Optimizing AlphaFold for Accessible Computational Biology

Global Open OnDemand Conference 2025

Vinay Saji Mathew
PhD Student, IEOR
Laboratory for Intelligent Systems and Analytics, Penn State

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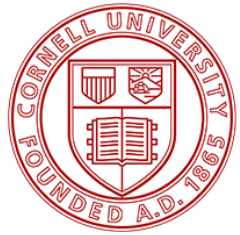

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Presentation Overview

1. Introduction
2. Objectives
3. Challenges & Solutions
4. Implementation
5. Impact
6. Future Work

Introduction

AlphaFold Achievement

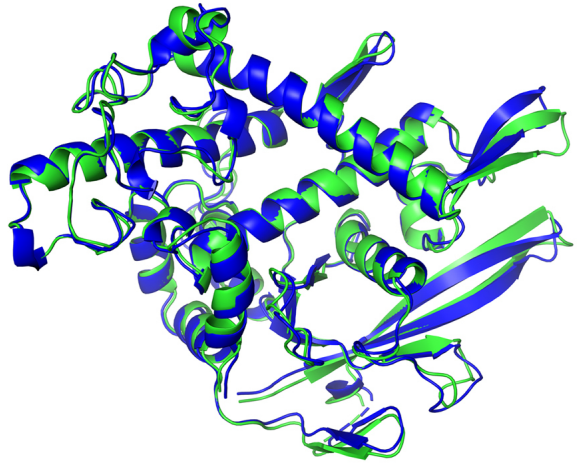
2024 Chemistry Nobel Prize Winner

Shared by John Jumper, Demis Hassabis, and David Baker

FASTA Sequence

```
>Protein
MKTIIALSYIFCLVFADYKDDDDK
FDKAKKLVFAATDGFYSVDVVK
...
```

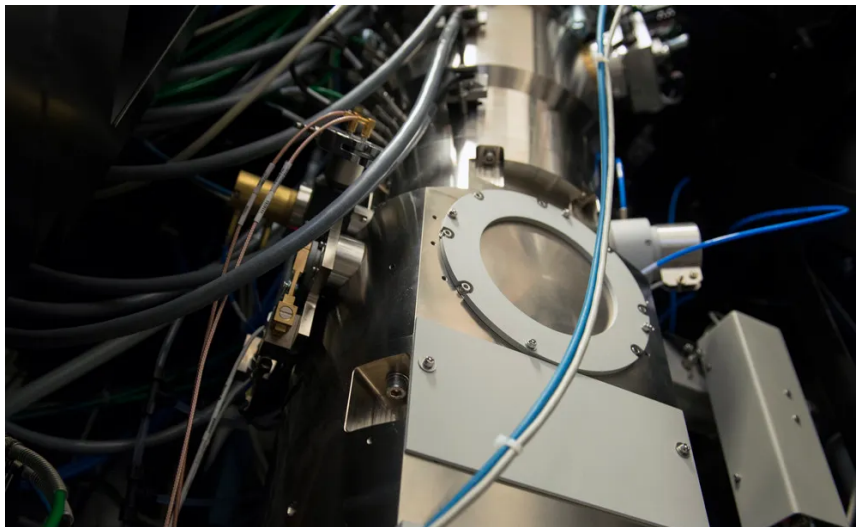
$\Rightarrow$



Biological Significance

Why Protein Structure Prediction Matters

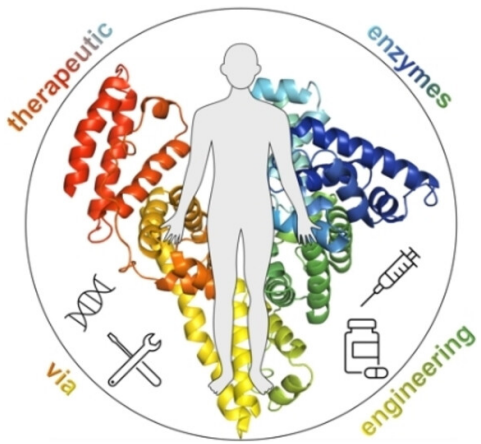
- Proteins are molecular machines governing biological processes
- AlphaFold achieves 92.5% experimental-level accuracy
- Billions of sequences produced annually
- Traditional methods (X-ray, cryo-EM) are resource-limited



