HIGH PERFORMANCE RESEARCH COMPUTING

Introduction to AlphaFold3 for 3D Protein Structure Prediction

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Research Computing
DIVISION OF RESEARCH

AlphaFold3 for 3D Protein Structure Prediction

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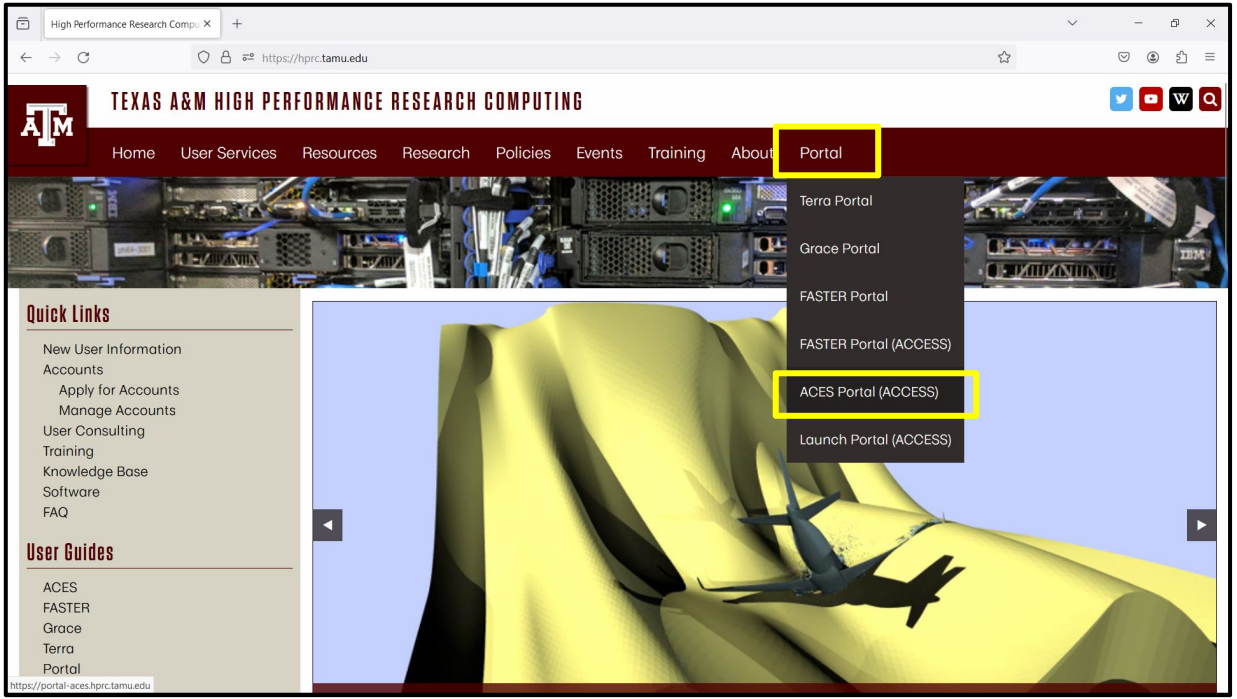
AlphaFold3 License Agreement

AlphaFold3 requires non-commercial users to agree to the terms of use in a Google form in order to download the af3.bin.zst model parameters file.

You will need the af3.bin.zst model parameters file to run AlphaFold3 on the ACES cluster.

