OmegaFold and Protein Structure Prediction

CCATS Group

OmegaFold

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Title: High-resolution *de novo* structure prediction from primary sequence

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How is OmegaFold Different?

- Based on the understanding that

  1. MSA does not always work, especially for fast-evolving antibodies, and orphan proteins.

  2. Protein folds in a natural setting without exploiting evolutionary information.

- **OmegaFold** predicts protein structure from a single primary sequence alone, i.e. *alignment-free*

- It uses a **pre-trained** protein language model (PLM) to generate single- and pair-wise embeddings (i.e. representations)

  - training on a large collection of unaligned and unlabelled protein sequences

  - fed into Geoformer, which will further distill structural/physical pairwise relationships

Installing OmegaFold

- On OSCER, clone:

  git clone https://github.com/HeliXonProtein/OmegaFold

- Make new Conda environment:

  conda create -n omegafold python=3.9

  conda activate omegafold

- The two types of GPUs on OSCER are NVIDIA K80m and A100
  - 1 K80m on 1 node (c302, c307), 2 K80m on 1 node (c301), and 2 A100 on 1 node (c736)
  - All are not supported by > PyTorch 1.10 (Omegafold was written with Pytorch 1.12)
- Thank you Nelson Liu for developing back support for old GPUs
  - https://github.com/nelson-liu/pytorch-manylinux-binaries/releases

Installing OmegaFold

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- Remake requirements.txt > req_backsupport.txt (PyTorch 1.9.0)

- In the omegafold conda environment

  pip install -r req_backsupport.txt

- Finally,

  python ./setup.py install

- To run: **omegafold [input.fasta] [working directory]**

Tutorial on OmegaFold

- Copy the following directory to your home:

```
cp -r /home/van/MacroMol_Modelling_Tutorial/04_omegafold/ .
```

- The folder is organized as follow:
  - 04_omegafold
    - Results
    - Tutorial
      - bax
      - parDE
        - paparde.fasta
        - of_monomer.slurm

04_omegafold/Tutorial/bax

- Bax.fasta
  - Amino acid sequence
- of_monomer.slurm
  - SLURM script to run OmegaFold
- To run:

  sbatch of_monomer.slurm

K80m (c307)
Wall Time: ~7 min
Prediction Time: ~172 sec
A100
Wall Time: ~5 min
Prediction Time: ~16 sec

```
>bax
MDGSGEQPRGGGPTSSEQIMKTGALLLQGFIQDRAGRMGGEAPEL
ALDPVPQDASTKKLSECLKRIGDELDSNMELQRMIAAVDTDSPRE
VFFRVAADMFSDGNFNWGRVVALFYFASKLVLKALCTKVPELIRT
IMGWTLDFLRERLLGWIQDQGGWDGLLSYFGTPTWQTVTIFVAGV
LTASLTIWKKMG
```

```
#!/bin/bash
#SBATCH --partition=gpu
#SBATCH --ntasks=10
#SBATCH --output=%j.out
#SBATCH --error=%j.err
#SBATCH --time=00:30:00
#SBATCH --job-name=bax
#SBATCH --exclude=c736

date
hostname

module load CUDA/11.3.1

eval "$(/ourdisk/hpc/ccats/dont_archive/van/.Programs/miniconda3/bin/conda shell.bash hook)"
conda activate omegafold

# To Run:
# omegafold [input.fasta] [working directory - output here]
omegafold bax.fasta .

date
```

