BetaFold: A Lightweight Protein Prediction Architecture

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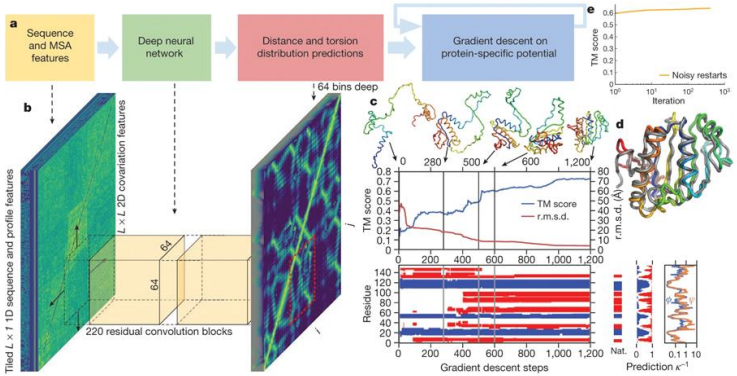
Outline

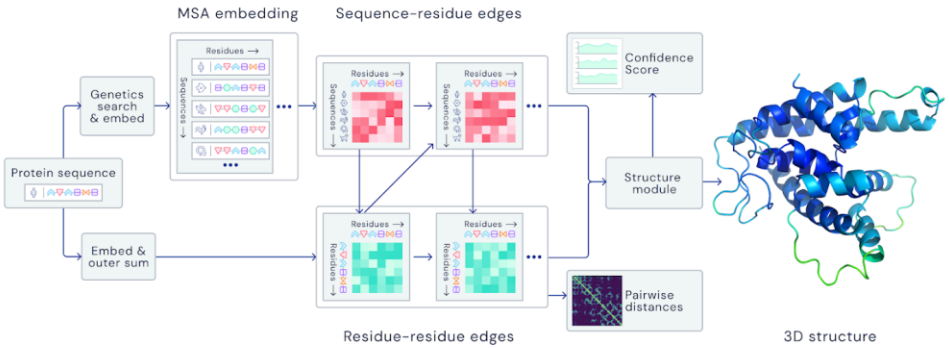
- Problem Definition
- Method
- Implementation
- Evaluation
- Conclusion

Problem Definition

AlphaFold I



AlphaFold II



Bottlenecks:

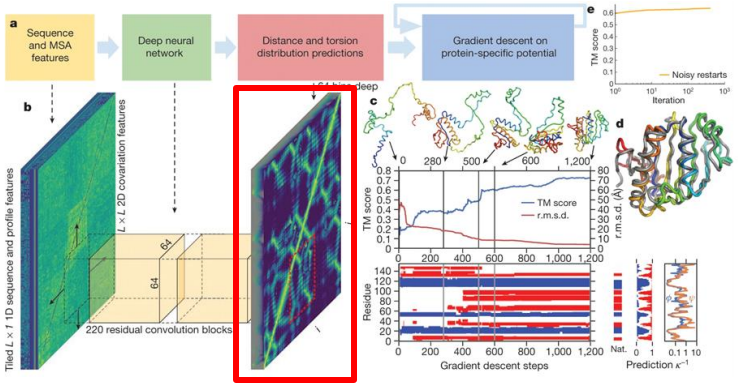
- Open-source implementation for running the inference and not the training
- Released code does not help determine the preprocessing.
- The inference per amino-acid sequence is around 10 mins on a 8 GB Quattro RTX 400, 128 GB machine.
- A major portion of inference is due to Multi-Sequence Alignment (MSA).
- Total size of the original data is around 2TB and ore-training time is over 2 weeks.

Method

BetaFold as a step towards solution:

- Breakdown Alphafold into its constituent and concentrate on Evoformer
- Skip Alphafold preprocessing (not available openly) instead use preprocessing as mentioned in [1].
- Skip MSA prediction: harder to handle 400 channel input feature on a small GPU.
- Focus on distogram prediction as it can be handled as an “image”-to-“image” translation task.