Save your af3.bin.zst file to your ACES $SCRATCH directory

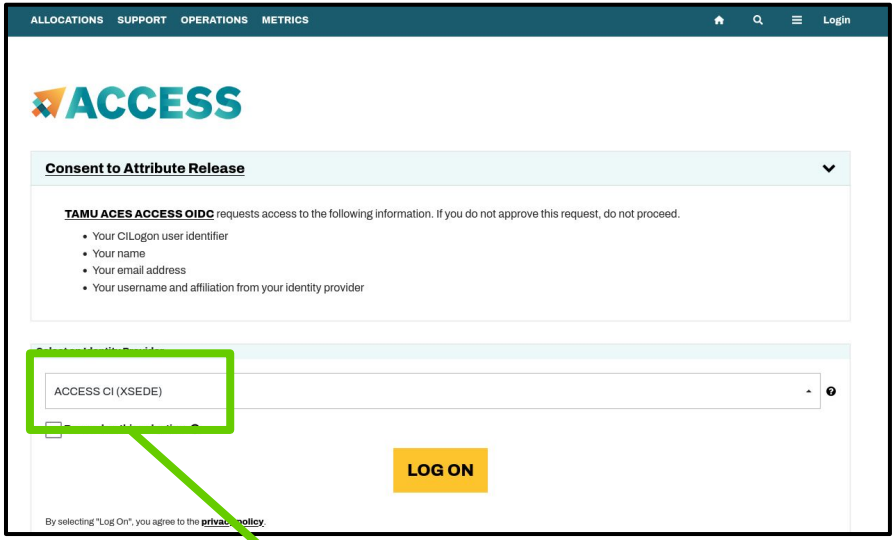
Accessing the HPRC ACES Portal

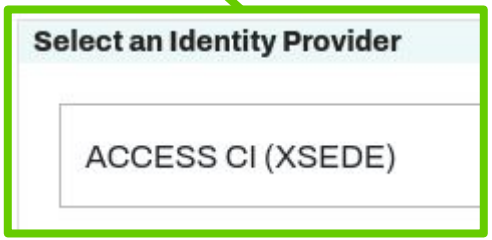


HPRC webpage: hprc.tamu.edu

Apply for an ACCESS ID if you don't already have one

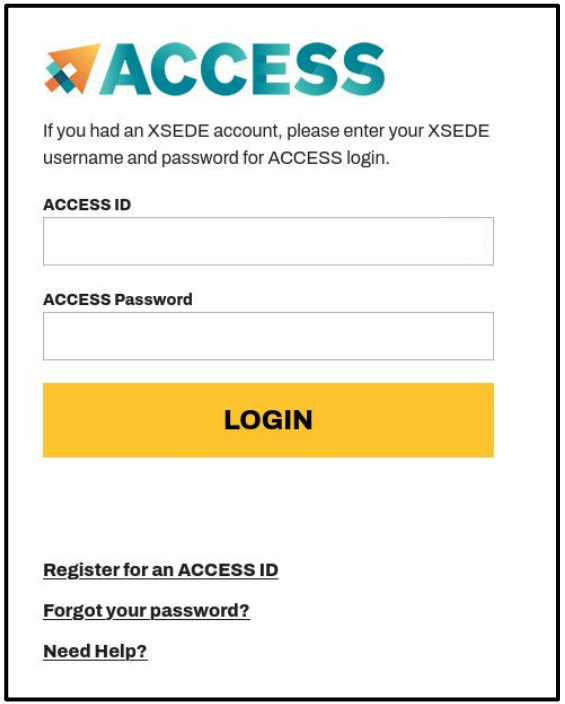
Accessing ACES via the Portal (ACCESS)