Biological Significance

Several Research Applications

- Drug discovery through virtual screening
- Host-pathogen interaction modeling
- Enzyme and therapeutic protein engineering
- Evolutionary relationship analysis



Introduction

Current Challenges

- Computationally demanding
- GPU utilization inefficiencies
- **Accessibility limitations**

Objectives

1. Optimize computational workflow
2. Enhance accessibility
3. Remain open-source for deployment.

Challenges and Observations

Optimize computational workflow

- Complex deployment process (initially Docker-only, problematic for HPC systems)
- Current setup has 75% CPU-bound operations while GPU is idle
- Wasted GPU utilization
- Potential Multi Instance GPU Support (!)
- 5TB+ database requirements
  - Regular updates needed
  - **Redundant storage across users**
  - Cron job maintenance

Current HPC Deployment Issues

Current HPC Deployment Issues

- Resource wastage during CPU phases
- Complex setup requirements
- Duplicate database storage waste

Technical Implementation Details

Container Implementation

- Singularity/Apptainer based
- Modular design for CPU/GPU phases
- High-performance database access (VAST via NFS - ROAR)

System Requirements

- Minimum: Half an A100 GPU for vGPU (1/7th slice of a MIG A100)
- 5 TB database storage

Cross-Platform Validation

Benchmarked Clusters

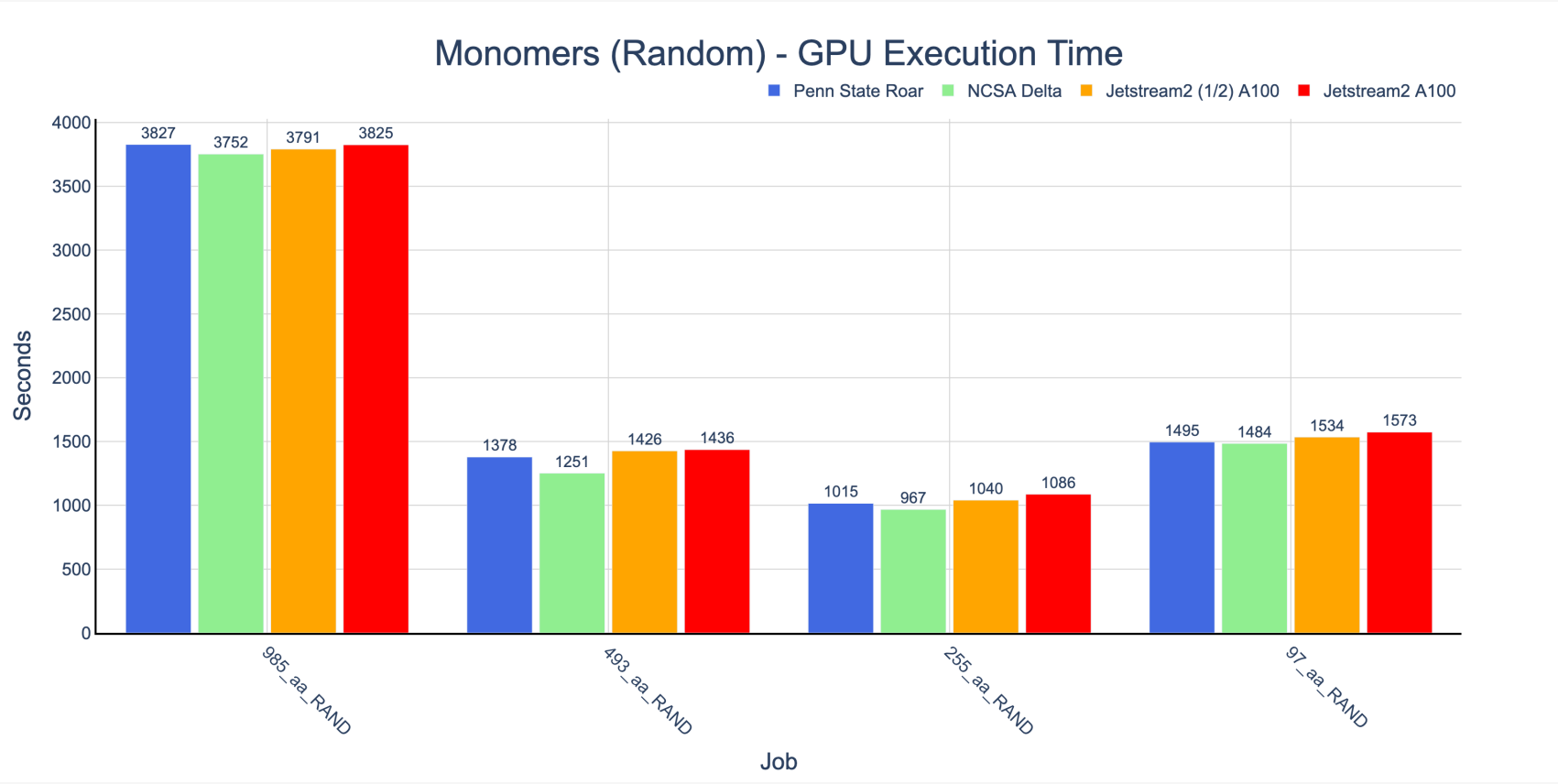
- NCSA Delta
- Jetstream2 by IU
- ROAR by Penn State