AlphaFold I



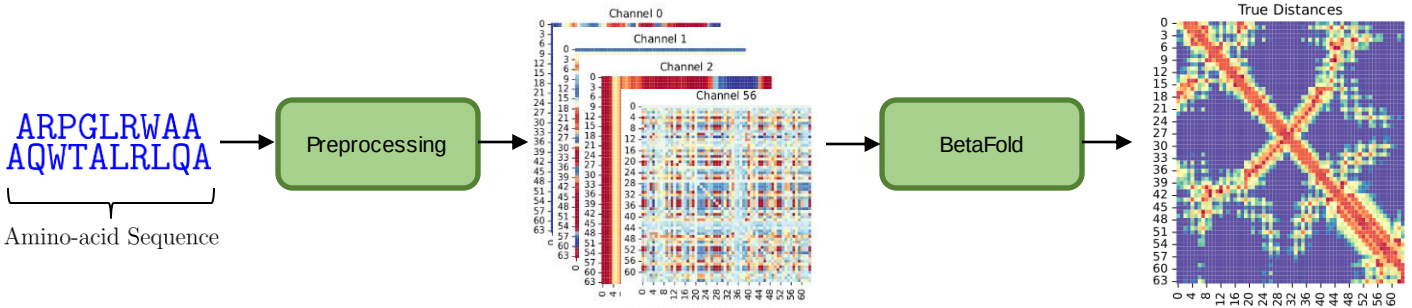
AlphaFold II

1) Jones, D. T. and Kandathil, S. M. High precision in protein contact prediction using fully convolutional neural netw orks and minimal sequence features. Bioinformatics, 34(19):3308–3315, 2018.

Method

BetaFold as a step towards solution:

- Amino-acid sequence preprocessing as proposed in [1].
- Distogram prediction as an “image”-to-“image” translation task.



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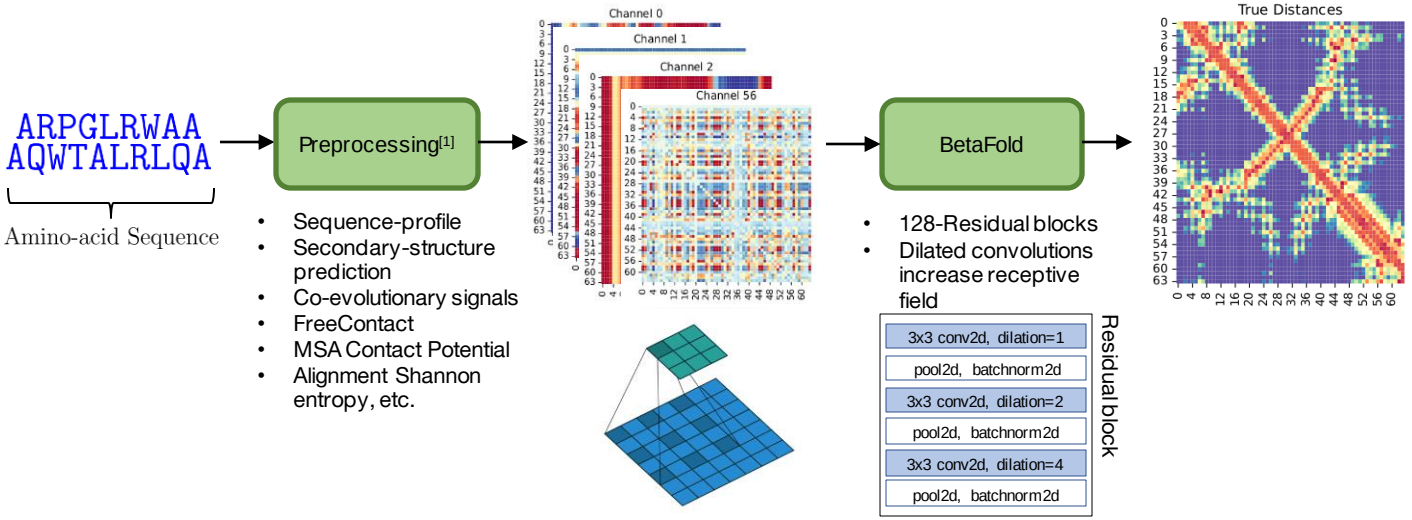
Implementation

BetaFold as a step towards solution:

- Amino-acid sequence preprocessing as proposed in [1].
- Distogram prediction as an “image”-to-“image” translation task.



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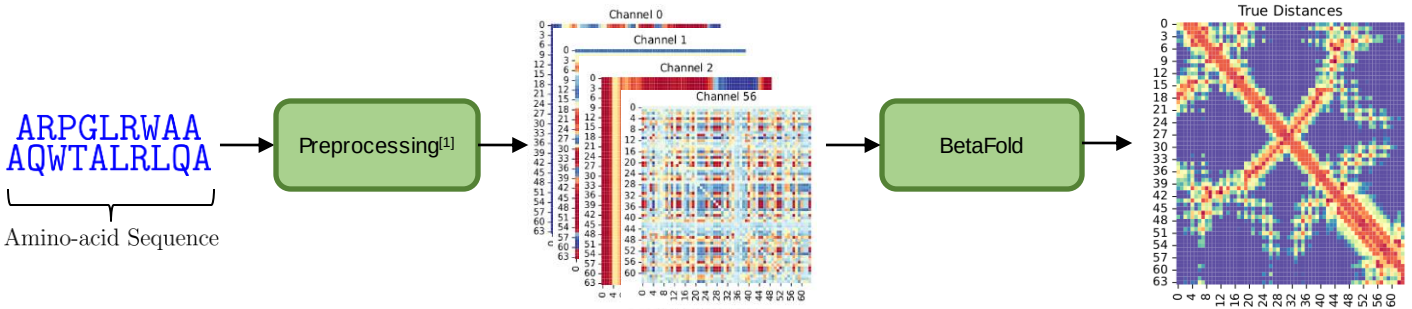
Implementation