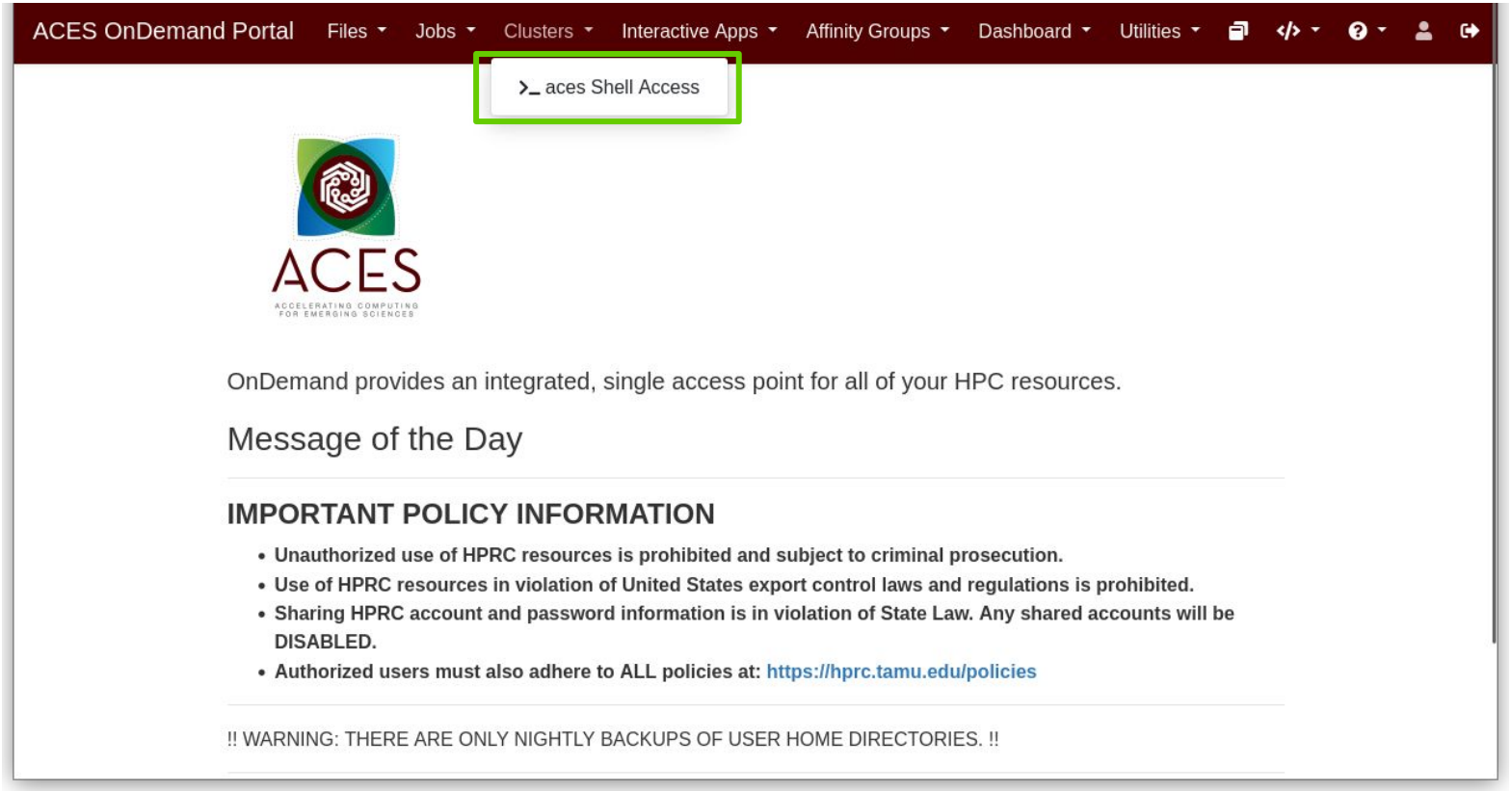


Select the Identity Provider appropriate for your account.

Log-in using your ACCESS credentials.



Shell Access via the Portal



AlphaFold History

- An Artificial Intelligence program developed by DeepMind
- 2018 AlphaFold 1 placed 1st at CASP 13
  - Critical Assessment of protein Structure Prediction
- 2020 AlphaFold 1 code released as open source
- 2020 AlphaFold2 placed 1st at CASP 14
- 2021 AlphaFold publication in Nature
  - Highly accurate protein structure prediction with AlphaFold
- 2021 AlphaFold2 code released as open source on GitHub
- 2024 AlphaFold AI system Awarded Nobel Prize in Chemistry
- 2024 AlphaFold3 available on the DeepMind AlphaFold Server
  - 20 jobs per day allowed for academic researchers
- 2024 AlphaFold3 code available on github
- 2025 AlphaFold3 available on the HPRC clusters

Selection and Limitations of Resources

Resource Limitations

- Currently AlphaFold(2,3) can only utilize one GPU
- AlphaFold2 minimum amino acid length: 16
- AlphaFold2 maximum amino acid lengths are as follows:
  - 2,700 proteomes / Swiss-Prot
  - 1,280 all other UniProt
- AlphaFold3 maximum amino acid (token) length: 5,000

Running AlphaFold3 on ACES

ALPHAFOLD 3 MODEL PARAMETERS TERMS OF USE

Last Modified: 2024-11-09

AlphaFold 3 is an AI model developed by Google DeepMind and Isomorphic Labs. It generates 3D structure predictions of biological molecules, providing model confidence for the structure predictions. We make the trained model parameters and output generated using those available free of charge for certain non-commercial uses, in accordance with these terms of use and the AlphaFold 3 Model Parameters Prohibited Use Policy.

Key things to know when using the AlphaFold 3 model parameters and output

1. The AlphaFold 3 model parameters and output are **only** available for non-commercial use by, or on behalf of, non-commercial organizations (*i.e.*, universities, non-profit organizations and research institutes, educational, journalism and government bodies). If you are a researcher affiliated with a non-commercial organization, provided **you are not a commercial organisation or acting on behalf of a commercial organisation,** this means you can use these for your non-commercial affiliated research.
2. You **must not** use nor allow others to use:
   i. AlphaFold 3 model parameters or output in connection with **any commercial activities, including research on behalf of commercial organizations;** or
   ii. AlphaFold 3 output to **train machine learning models** or related technology for **biomolecular structure prediction** similar to AlphaFold 3.
3. You ***must not*** **publish or share AlphaFold 3 model parameters**, except sharing these within your organization in accordance with these Terms.
4. You ***can*** **publish, share and adapt AlphaFold 3 *output*** in accordance with these Terms, including the requirements to provide clear notice of any modifications you make and that ongoing use of AlphaFold 3 output and derivatives are subject to the AlphaFold 3 Output Terms of Use.

https://github.com/google-deepmind/alphafold3/blob/main/WEIGHTS_TERMS_OF_USE.md

AlphaFold2 vs AlphaFold3

The new AlphaFold model demonstrates substantially improved accuracy over many previous specialized tools: far greater accuracy for protein–ligand interactions compared with state-of-the-art docking tools, much higher accuracy for protein–nucleic acid interactions compared with nucleic-acid-specific predictors and substantially higher antibody–antigen prediction accuracy compared with AlphaFold-Multimer v.2.37,8.

(from AlphaFold3 Abstract)

Abramson, J., Adler, J., Dunger, J. *et al.* Accurate structure prediction of biomolecular interactions with AlphaFold 3. *Nature* 630, 493–500 (2024). https://doi.org/10.1038/s41586-024-07487-w

AlphaFold3 requires non-commercial users to agree to the terms of use in a Google form in order to download the model parameters file.