Performance Analysis - Monomers (CPU)

CPU Execution Time for Monomers

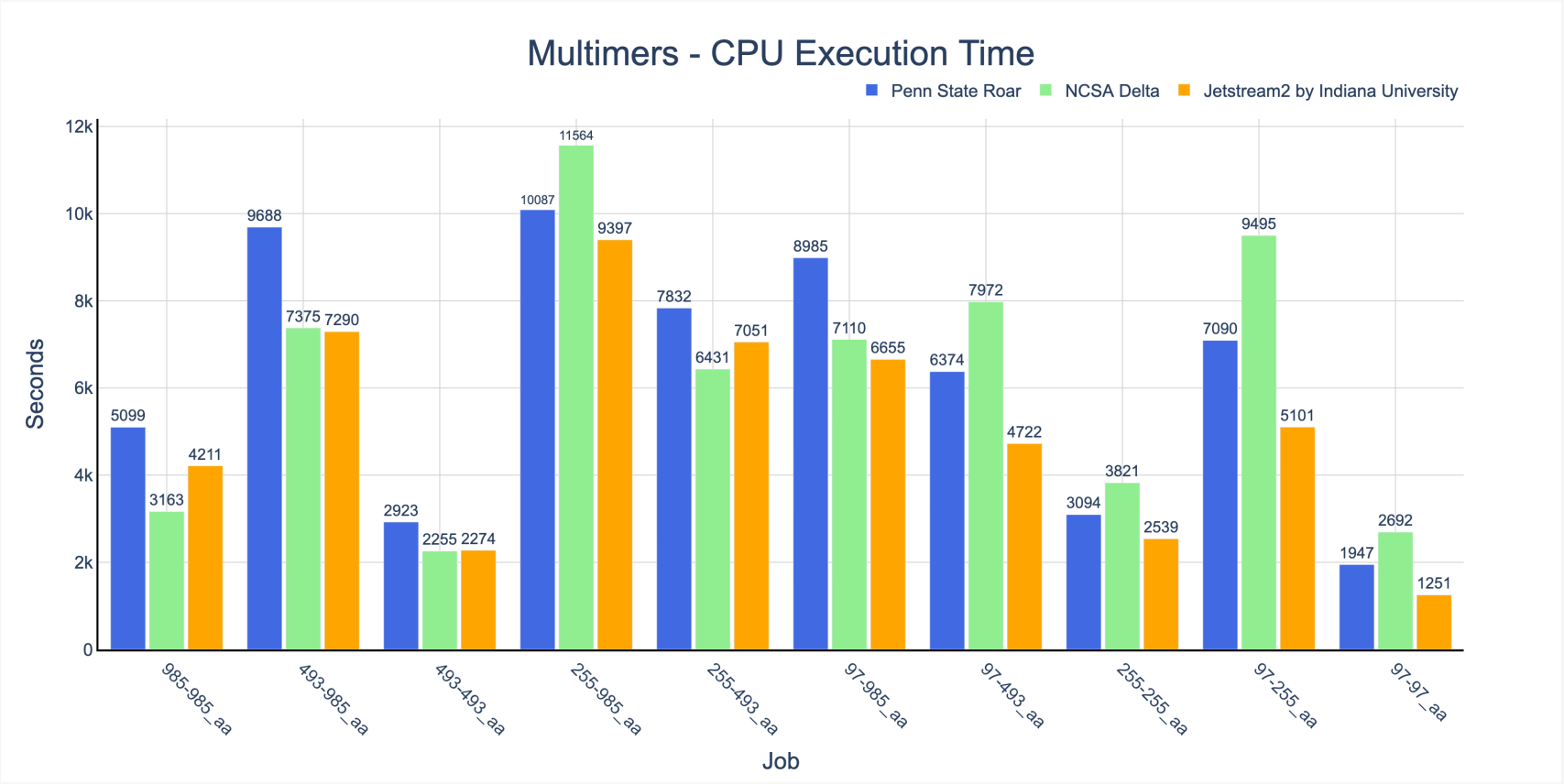
Performance Analysis - Monomers (GPU)

