Deep Mind Research Overview

Focus on 3 high profile applications:
- AlphaFold
- WaveNet
- AlphaGo

AlphaFold

- Accurately predicts 3D model of protein structures

- Proteins are building blocks of all living organisms and these are made up of a string of amino acids

- Protein folding problem is about predicting the shape of a protein based on its amino acids

- The 3D structure of a protein is important as it determines the function of the protein

AlphaFold Information

- ***Intro Video***

  https://www.youtube.com/watch?v=KpedmJdrTpY

- ***Paper in Nature***

  https://www.nature.com/articles/s41586-021-03819-2

- ***Explainer video***

  https://www.youtube.com/watch?v=B9PL__gVxLI
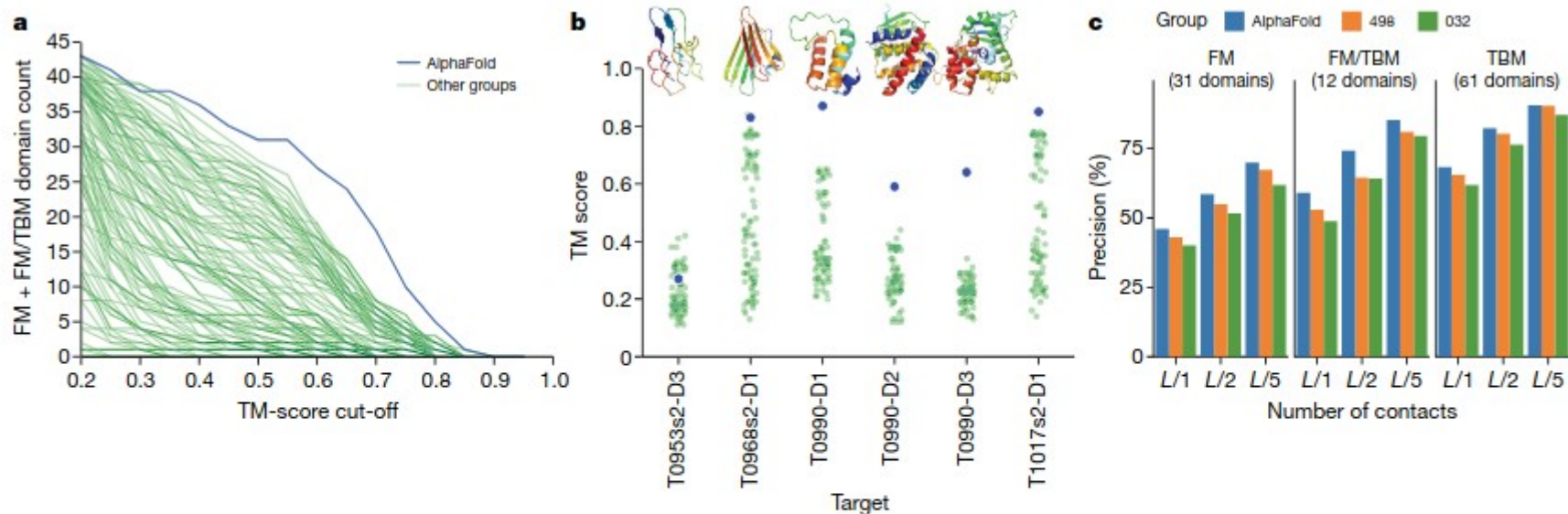
- ***Code on Github***

  https://github.com/deepmind/alphafold

Two iterations

- AlphaFold – better at predicting 3D structure of proteins than other algorithms (2019)

- AlphaFold2 – "solved" the protein folding problem (2021)