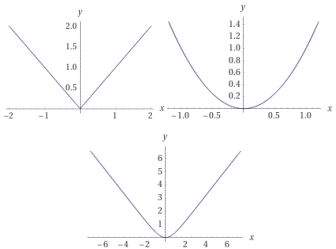
- Two types of task: (i) contact prediction, (ii) true distance prediction
- Contact prediction: binary classification with threshold of 6 angstrom using binary cross-entropy loss
- True distance prediction: using log_cosh and inv_log_cosh, s.t.,

$$\mathtt{log\_cosh}(\mathrm{y}, \hat{\mathrm{y}}) = \log(\cosh(\hat{\mathrm{y}} - \mathrm{y}))$$

$$\mathtt{inv\_log\_cosh}(\mathrm{y}, \hat{\mathrm{y}}) = \log\left[\cosh\left(\frac{\mathrm{K}}{\hat{\mathrm{y}} + \varepsilon} - \frac{\mathrm{K}}{\mathrm{y} + \varepsilon}\right)\right]$$

works like MSE for small values and MAE for large values (i.e., not strongly affected by outliers)

- In practice log-cosh works better but with inverted distances (K/y).
- Implementation at: https://github.com/shams-sam/BetaFold



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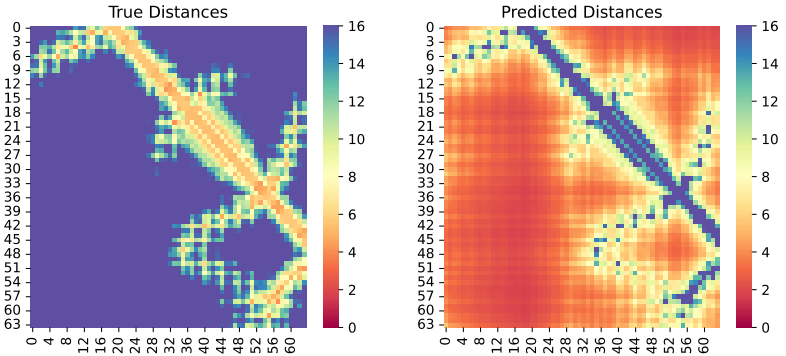
Evaluation

#	Task	Hyper-parameters	Metric	Performance
1	True Distance Pred.	$\texttt{loss} = \texttt{inv\_log\_cosh}, \texttt{lr} = \texttt{1e} - 2$	MAE	0.27
2	True Distance Pred.	$\texttt{loss} = \texttt{inv\_log\_cosh}, \texttt{lr} = \texttt{1e} - 3$	MAE	0.14
3	True Distance Pred.	$\texttt{log\_cosh}, \texttt{lr} = \texttt{1e} - 2$	MAE	0.30
4	True Distance Pred.	$\texttt{log\_cosh}, \texttt{lr} = \texttt{1e} - 3$	MAE	0.31
5	True Distance Pred.	$\texttt{log\_cosh}, \texttt{lr} = \texttt{1e} - 2$ with inverted distances	MAE	0.08
6	True Distance Pred.	$\texttt{log\_cosh}, \texttt{lr} = \texttt{1e} - 3$ with inverted distances	MAE	0.08
7	Contact Pred.	$\texttt{log\_cosh}, \texttt{lr} = \texttt{1e} - 2$	Accuracy	0.93
8	Contact Pred.	$\texttt{log\_cosh}, \texttt{lr} = \texttt{1e} - 3$	Accuracy	0.92



Conclusion

- AlphaFold is a highly specialized architecture with huge networks trained on really large dataset.
- Lightweight architectures are only possible if we can think of solutions around shrinking the MSA representations.
- Possibly use domain knowledge to bake more inductive priors within the network. Currently attention does the work.

- We try to emulate the task of Evoformer as an “image”-to-“image” translation task.
- Possible application of manifold learning in predicting the 3D structures from 2D distograms.

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Thank you!

Any questions/feedback?

- Email: azam1@purdue.edu

References

1. Jumper, John, et al. "Highly accurate protein structure prediction with AlphaFold." *Nature* 596.7873 (2021): 583-589.
2. Senior, Andrew W., et al. "Improved protein structure prediction using potentials from deep learning." *Nature* 577.7792 (2020): 706-710.