Create a New Working Directory

Create a working directory.

```
mkdir $SCRATCH/af3_demo
cd $SCRATCH/af3_demo
```

You can save your af3.bin.zst file in your $SCRATCH directory.

AlphaFold3 uses .json input format not FASTA

The Singularity image on ACES was built using AlphaFold3 version 3.0.1

alphafold3jobscript

The **`alphafold3jobscript`** utility is available on ACES which will generate one job script that is configured to run AlphaFold3 in two steps:

1. run the four parallel multiple sequence alignment steps in a non-GPU job
2. run the structure prediction step in a separate GPU job launched from within the same job script

alphafold3jobscript

alphafold3jobscript --help

```
Synopsis:
       alphafold3jobscript is a script to create an AlphaFold3 job script to run first a CPU-only job for the
       sequence alignment step and a second GPU job for the prediction step.

Required:
       --json_path /full/path/to/input.json         # full path to your input.json file
       --model_dir /full/path/to/model/dir          # full path to the directory containing your af3.bin.zst model file

Optional:
       --max_template_date date          # format YYYY-MM-DD   (default: 2025-01-01)
       --num_recycles int                # (default: 3)
       --output_dir /full/path/to/dir    # (default: $PWD/output_NAME_JOBID)
       --gpu_type type                   # a30, h100  (default: first available)

Example Command:
       alphafold3jobscript --json_path /full/path/to/my/alphafold_input.json --model_dir /full/path/to/my/model/dir/

Example .json Files
       /scratch/data/bio/alphafold3/examples/
```

alphafold3jobscript

Generate a jobscript to run AlphaFold3 using an example input .json file

```
alphafold3jobscript --json_path
/scratch/data/bio/alphafold3/examples/alphafold_input_2pv7.json
--model_dir $SCRATCH
```

Submit and Monitor the Job

- Submit the job script to the Slurm scheduler.
  - completes in about 10 minutes
    - 8 minutes for the CPU job
    - 2 minutes for the GPU job

```
[userid@aces ~]$ sbatch run_alphafold_3.0.1_2PV7_aces.sh

Submitted batch job 1008938
```

- Monitor the job status.

```
[userid@aces ~]$ squeue --me

JOBID     NAME             USER      PARTITION  NODES  CPUS  STATE    TIME    TIME_LEFT   START_TIME         REASON  NODELIST
1008938   alphafold3-cpu   userid    cpu        1      32    RUNNING  2.59    23:57:01    2025-04-3T16:11    None    ac046
```

Example alphafold_input_2pv7.json


```
{
  "name": "2PV7",
  "sequences": [
        {
        "protein": {
        "id": ["A", "B"],
        "sequence":
"GMRESYANENQFGFKTINSDIHKIVIVGGYGKLGGLFARYLRASGYPISILDREDWAVAESILANADVVIVSVPINLTLE
TIERLKPYLTENMLLADLTSVKREPLAKMLEVHTGAVLGLHPMFGADIASMAKQVVVRCDGRFPERYEWLLEQIQIW
GAKIYQTNATEHDHNMTYIQALRHFSTFANGLHLSKQPINLANLLALSSPIYRLELAMIGRLFAQDAELYADIIMDKSE
NLAVIETLKQTYDEALTFFENNDRQGFIDAFHKVRDWFGDYSEQFLKESRQLLQQANDLKQG"
        }
        }
  ],
   "modelSeeds": [1],
   "dialect": "alphafold3",
   "version": 1
}
```


https://github.com/google-deepmind/alphafold3/blob/main/docs/input.md

ACES Cluster Utilities

A number of cluster utilities are available to help you query resources from the command line, such as available nodes, GPUs, cores, memory, template job scripts, and shared conda and Python environments.

myjob	**gpuavail***
maxconfig	**cpuavail***
gcatemplates	**envsavail***
jobstats	**venvavail***
maintenance	**toolchains***

Use the **-h** or **--help** flag with any utility to see available options.

* also available on the portal

Show Your Job Details using myjob

The myjob command

- can be used to see detailed information related to your job.
  - Status (PENDING, RUNNING, COMPLETED, FAILED, …)
  - Node List
  - Submit time, Start time, End time, Total runtime
  - CPU Efficiency
  - Memory Utilized, Memory Efficiency
- will advise you if your job is PENDING due to a scheduled maintenance.
- will advise you if your job FAILED due to CRLF characters in the job script and provide a link to the HPRC documentation on how to resolve this issue.
- will advise you if your job FAILED due to file or disk quota being reached.
  - will show you the directory in your $HOME directory that has the most files when $HOME file quota is reached.