SLURM Allocation requests

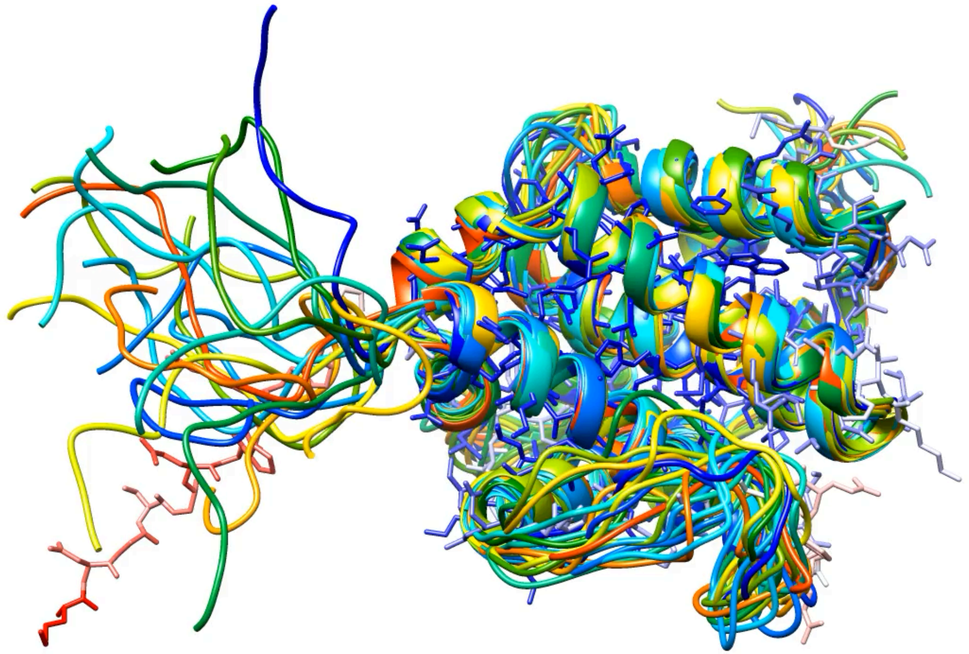
hostname = get name of node

Load CUDA

Omegafold conda environment

Running OmegaFold

bax.pdb



PDB 1F16
OmegaFold

04_omegafold/Tutorial/parDE1

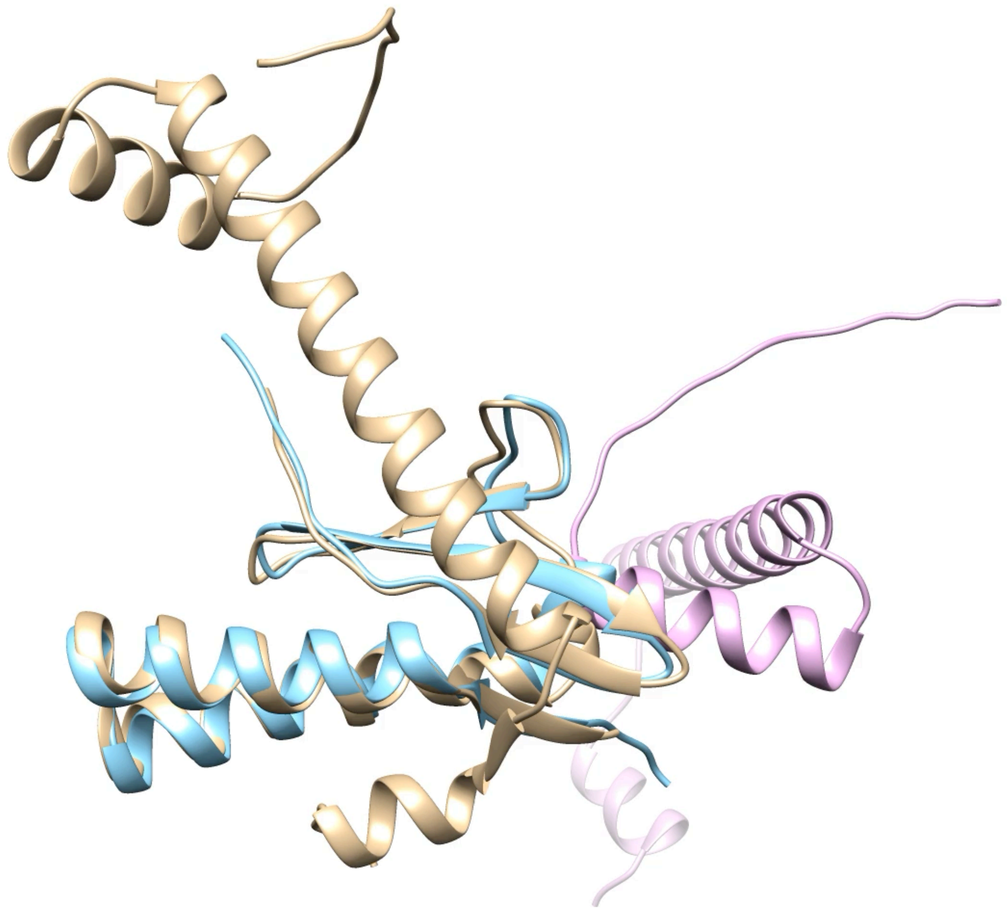
- Currently, OmegaFold can only predict monomers
- However, input can take in multiple sequences and predict them individually
- paparde.fasta
  - Both ParD and ParE sequence
- of_monomer.slurm
  - SLURM script to run OmegaFold
- To run:

  sbatch of_monomer.slurm

```
1 >ParD
2 GSHMMSLKWTRKAAADLDAIYDHYVVLIGPEKALKAVQDIVEQVKP
  LQQVANQGAGRPSEVPGVRTLTLERWPFSAPFRVKGKEIQILRIDR
  VEITP
3 >ParE
4 GSHMMSTVVSFRADDALVAALDELARATHRDRPYHLRQALAQYLER
  QQWQVAAIDEGLADANAGRLLEHIEIEKRWGLQ
```

K80m (c307)
Wall Time: ~6 min
Prediction Time:
ParD ~39 sec
ParE ~50 sec

ParDE



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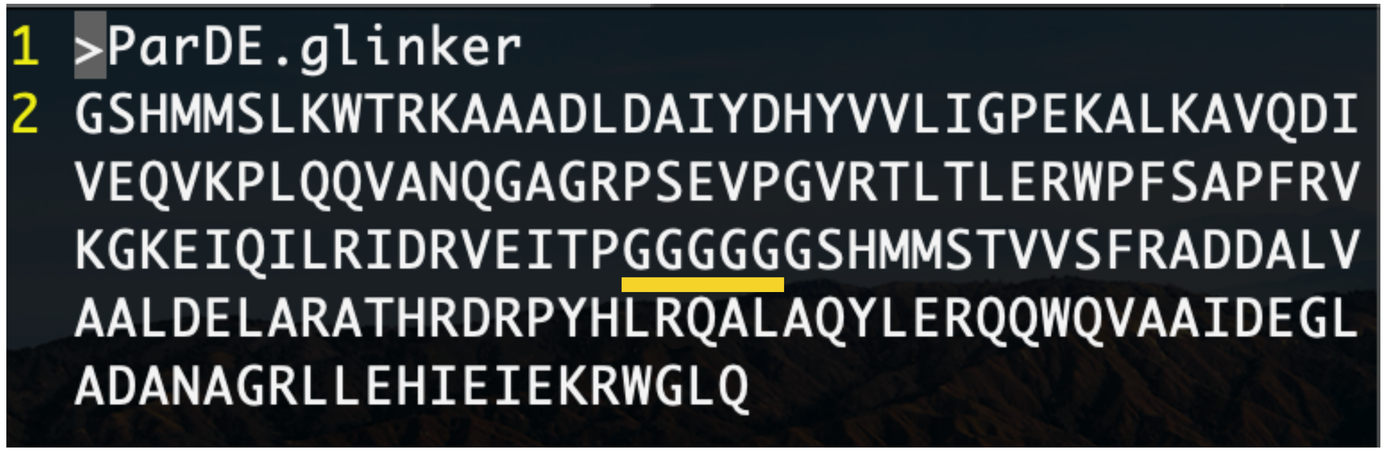
04_omegafold/Tutorial/parDE2

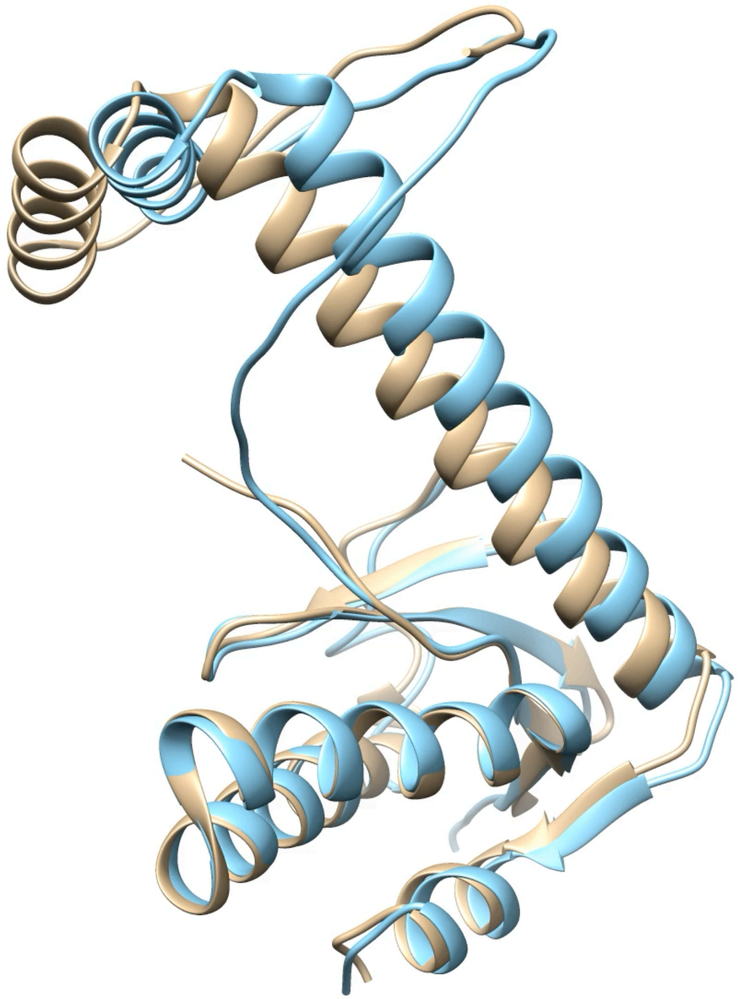
- Lets modify the FASTA input so that we can predict the complex.
- paparde.fasta
  - 4 G are added to connect ParD -> ParE
- of_monomer.slurm
  - SLURM script to run OmegaFold
- To run:

```
sbatch of_monomer.slurm
```



