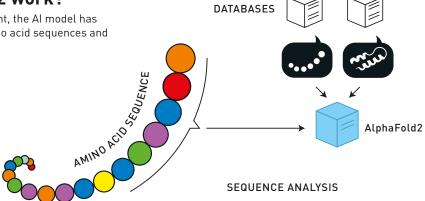
## How does AlphaFold2 work?

As part of AlphaFold2's development, the Al model has been trained on all the known amino acid sequences and determined protein structures.

## 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.



Have co-evolved

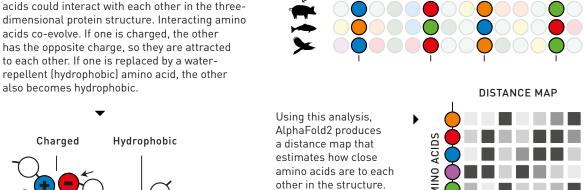
Have co-evolved

AMINO ACIDS

## 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 threedimensional 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 waterrepellent (hydrophobic) amino acid, the other



← Furthest

apart

Closest →

UNKNOWN

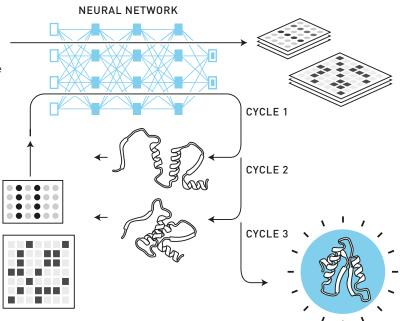
AMINO ACIDS IN FOLDED PROTEIN **STRUCTURE** 

## 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.



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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