https://hprc.tamu.edu/kb/Software/useful-tools/myjob

Show Your Job Details using myjob

```
[userid@aces ~]$ myjob 1008938

              Job ID: 1008938
             Cluster: aces
          User/Group: userid/userid
             Account: 123456789101
               State: COMPLETED (exit code 0)
           Partition: cpu
          Node Count: 1
            NodeList: ac046
      Cores per node: 32
        CPU Utilized: 00:53:56
      CPU Efficiency: 22.13% of 4:03:44 core-walltime
         Submit time: 2025-04-03 15:53:22
          Start time: 2025-04-03 16:11:01
            End time: 2025-04-03 16:18:38
 Job Wall-clock time: 00:07:37
     Memory Utilized: 552.50 MB
   Memory Efficiency: 0.54% of 100.00 GB
            Job Name: 0.54% of 100.00 GB
Job Submit Directory: /scratch/user/userid/af3_demo
         Submit Line: sbatch run_alphafold_3.0.1_2PV7_aces.sh
```

PENDING Job due to a Scheduled Maintenance

```
[userid@aces ~]$ myjob 1320633

               Job ID: 1320633
              Cluster: aces
           User/Group: userid/userid
              Account: 123456789101
                State: PENDING
               Reason: ReqNodeNotAvail, Reserved for maintenance
          Submit time: 2024-10-14 10:09:59
            Partition: cpu
           Node Count: 1
             NodeList: None assigned
                Cores: 1
                 Note: Efficiency not available for jobs in the PENDING state.
             Job Name: picard
Job Submit Directory: /scratch/user/userid/myproject/picard
          Submit Line: sbatch run_bwa_samtools_pilon_faster.sh
                 Note: job is PENDING due to runtime overlapping with maintenance window.
                 Note: maintenance will begin in  22 hours, and 49 minutes.
```

Viewing Maximum Available Resources

The **maxconfig** command will show the recommended Slurm parameters for the maximum available resources (cores, memory, time) per node for a specified accelerator or partition (default ACES partition: cpu).

```
[userid@aces ~]$ maxconfig

  ACES partitions:   cpu  gpu  pvc  bittware  d5005  memverge  nextsilicon
  ACES GPUs in gpu partition:  a30:2  h100:2  h100:4  h100:8  pvc:2  pvc:4  pvc:6  pvc:8

  Showing max parameters (cores, mem, time) for partition cpu

#!/bin/bash
#SBATCH --job-name=my_job
#SBATCH --time=7-00:00:00
#SBATCH --nodes=1       # max 64 nodes for partition cpu
#SBATCH --ntasks-per-node=1
#SBATCH --cpus-per-task=96
#SBATCH --mem=488G
#SBATCH --output=stdout.%x.%j
#SBATCH --error=stderr.%x.%j
```

https://hprc.tamu.edu/kb/Software/useful-tools/maxconfig

Viewing Maximum Available Resources

See the recommended Slurm parameters for requesting 1 x H100 GPU with ¼ the total CPUs and memory since there are 4 x H100s per node.

```
[userid@aces ~]$ maxconfig -g h100 -G 1

  ACES partitions:   cpu  gpu  pvc  bittware  d5005  memverge  nextsilicon
  ACES GPUs in gpu partition:  a30:2  h100:2  h100:4  h100:8  pvc:2  pvc:4  pvc:6  pvc:8

  Showing 1/4 of total cores and memory for using 1 x h100 GPU

#!/bin/bash
#SBATCH --job-name=my_job
#SBATCH --time=2-00:00:00
#SBATCH --partition=gpu
#SBATCH --nodes=1       # max 8 nodes for partition gpu
#SBATCH --ntasks-per-node=1
#SBATCH --cpus-per-task=24
#SBATCH --mem=125G
#SBATCH --gres=gpu:h100:1
#SBATCH --output=stdout.%x.%j
#SBATCH --error=stderr.%x.%j
```

https://hprc.tamu.edu/kb/Software/useful-tools/maxconfig

Checking GPU Configuration & Availability on ACES

- Use the command line (shell) to see the current GPU configuration and availability.
- The GPU configuration can change since ACES is a composable resource cluster.
- If there are no GPUs in the AVAILABILITY output, it means that a GPU job that you submit may take a while to start.
- AlphaFold does not support running on PVC GPUs.

```
[userid@aces ~]$ gpuavail

    CONFIGURATION
NODE           NODE
TYPE           COUNT
---------------------
gpu:pvc:4      16
gpu:pvc:2      11
gpu:pvc:8      4
gpu:h100:4     3
gpu:h100:8     2
gpu:h100:2     1
gpu:a30:2      1
gpu:pvc:6      1
               AVAILABILITY
NODE   GPU     GPU    GPUs     CPUs    GB MEM
NAME   TYPE    COUNT  AVAIL    AVAIL   AVAIL
-----------------------------------------------
ac065  a30     2      2        96      488
ac041  h100    4      1        87      421
ac045  h100    2      1        88      422
ac051  pvc     2      2        96      488
```