GPU Execution Time for Monomers



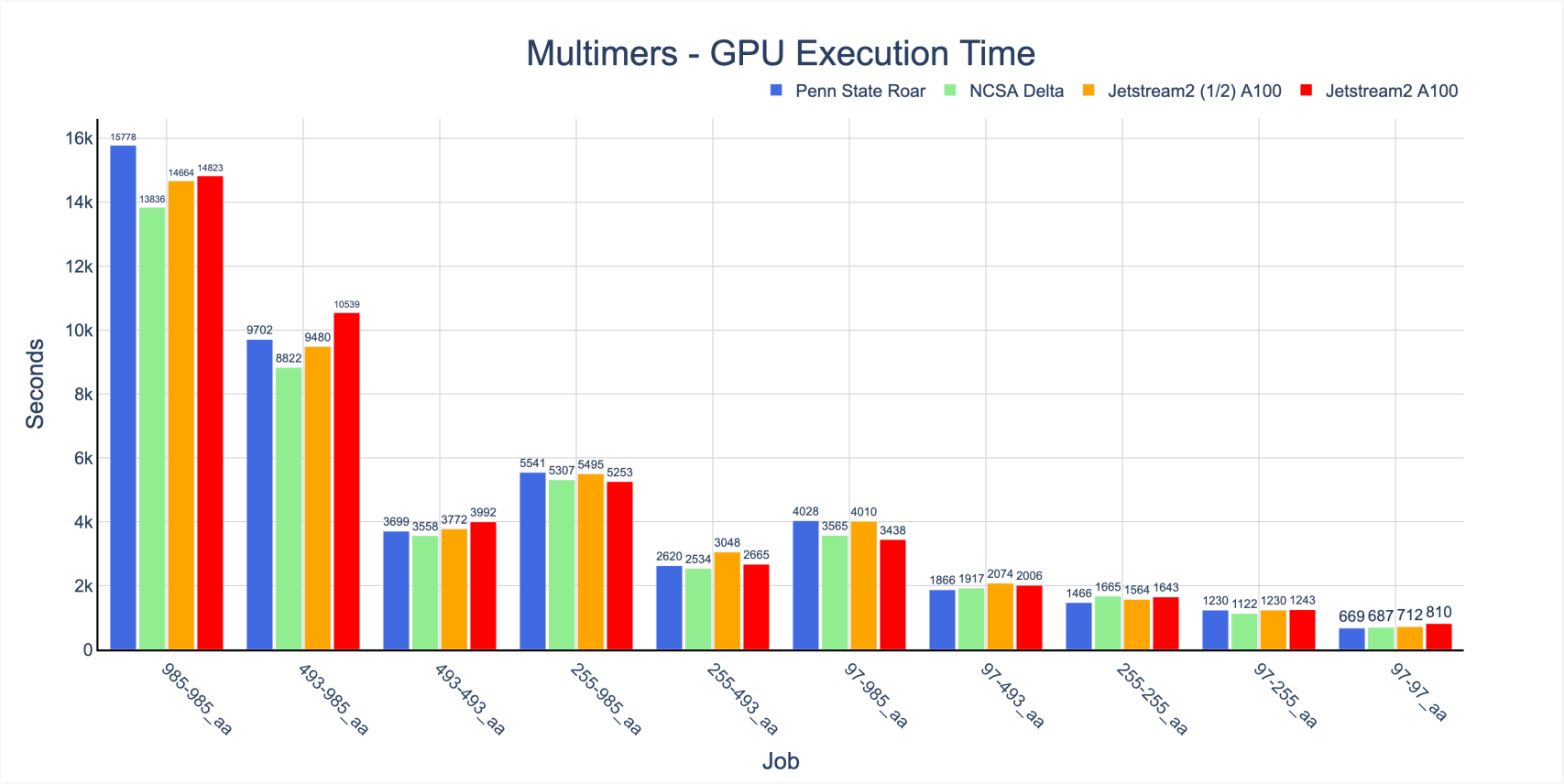
Performance Analysis - Multimers (CPU)

