



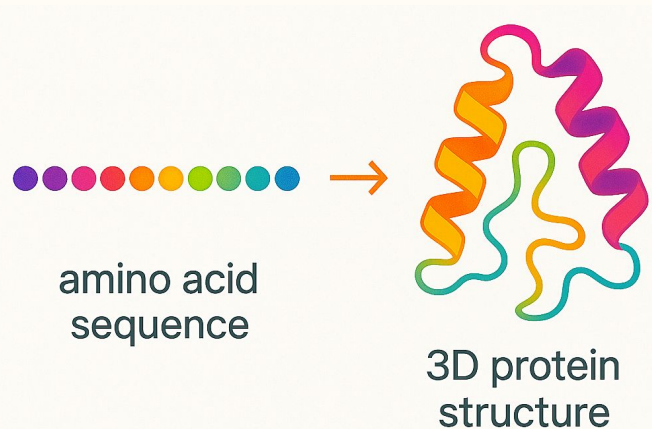
AlphaFold2 & ColabFold: Next-Gen Protein Structure Prediction

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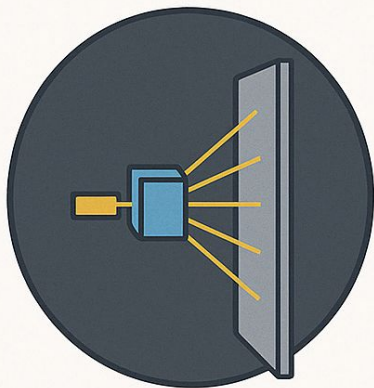
Why Is Protein Structure Important?



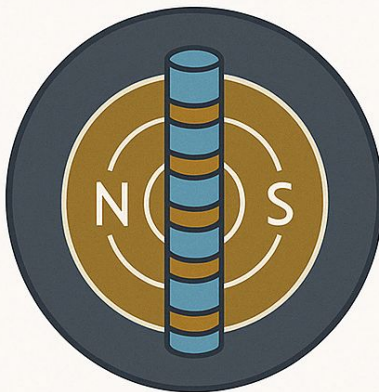
- Proteins: chains of amino acids → 3D structure → biological function
- Predicting structures from sequences = major scientific challenge
- Traditional experimental methods slow & expensive
- Millions of proteins structurally unknown
- Importance: drug discovery, biological understanding

What are the Experimental Methods?

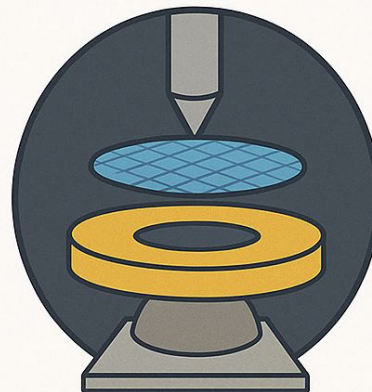
X-Ray
crystallography



Nuclear magnetic
resonance spectroscopy



Cryoelectron
microscopy



What is CASP (Critical Assessment of Structure Prediction) ?

CASP is a community-wide, blind experiment held every two years that rigorously evaluates the accuracy and progress of computational **protein structure prediction** methods



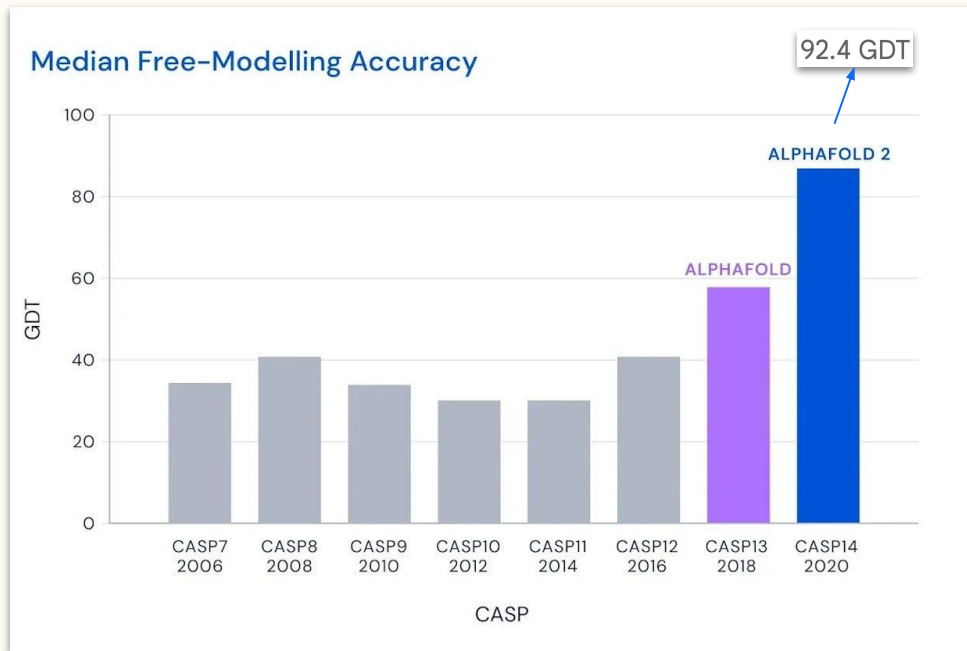
How Did AlphaFold2 Revolutionize Prediction?