https://hprc.tamu.edu/kb/Software/useful-tools/gpuavail

Check non-GPU node Availability

Use the **cpuavail** command to see non-GPU nodes readily available for jobs.

```
[userid@aces ~]$ cpuavail

    CONFIGURATION                          AVAILABILITY
  NODE          NODE                  NODE     CPUs       GB MEM
  TYPE          COUNT                 NAME     AVAIL      AVAIL
  --------------------                ----------------------------
  CPU-only          57                ac006        8          196
  GPU               38                ac007        6          86
  other             12                ac017        8          88
                                      ac021        44         4
                                      ac022        4          190
                                      ac042        54         214
                                      ac043        12         92
                                      ac052        60         244
                                      ac053        64         248
                                      ac063        12         228
                                      ac073        8          88
                                      ac080        1          121
```

https://hprc.tamu.edu/kb/Software/useful-tools/cpuavail

ACES Cluster maintenance

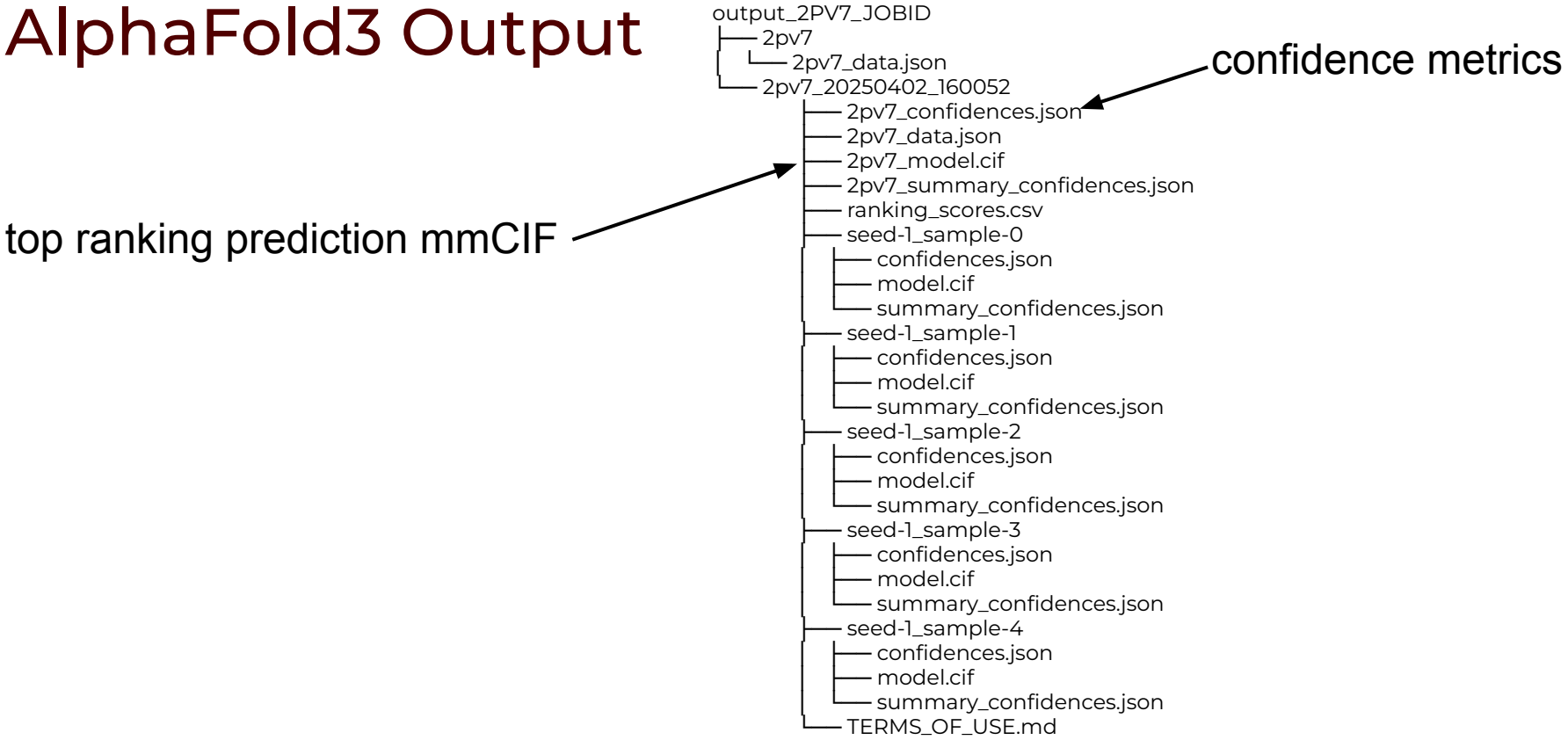
- You can use the maintenance command to see if there is a scheduled cluster maintenance.

```
[userid@aces ~]$ maintenance

 The scheduled 11 hour ACES maintenance will start in:

   3 days    16 hours    41 minutes

 Scheduled jobs will not start if they overlap with this maintenance window.
```

A 7-day job submitted at the time of the above message will remain queued and will not start until after the maintenance is complete.