AlphaFold Results

Fig. 1 | The performance of AlphaFold in the CASP13 assessment. a, Number of FM (FM + FM/TBM) domains predicted for a given TM-score threshold for AlphaFold and the other 97 groups. **b,** For the six new folds identified by the CASP13 assessors, the TM score of AlphaFold was compared with the other groups, together with the native structures. The structure of T1017s2-D1 is not available for publication. **c,** Precisions for long-range contact prediction in CASP13 for the most probable L, $L/2$ or $L/5$ contacts, where L is the length of the domain. The distance distributions used by AlphaFold in CASP13, thresholded to contact predictions, are compared with the submissions by the two best-ranked contact prediction methods in CASP13: 498 (RaptorX-Contact[26]) and 032 (TripletRes[32]) on 'all groups' targets, with updated domain definitions for T0953s2.
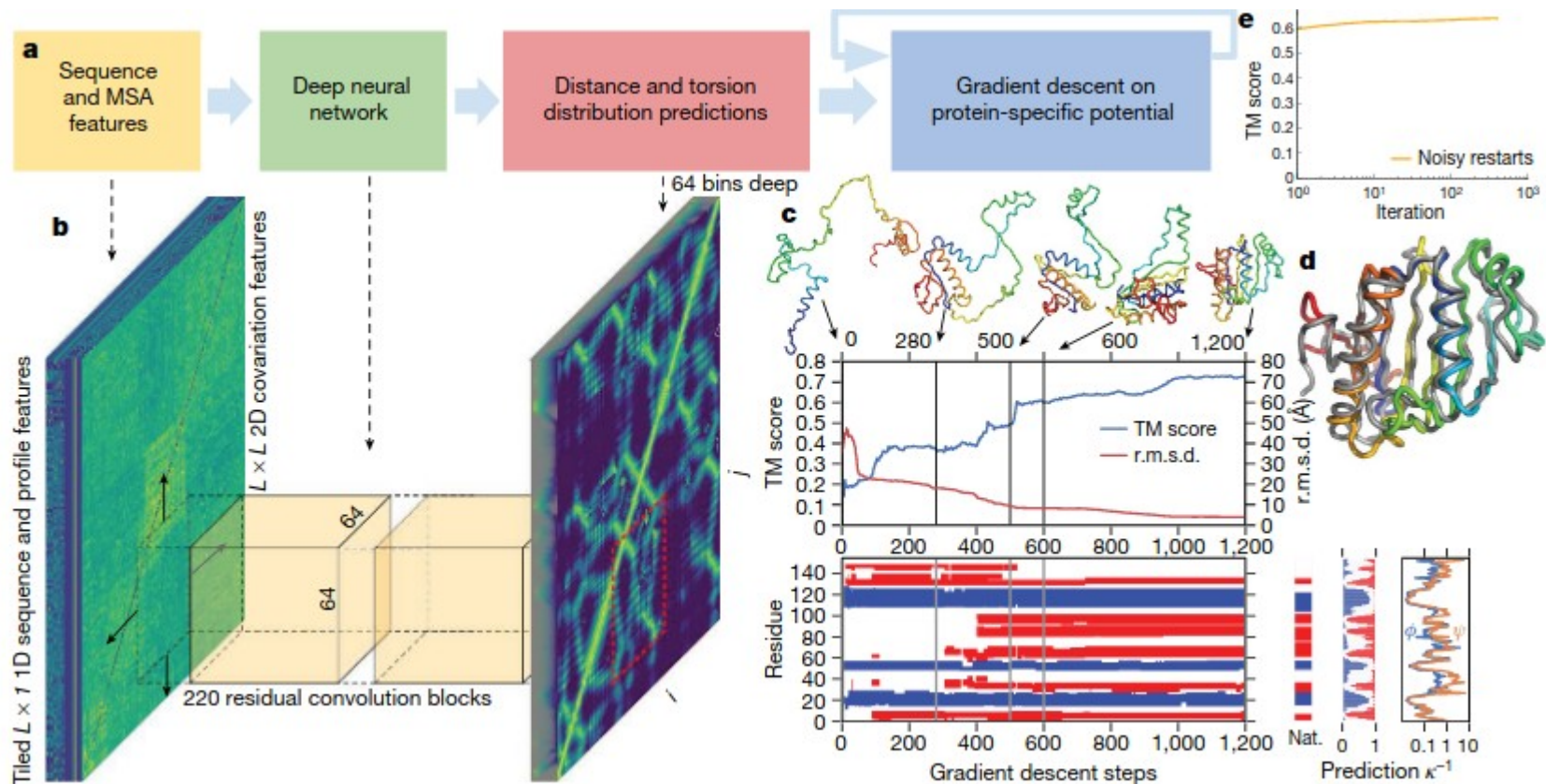
Abstract of 2019 AlphaFold paper