Previous CASP winners:

- Predicted parts of protein structure, e.g., which amino acids are close together.
- Built full 3D shape using separate physics-based tools.

AlphaFold:

- Uses a deep learning model to directly predict a protein's 3D structure from its sequence.
- Trained on large databases of protein sequences and structures.
- Combines evolutionary patterns with geometric reasoning.
- Achieves higher accuracy and speed compared to previous methods



"... a score of around 90 GDT is informally considered to be competitive with results obtained from experimental methods."
~ **John Moult** (one of the founders of CASP)

Team

Demis Hassabis & John Jumper were co-awarded the **2024 Nobel Prize** in Chemistry for their work developing **AlphaFold** ([Highly accurate protein structure prediction with AlphaFold](#))



Sir Demis Hassabis

(Co-founder and CEO of Google DeepMind and Isomorphic Labs)

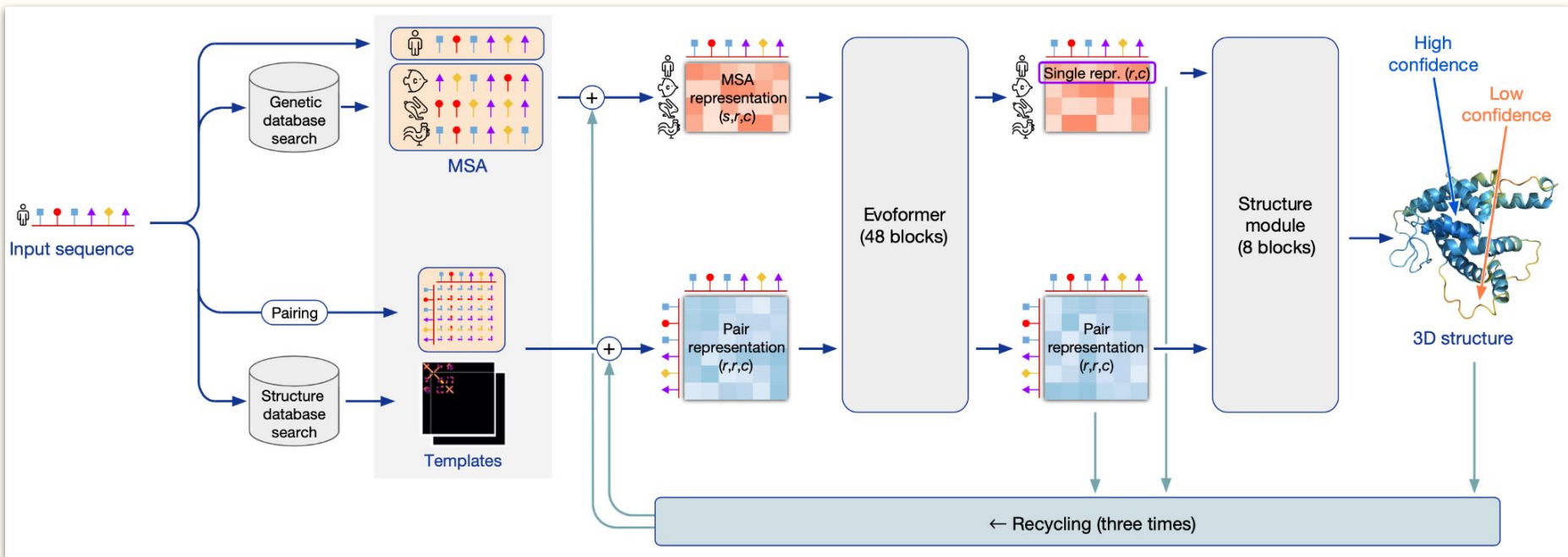


Dr. John Jumper

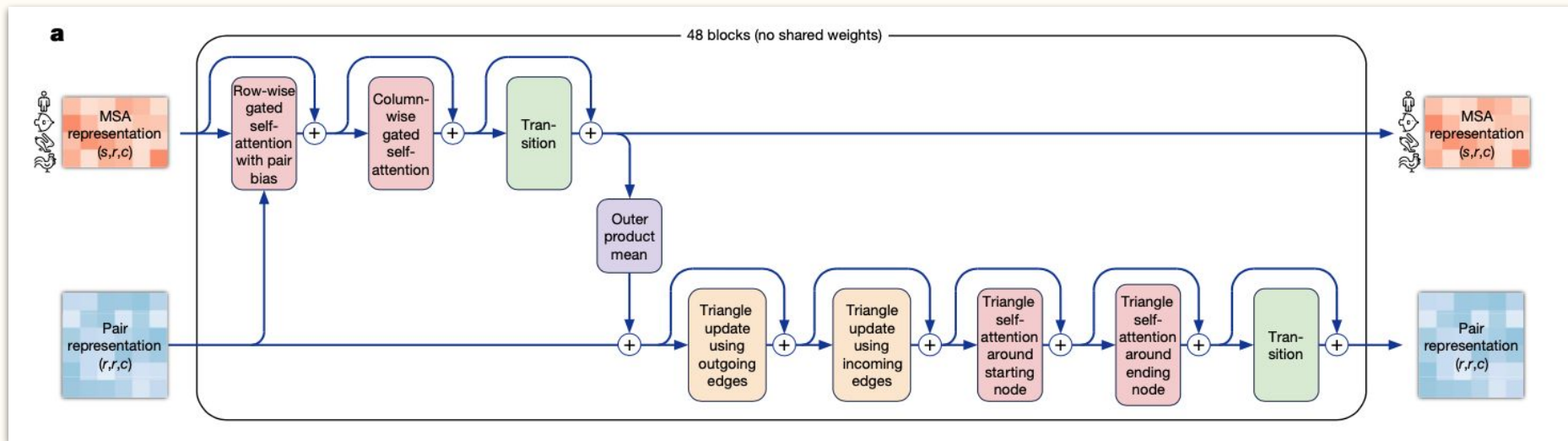
(Google DeepMind Director)

What Are Key Components of AlphaFold2?

