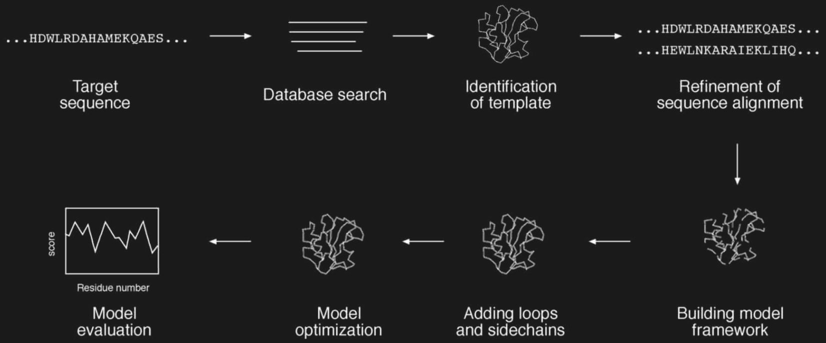
Homology modeling



...HDWLRDAHAMEKQAES...

Target sequence

Database search

Identification of template

...HDWLRDAHAMEKQAES...
...HEWLNKARAIEKLIHQ...

Refinement of sequence alignment

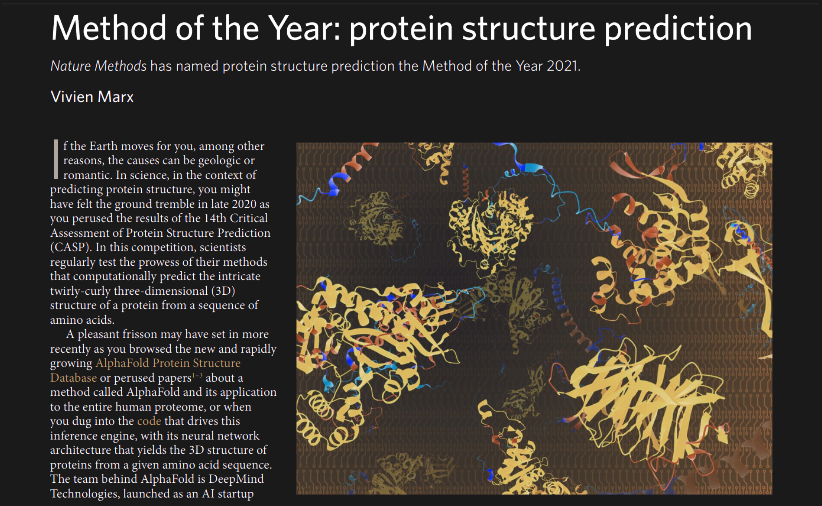
Building model framework

Adding loops and sidechains

Model optimization

Model evaluation

ANNs : AlphaFold



Method of the Year: protein structure prediction

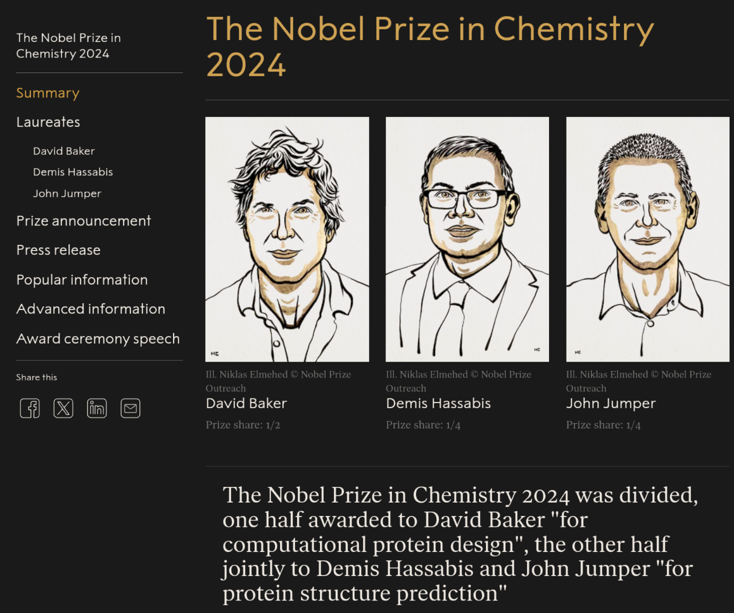
Nature Methods has named protein structure prediction the Method of the Year 2021.