Protein structure prediction can be used to determine the three-dimensional shape of a protein from its amino acid sequence[1]. This problem is of fundamental importance as the structure of a protein largely determines its function[2]; however, protein structures can be difficult to determine experimentally. Considerable progress has recently been made by leveraging genetic information. It is possible to infer which amino acid residues are in contact by analysing covariation in homologous sequences, which aids in the prediction of protein structures[3]. Here we show that we can train a neural network to make accurate predictions of the distances between pairs of residues, which convey more information about the structure than contact predictions. Using this information, we construct a potential of mean force[4] that can accurately describe the shape of a protein. We find that the resulting potential can be optimized by a simple gradient descent algorithm to generate structures without complex sampling procedures. The resulting system, named AlphaFold, achieves high accuracy, even for sequences with fewer homologous sequences. In the recent Critical Assessment of Protein Structure Prediction[5] (CASP13)—a blind assessment of the state of the field—AlphaFold created high-accuracy structures (with template modelling (TM) scores[6] of 0.7 or higher) for 24 out of 43 free modelling domains, whereas the next best method, which used sampling and contact information, achieved such accuracy for only 14 out of 43 domains. AlphaFold represents a considerable advance in protein-structure prediction. We expect this increased accuracy to enable insights into the function and malfunction of proteins, especially in cases for which no structures for homologous proteins have been experimentally determined[7].

Data – PDB

- Data is freely available on the Protein Data Bank website compiled by scientists https://www.wwpdb.org/ftp/pdb-ftp-sites

- Atomic co-ordinates, X-ray data, NMR data

- 1000s of proteins and their experimentally determined structure

AlphaFold Model

WaveNet – Intro

- Creates more natural sounding speech

- Deep Mind blog post

  https://www.deepmind.com/blog/wavenet-a-generative-model-for-raw-audio

- Paper 2016

  https://arxiv.org/pdf/1609.03499.pdf

WaveNet – Text to speech

- Text to Speech often relies on concatenating sounds from a database of speech fragments

- This results in unnatural sounding computer generated speech

- Parametric TTS has been tried, where the information required to generate the audio are parameters in the model and the characteristics of the speech can be controlled by inputs. However, this typically sounds even less natural.

- WaveNet improves on this by modelling the raw waveform of the audio one sample at a time. Inspired by PixelRNN and PixelCNN used to generate complex natural images.

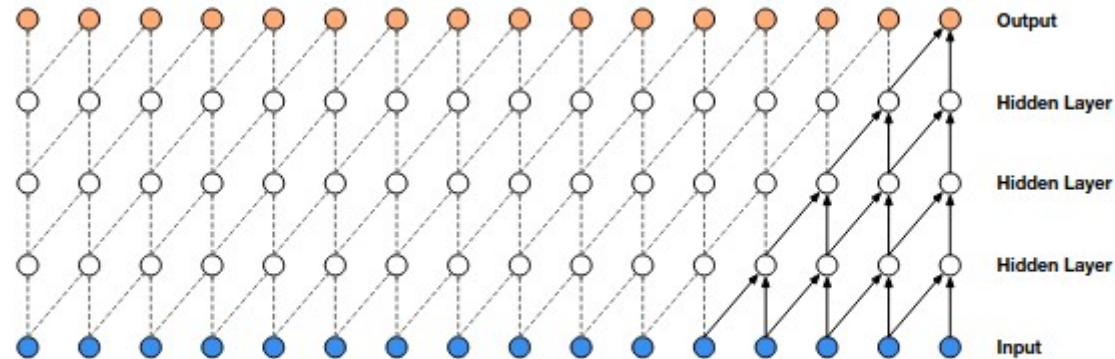# WaveNet – Model

- WaveNet uses Causal Convolution

Figure 2: Visualization of a stack of causal convolutional layers.

WaveNet – Data

- Used a database of North American English and Mandarin Chinese on which Google's current TTS algorithms are based.

- These contain 24.6 hours and 34.8 hours of speech data by professional female speakers

How to test quality/ accuracy?