CPU Execution Time for Multimers



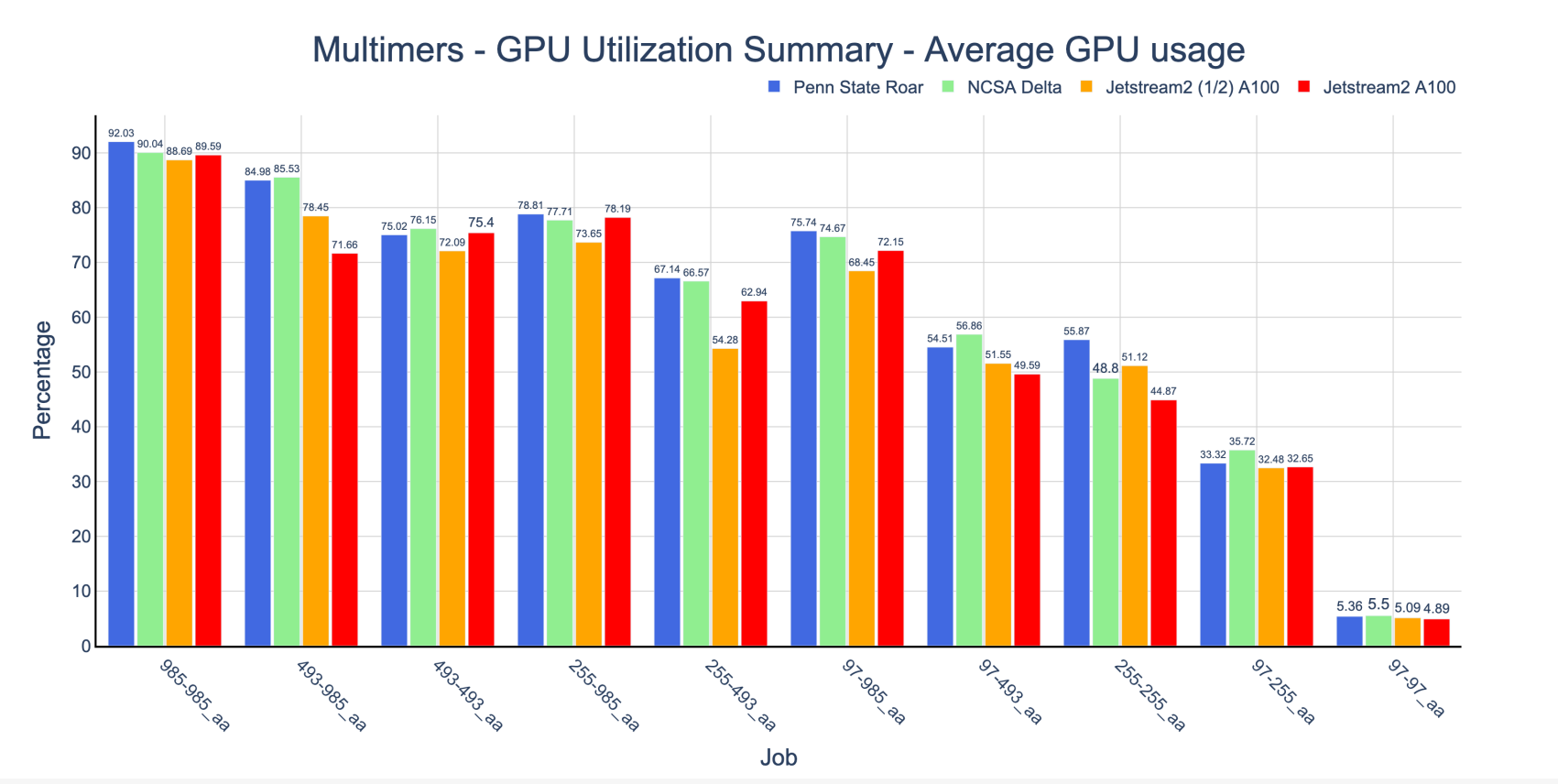
Performance Analysis - Multimers (GPU)