Vivien Marx

If the Earth moves for you, among other reasons, the causes can be geologic or romantic. In science, in the context of predicting protein structure, you might have felt the ground tremble in late 2020 as you perused the results of the 14th Critical Assessment of Protein Structure Prediction (CASP). In this competition, scientists regularly test the prowess of their methods that computationally predict the intricate twirly-curly three-dimensional (3D) structure of a protein from a sequence of amino acids.

A pleasant frisson may have set in more recently as you browsed the new and rapidly growing AlphaFold Protein Structure Database or perused papers[1–3] about a method called AlphaFold and its application to the entire human proteome, or when you dug into the code that drives this inference engine, with its neural network architecture that yields the 3D structure of proteins from a given amino acid sequence. The team behind AlphaFold is DeepMind Technologies, launched as an AI startup

ANNs : AlphaFold



The Nobel Prize in Chemistry 2024

Summary

Laureates

- David Baker
- Demis Hassabis
- John Jumper

Prize announcement

Press release

Popular information

Advanced information

Award ceremony speech

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The Nobel Prize in Chemistry 2024

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David Baker

Prize share: 1/2

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Demis Hassabis

Prize share: 1/4

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John Jumper

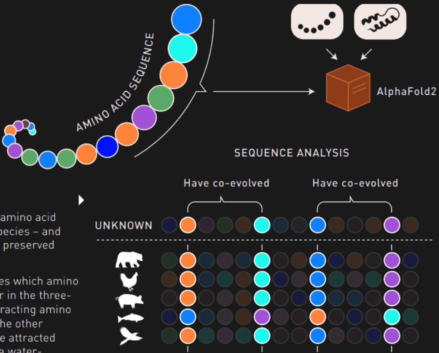
Prize share: 1/4

The Nobel Prize in Chemistry 2024 was divided, one half awarded to David Baker "for computational protein design", the other half jointly to Demis Hassabis and John Jumper "for protein structure prediction"

ANNs : AlphaFold

1. DATA ENTRY AND DATABASE SEARCHES

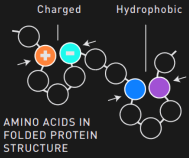
An amino acid sequence with unknown structure is fed into AlphaFold2, which searches databases for similar amino acid sequences and protein structures.



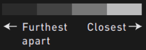
2. SEQUENCE ANALYSIS

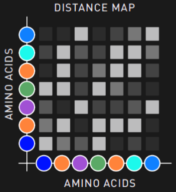
The AI model aligns all the similar amino acid sequences – often from different species – and investigates which parts have been preserved during evolution.

In the next step, AlphaFold2 explores which amino acids could interact with each other in the three-dimensional protein structure. Interacting amino acids co-evolve. If one is charged, the other has the opposite charge, so they are attracted to each other. If one is replaced by a water-repellent (hydrophobic) amino acid, the other also becomes hydrophobic.

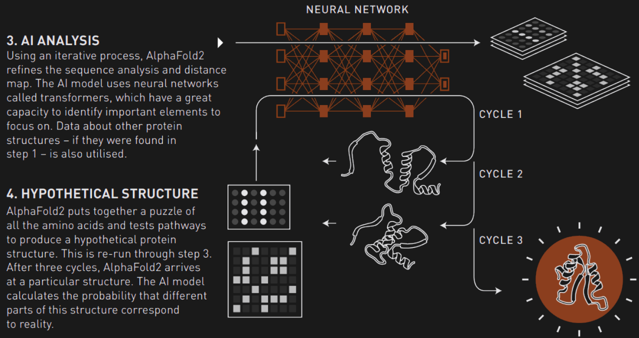


Using this analysis, AlphaFold2 produces a distance map that estimates how close amino acids are to each other in the structure.





ANNs : AlphaFold



3. AI ANALYSIS

Using an iterative process, AlphaFold2 refines the sequence analysis and distance map. The AI model uses neural networks called transformers, which have a great capacity to identify important elements to focus on. Data about other protein structures – if they were found in step 1 – is also utilised.

4. HYPOTHETICAL STRUCTURE

AlphaFold2 puts together a puzzle of all the amino acids and tests pathways to produce a hypothetical protein structure. This is re-run through step 3. After three cycles, AlphaFold2 arrives at a particular structure. The AI model calculates the probability that different parts of this structure correspond to reality.

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