- Used a Mean Opinion Score (1-5) from blind tests with human subjects based on 500 ratings over 100 test sentences
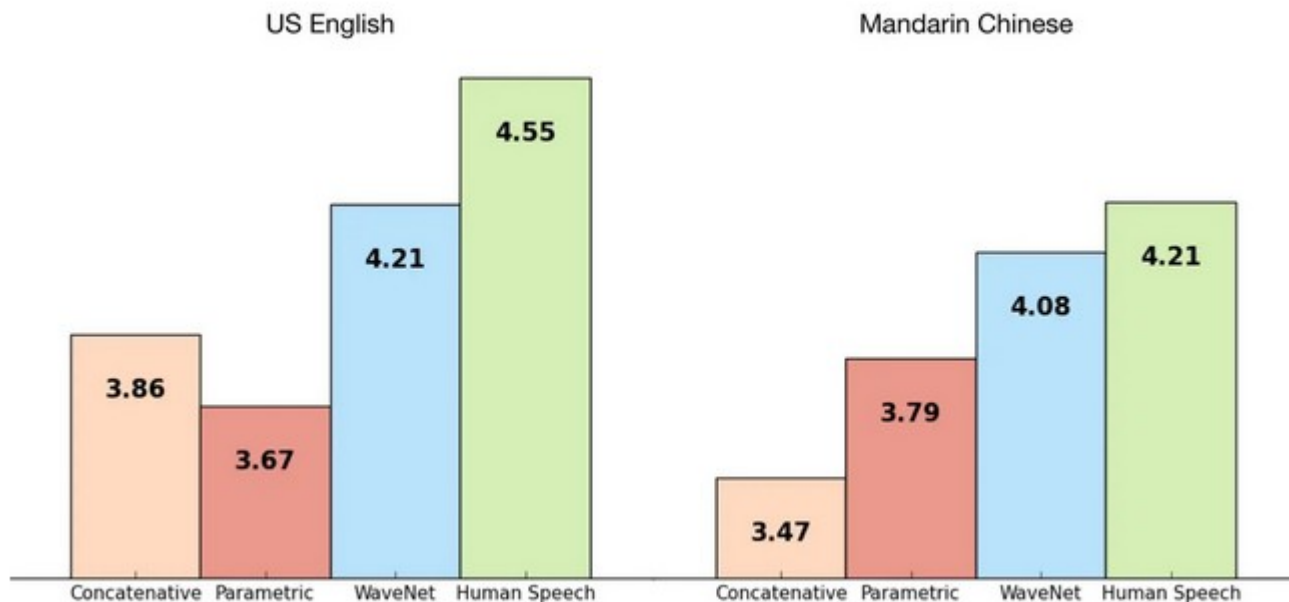
Other applications

- Since WaveNet works on audio it can be used for music as well as speech

- Can be trained on classic music to generate a new composition

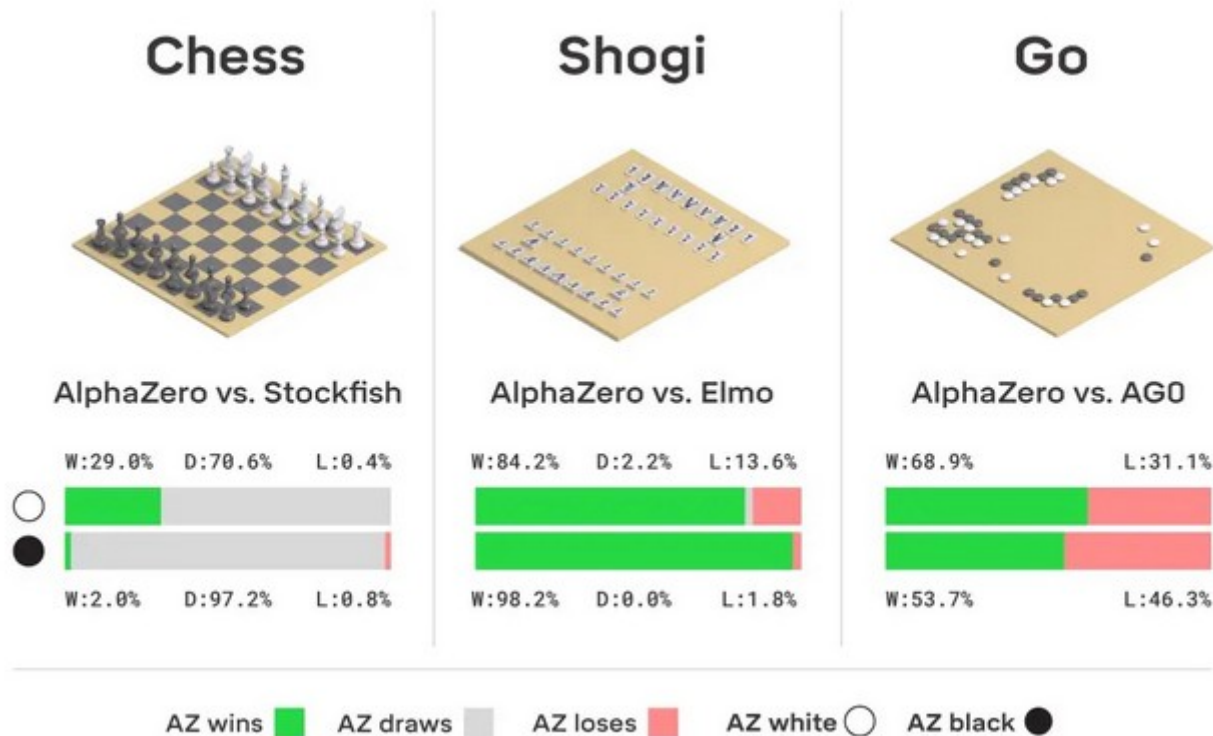- Can also be used for speech recognition