GPU Execution Time for Multimers



GPU Utilization Analysis

Multimer GPU Usage Summary



System-Specific Implementations

Cluster-Specific Observations

- **NCSA Delta & ROAR**
  - MIG-enabled GPU support
  - Parallel job submission
  - Queue-based workload distribution
  - Tested on MIG GPU partitions down to 1/7th of an A100. Performance degrades but completes on partitioned A100
- **Jetstream2**
  - Virtual GPU allocation
  - Anything less than half an A100 on vGPU setup crashes
  - Sequential job processing
  - Dedicated system assignment

Our Approach: Optimized OOD Implementation

Workflow Optimization

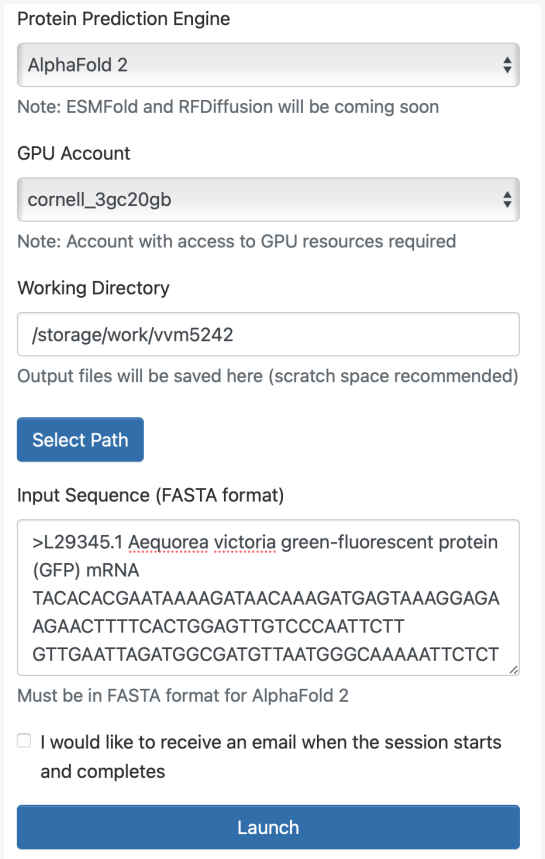
- CPU/GPU phase separation
- GPU allocation is dependent on successful completion and verification of output from MSA search.
- 75% reduction in GPU allocation

User Interface

- Easy Open On Demand interface
- Single input requirement
- Real time progress and Logs

AlphaFold2 User Interface

Open OnDemand Form



AlphaFold3 User Interface

Form Part 1

Protein Prediction

This app will generate a predicted structure for the input amino acid sequence using the selected engine.

Protein Prediction Engine

AlphaFold 3

Note: ESMFold and RFDiffusion will be coming soon

GPU Account

cornell_3gc20gb

Note: Account with access to GPU resources required

Working Directory

/storage/work/vvm5242

Output files will be saved here (scratch space recommended)

Select Path

Form Part 2

Input Sequence (JSON format)

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

Must be in compatible JSON format (specifications are in the AlphaFold 3 documentation).