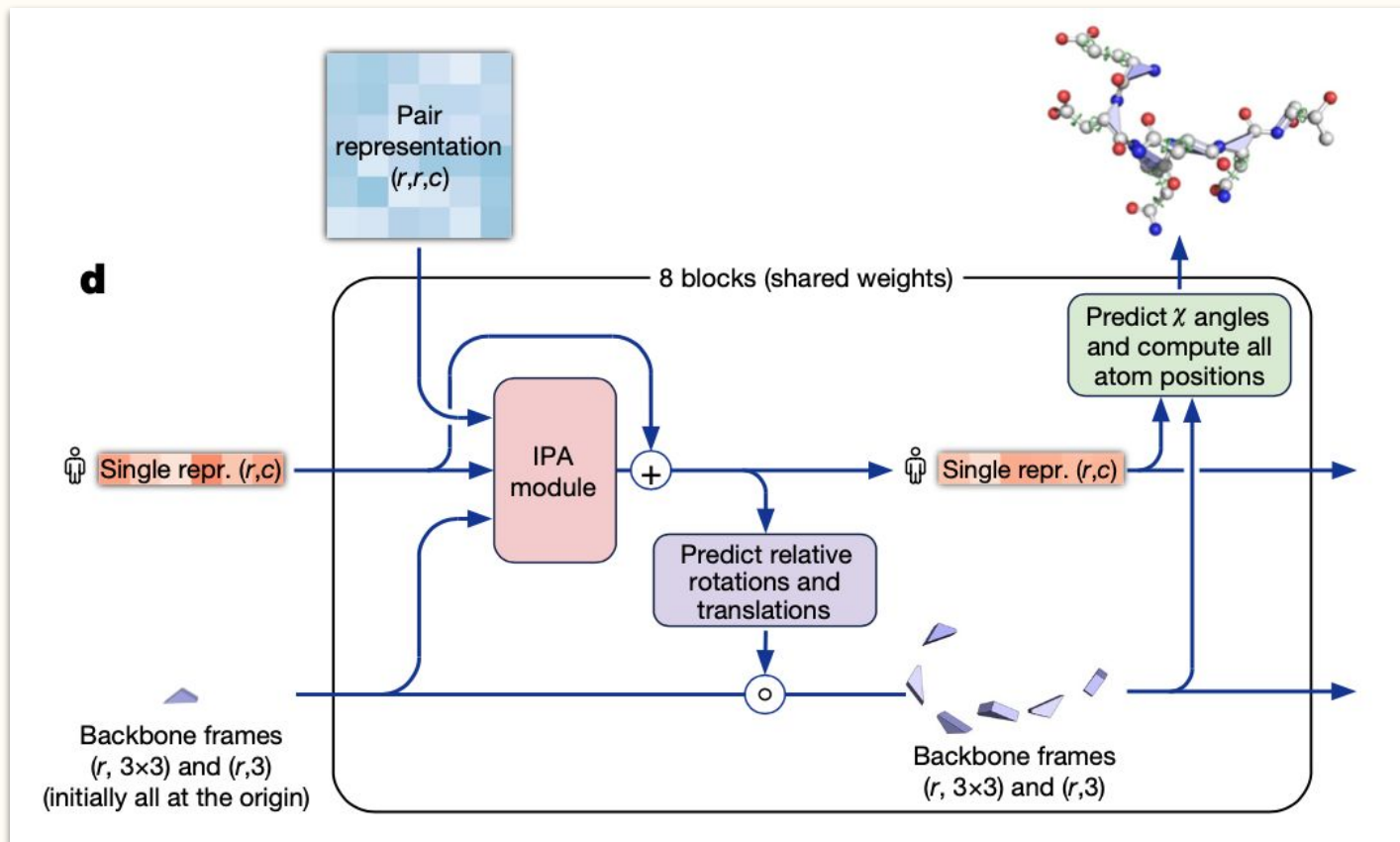
7



What happens inside the Evoformer?