AlphaGo

- Strongest computer program at playing the game of Go

- Deep Neural Network + Advanced search tree

- Reinforcement learning – given the rules of Go and plays against different versions of itself thousands of times learning better decision making

- Also applied the technique to Chess and Shogi

AlphaGo – Info

- AlphaGo movie (story about how AlphaZero beat the Go champion Lee Sedol)

- https://www.youtube.com/watch?v=WXuK6gekU1Y

- Deep Mind blog post

- https://www.deepmind.com/blog/alphazero-shedding-new-light-on-chess-shogi-and-go

- Paper 2017

- https://storage.googleapis.com/deepmind-media/DeepMind.com/Blog/alphazero-shedding-new-light-on-chess-shogi-and-go/alphazero_preprint.pdf

Comparison to traditional algorithms

Chess	Shogi	Go
AlphaZero vs. Stockfish	AlphaZero vs. Elmo	AlphaZero vs. AG0

Chess: W:29.0% D:70.6% L:0.4% (AZ white); W:2.0% D:97.2% L:0.8% (AZ black)

Shogi: W:84.2% D:2.2% L:13.6% (AZ white); W:98.2% D:0.0% L:1.8% (AZ black)

Go: W:68.9% L:31.1% (AZ white); W:53.7% L:46.3% (AZ black)

AZ wins ▮ AZ draws ▮ AZ loses ▮ AZ white ○ AZ black ●
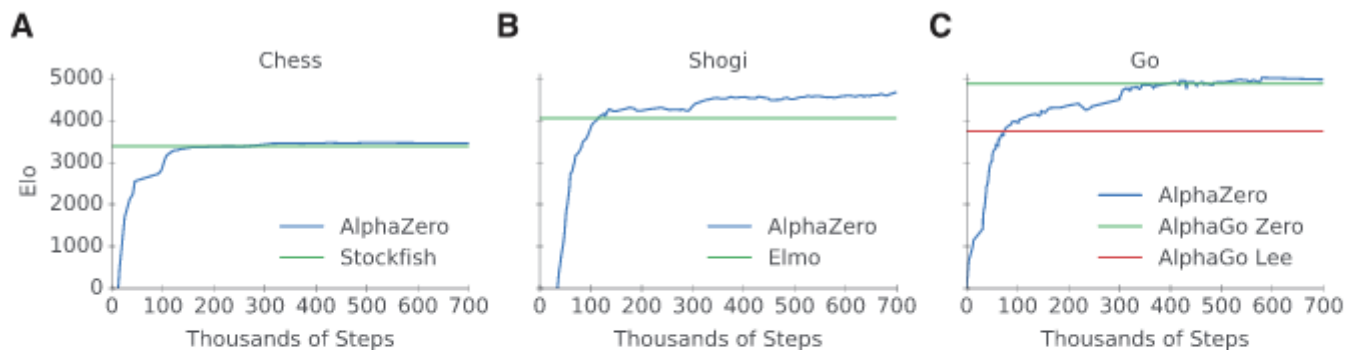
Training AlphaZero

Figure 1: **Training AlphaZero for 700,000 steps.** Elo ratings were computed from games between different players where each player was given one second per move. (**A**) Performance of AlphaZero in chess, compared with the 2016 TCEC world-champion program Stockfish. (**B**) Performance of AlphaZero in shogi, compared with the 2017 CSA world-champion program Elmo. (**C**) Performance of AlphaZero in Go, compared with AlphaGo Lee and AlphaGo Zero (20 blocks over 3 days).

Chess playing style

- Some of the games from the match against Stockfish were released in the paper

- AlphaZero plays in a very dynamic style often sacrificing material for long term attacking possibilities

- Likes the Berlin Defence and the Queen's Gambit