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Job Monitoring and Results

Progress During Run

Protein Prediction (33287050)

1 node | 1 core | Running

Host: >_ p-bc-5006

Delete

Created at: 2025-02-23 00:06:39 EST

Time Remaining: 23 hours and 56 minutes

Session ID: 106f12f0-435a-4466-b24e-541b472cc950

Problems with this session? Submit support ticket

Current Status

Job IDs: CPU = 33287054 | GPU = 33287055 View My Jobs

Run Directory: /storage/work/vvm5242/pp1740287199

Phase: AlphaFold 3 CPU Phase - MSA Generation

Step: Completed Jackhmmer search

25%

Progress:

- Detected AlphaFold 3 input format
- Getting protein MSAs
- Started Jackhmmer search
- Completed Jackhmmer search

CPU Phase Log

```
I0223 05:07:29.417441 22982725124096 folding_input.py:1044] Detected /root/af_inpu
```

After Completion

CPU Phase Log

```
I0213 21:42:51.090887 22878978326528 folding_input.py:1044] Detected /root/af_inpu
I0213 21:42:51.092551 22878978326528 pipeline.py:81] Getting protein MSAs for sequ
I0213 21:42:51.095661 22876702512704 jackhmmer.py:78] Query sequence: GMRESYANENQF
I0213 21:42:51.096306 22876696208960 jackhmmer.py:78] Query sequence: GMRESYANENQF
I0213 21:42:51.096395 22876700411456 jackhmmer.py:78] Query sequence: GMRESYANENQF
I0213 21:42:51.096657 22876698310208 jackhmmer.py:78] Query sequence: GMRESYANENQF
I0213 21:42:51.097247 22876702512704 subprocess_utils.py:68] Launching subprocess
I0213 21:42:51.097560 22876696208960 subprocess_utils.py:68] Launching subprocess
I0213 21:42:51.098170 22876700411456 subprocess_utils.py:68] Launching subprocess
I0213 21:42:51.098312 22876698310208 subprocess_utils.py:68] Launching subprocess
I0213 21:45:21.104391 22876698310208 subprocess_utils.py:97] Finished Jackhmmer in
I0213 21:51:36.808516 22876702512704 subprocess_utils.py:97] Finished Jackhmmer in
I0213 21:55:56.012930 22876696208960 subprocess_utils.py:97] Finished Jackhmmer in
I0213 22:00:35.508942 22876700411456 subprocess_utils.py:97] Finished Jackhmmer in
I0213 22:00:35.623793 22878978326528 pipeline.py:114] Getting protein MSAs took 16
```

GPU Phase Log

```
I0214 20:01:27.887957 23093135508608 xla_bridge.py:895] Unable to initialize backe
I0214 20:01:27.902343 23093135508608 xla_bridge.py:895] Unable to initialize backe
I0214 20:01:28.024057 23093135508608 folding_input.py:1044] Detected /root/af_outp
I0214 20:01:36.723238 23093135508608 pipeline.py:165] processing 2PV7, random_seed
I0214 20:01:36.760128 23093135508608 pipeline.py:258] Calculating bucket size for
I0214 20:01:36.760270 23093135508608 pipeline.py:264] Got bucket size 768 for inpu
Running AlphaFold 3. Please note that standard AlphaFold 3 model parameters are
only available under terms of use provided at
https://github.com/google-deepmind/alphafold3/blob/main/WEIGHTS_TERMS_OF_USE.md.
If you do not agree to these terms and are using AlphaFold 3 derived model
parameters, cancel execution of AlphaFold 3 inference with CTRL-C, and do not
use the model parameters.
Skipping running the data pipeline.
Found local devices: [CudaDevice(id=0)]
Building model from scratch...
Processing fold inputs.
```

Completion Information

Run Directory: /storage/work/vvm5242/pp1739482915

Structure Directory: /storage/work/vvm5242/pp1739482915/structure

Benefits and Outcomes

For HPC Centers

- Optimized resource utilization
- Ready for AlphaFold 2, 3 and Boltz
- Centralized compliance handling
- Available at: github.com/EpiGenomicsCode/ProteinStructure-OOD