K80m (c302)
Wall Time: ~10 min
Prediction Time: ~ 156 sec

ParDE Complex



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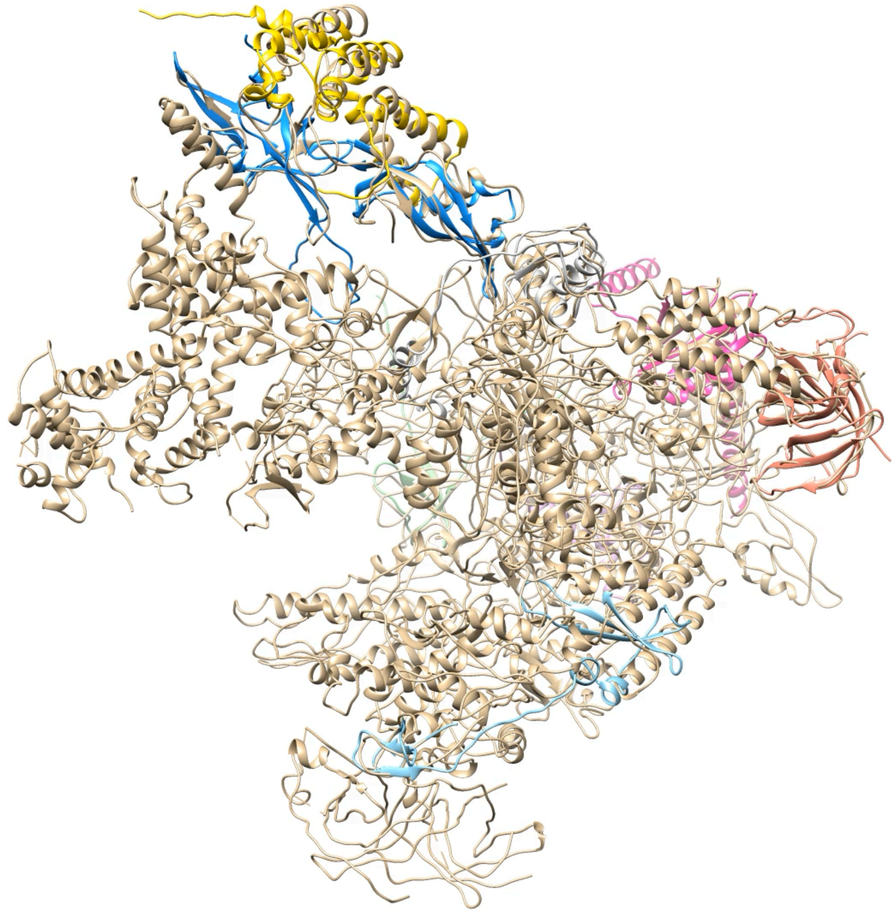
04_omegafold/Tutorial/pol3

- Lets try human RNA Pol3 (~1300 residues)
- PDB 7AST has Chain A-J (11)
- pol3.fasta
  - Ran this on K80m and out of memory (5 Gb total)



PDB 7AST
OmegaFold