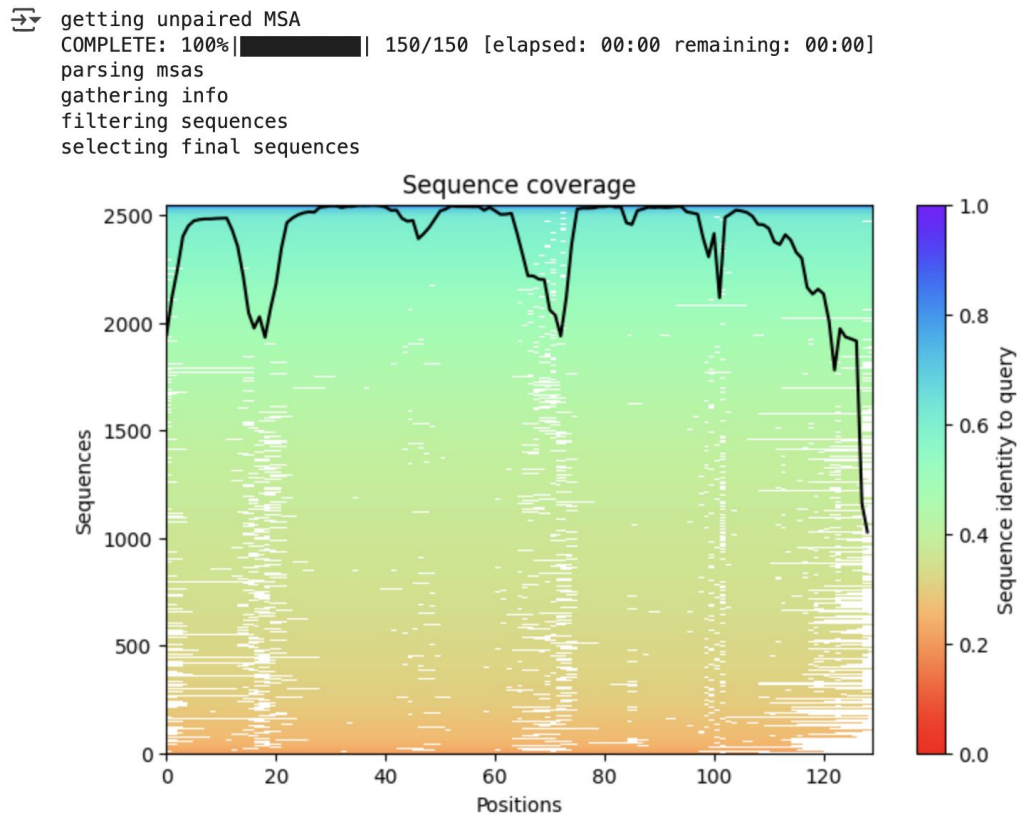
What happens inside the Structure Module?



What Is ColabFold?