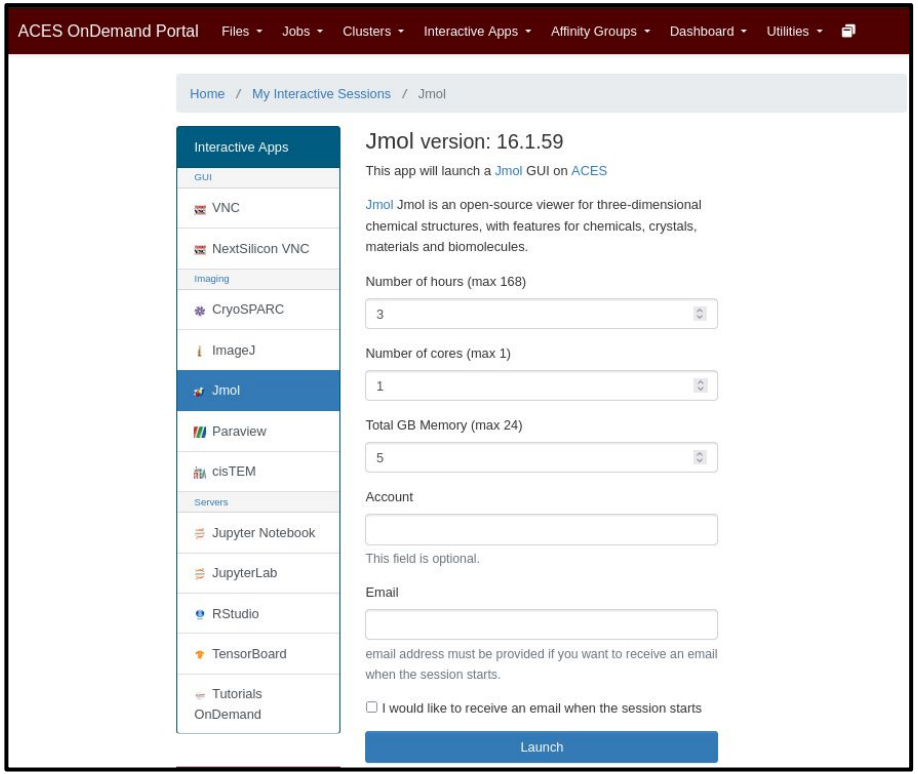
AlphaFold3 Results Visualization

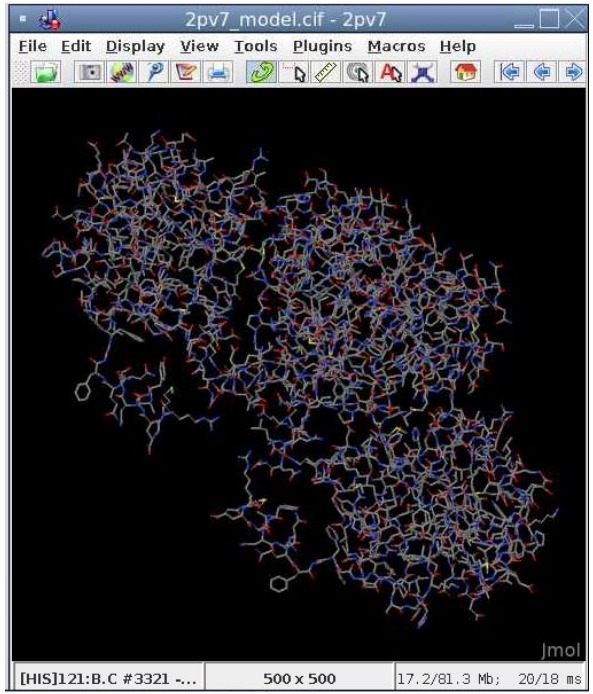
AlphaFold3 Output



https://github.com/google-deepmind/alphafold3/blob/main/docs/output.md

Visualize AlphaFold3 Results with Jmol on the ACES Portal





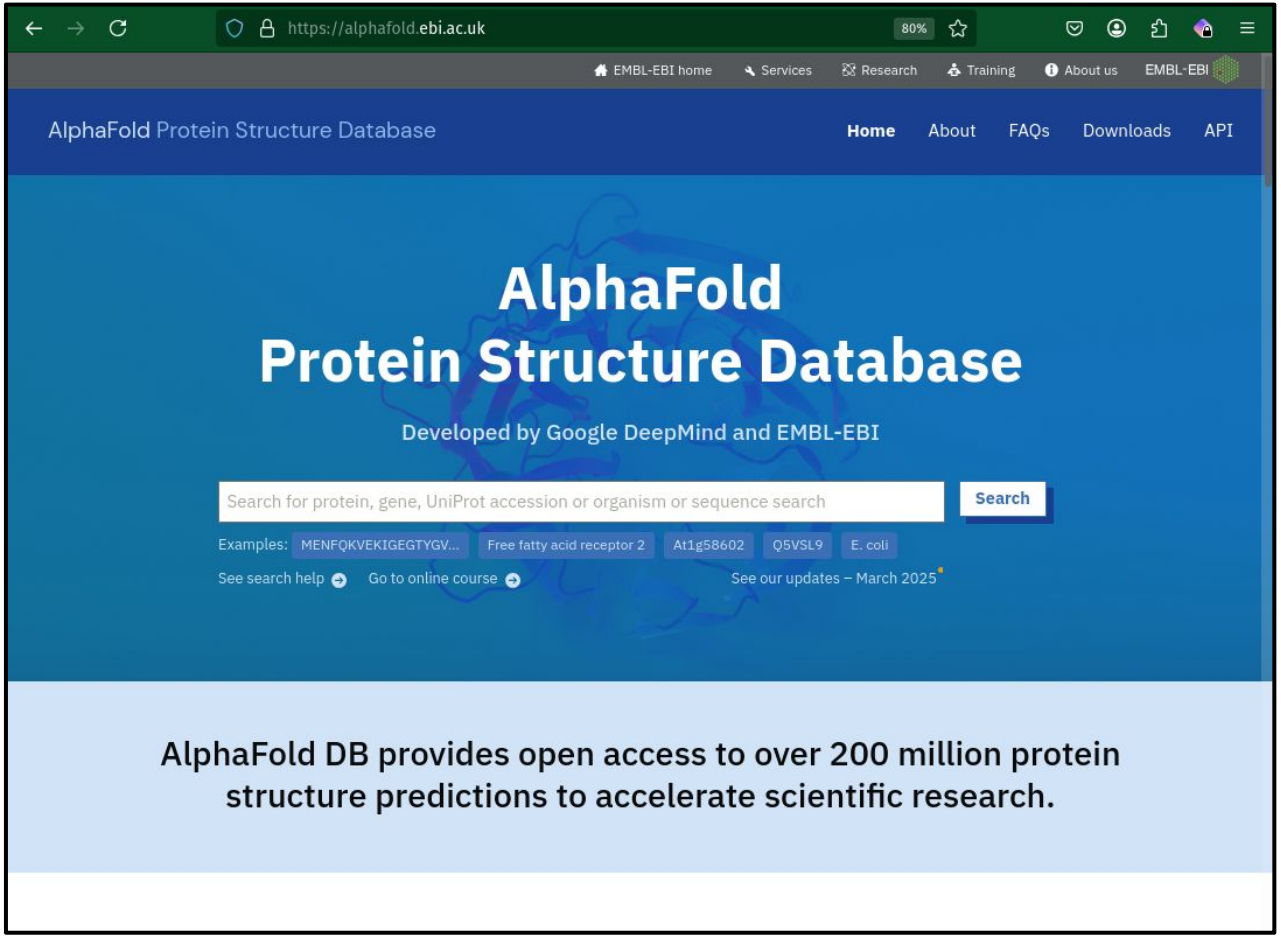
/scratch/training/alphafold/output_2PV7/2pv7_20250403_130646/2pv7_model.cif

Structure Database and References

DeepMind and EMBL's European Bioinformatics Institute (EMBL-EBI) have partnered to create AlphaFold DB to make these predictions freely available to the scientific community.

Search for your protein to see if it the structure has already been predicted using AlphaFold.

There were 992,316 predictions in 2022



References

Abramson, J., Adler, J., Dunger, J. et al. Accurate structure prediction of biomolecular interactions with AlphaFold 3. Nature 630, 493–500 (2024). https://doi.org/10.1038/s41586-024-07487-w

Tunyasuvunakool, K., Adler, J., Wu, Z. et al. Highly accurate protein structure prediction for the human proteome. Nature 596, 590–596 (2021). https://doi.org/10.1038/s41586-021-03828-1

Jumper, J., Evans, R., Pritzel, A. et al. Highly accurate protein structure prediction with AlphaFold. Nature 596, 583–589 (2021). https://doi.org/10.1038/s41586-021-03819-2

Zhong, B, et al. (2021) ParaFold doi.org/10.48550/arXiv.2111.06340

Arnold, M. J. (2021) AlphaPickle doi.org/10.5281/zenodo.5708709

ACES Documentation

- ACES KnowledgeBase Documentation hprc.tamu.edu/kb
- ACES User Guide hprc.tamu.edu/kb/User-Guides/ACES
- Email your questions to help@hprc.tamu.edu
  - Received emails generate helpdesk tickets.

Let us know when the issue has been resolved so we can close the helpdesk ticket.

HIGH PERFORMANCE RESEARCH COMPUTING
TEXAS A&M UNIVERSITY

https://hprc.tamu.edu

HPRC Helpdesk:

help@hprc.tamu.edu
Phone: 979-845-0219

Help us help you. Please include details in your request for support, such as, **Cluster** (ACES, FASTER, Grace, Launch), NetID (UserID), Job information (**JobID**(s), Location of your jobfile, input/output files, Application, Module(s) loaded, Error messages, etc), and Steps you have taken, so we can reproduce the problem.