automatically generated if it is not present.
- Templates in PDB format are automatically converted to the mmCIF format. `_entity_poly_seq` and `_pdbx_audit_revision_history.revision_date` are automatically generated.

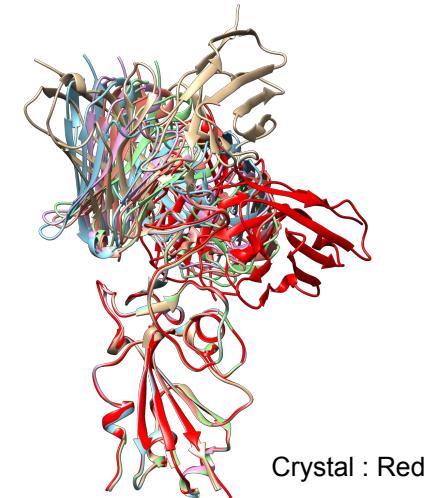
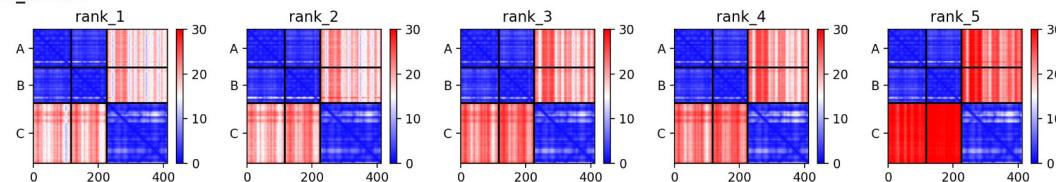
If you encounter problems, please report them to this [issue](#).

# Limitation of AlphaFold

Inaccurate prediction of complex,  
especially antibody-antigen complex

coevolution information is limited  
due to the unique generation mechanism of antibodies

Plots for 7bem\_89674



→ Ab-initio docking method, other deep learning based methods are being developed  
( And also, many other deep learning based ligand docking method are being developed )

# **Thank you for listening**