- **Open-source** adaptation of AlphaFold2 for easier use
- Utilizes **MMseqs2** for fast, efficient MSA generation
- Runs on platforms like Google Colab, making predictions accessible
- Provides **similar high accuracy** as AlphaFold2 with streamlined pre-processing
- Supports predictions for both single chains and protein complexes

Replication results....



Replication results....

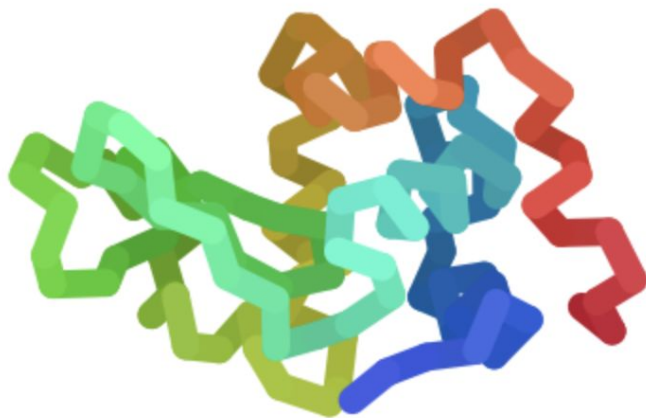


running prediction

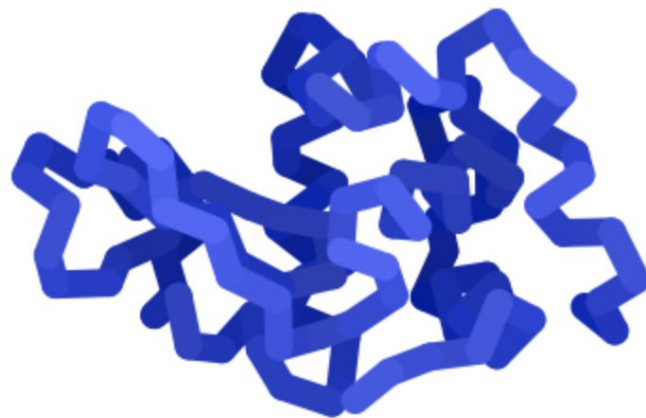
seed=0 model=model_1_ptm recycle=0 plddt=0.982 ptm=0.903

seed=0 model=model_1_ptm recycle=1 plddt=0.983 ptm=0.907 rmsd_tol=0.075

length

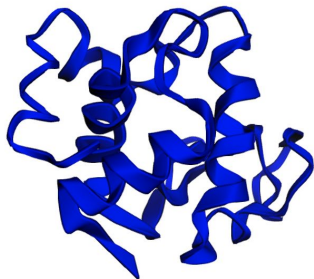


plddt

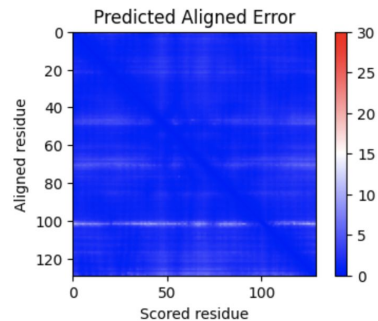
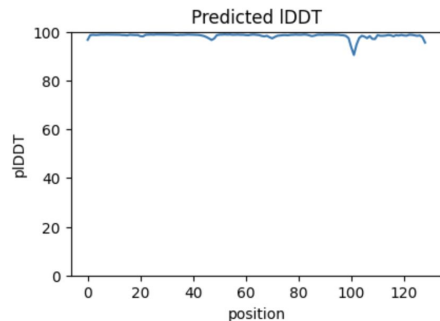


Replication results....

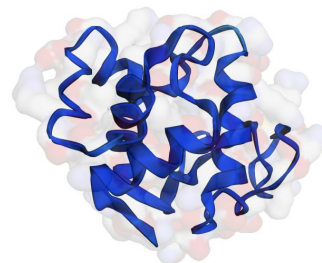
13



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

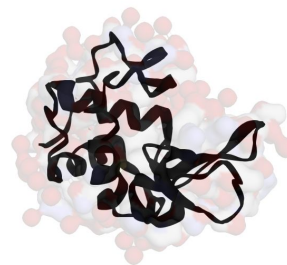


AlphaFold Prediction



<py3dmol.view at 0x784ed4387f90>
Visualization of AlphaFold Prediction using py3dmol

Experimental Structure (1LYZ)



<py3dmol.view at 0x784ed322e110>
Visualization of Experimental Structure (1LYZ) using py3dmol



A teeny-tiny DEMO!