For Researchers

- Simplified access to AlphaFold i.e., No coding requirements

Protein Design with RFDiffusion

Protein Design

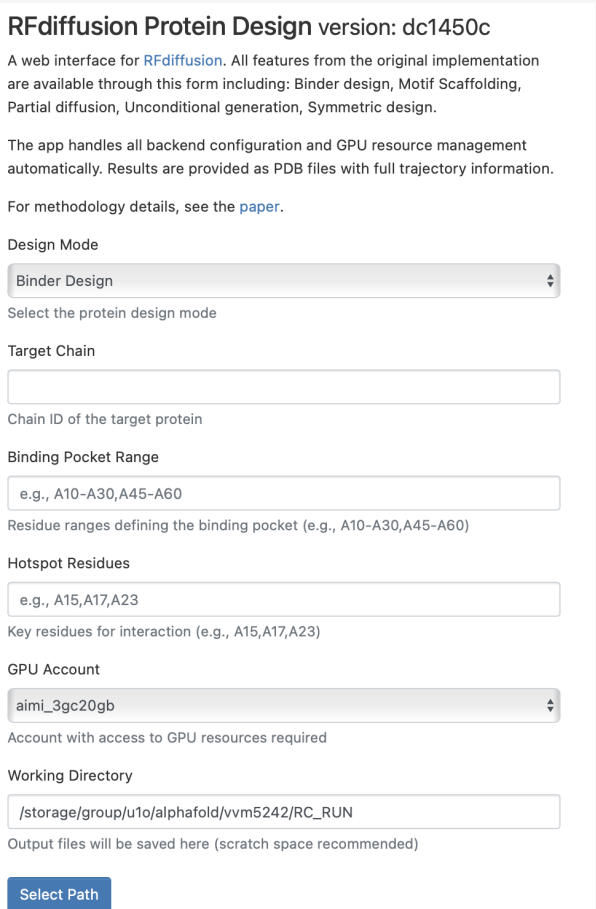
- Inverse problem to structure prediction
- Design proteins with specific functions
- Applications in drug development and enzyme engineering
- Complementary to AlphaFold's prediction capabilities

RFDiffusion OOD Implementation

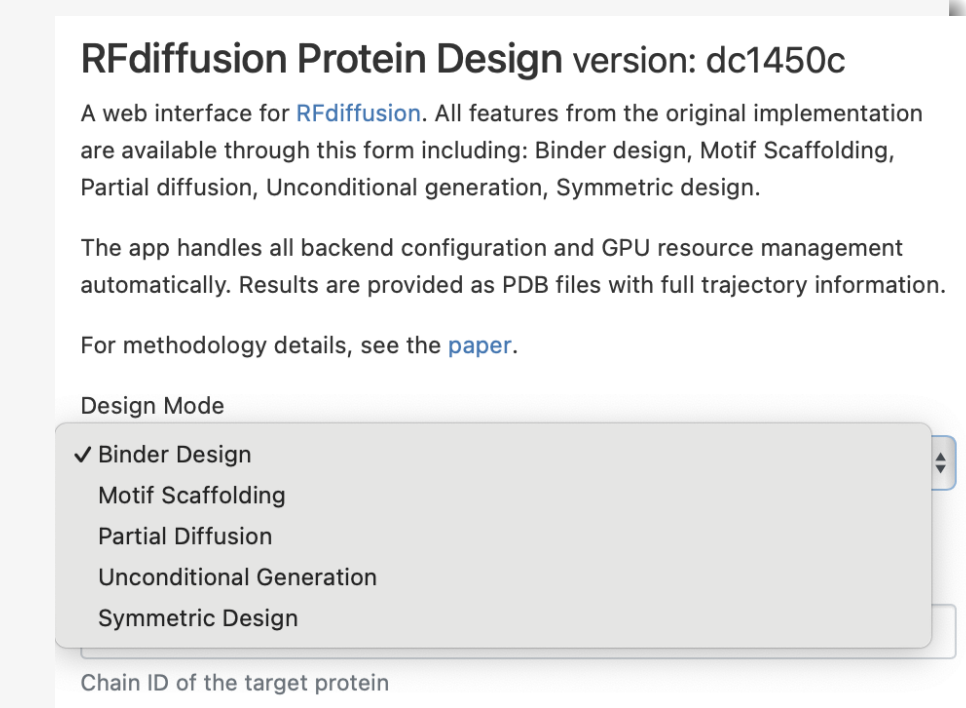
- Development app available at: github.com/EpiGenomicsCode/RFDiffusion-OOD
- Similar user-friendly interface

RFDiffusion Preview

RFDiffusion Interface



Design Modes



Acknowledgments

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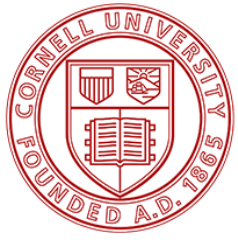

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