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Final Writeup

1 Distribution of Work

1.1 Yu-Kai (Steven) Wang

(a) Multihead self attention

(b) Outer product mean

(c) Triangular self attention

(d) IPA Module

(e) Parallelization of model so that it can run on any number of GPUs

(f) Dispatching jobs to the DCS cluster

(g) Optimization of evoformer trunk and structure module

1.2 Matthew Uryga

(a) Input feature projections

(b) Evoformer trunk structure

(c) Structure module, excluding the IPA module

    (i) Backbone update
    (ii) FAPE and torsion angle loss
    (iii) etc.

(d) Dataset for batching of crops for training/validation and whole sequences for testing

(e) Model training and validation loops

(f) Model evaluation

(g) Predicted/Ground truth structure visualization

1.3 Repository Link

The code for our implementation of the evoformer trunk can be found here:
https://github.com/mnuryga/MLBinfCapstone.

2 Method

2.1 Overall Implementation

For the most part, the Alphafold2 supplemental paper was followed closely when implementing the model structure. Some deviations include a reduced breadth of input data (no extra msa information) and some slight variations in the final computation of coordinates. It is also worth noting that the model was not designed to predict anything beyond the ϕ and ψ torsion angles and the locations of C, C_α, and N.

2.2 Parameters

Due to memory, time, and processing power limitations, the parameters of the model were decreased from the specifications in the Alphafold2 paper. Namely, the following parameters were altered:

$$\begin{aligned}
N_{res} &= 256 \longrightarrow 64 \\
N_{clust} &= 16 \longrightarrow 8 \\
c_m &= 256 \longrightarrow 128 \\
c_z &= 128 \longrightarrow 64 \\
c_z &= 128 \longrightarrow 64 \\
c_{MHSA} &= 32 \longrightarrow 16 \\
c_{outer\ prod\ mean} &= 32 \longrightarrow 16 \\
c_{trangular\ attn} &= 32 \longrightarrow 16
\end{aligned}$$

Without these parameter reductions, evaluation of the model would not be possible on the largest test sequences, as the GPUs would run out of memory to hold the entirety of the protein and its representations.

2.3 Tuning of Learning Rate

Because training took a significant amount of time, the learning rate could not be optimally tuned. However, through short validation runs, a learning rate of 0.001 was settled on. The learning rate was manually halved every 6 epochs.

2.4 Tuning of Dimension Parameters

Through a variety of limited experiments, it was found that increasing the

2.5 Training

Training was conducted on the DCS cluster so that the model could make use of 4 GPUs. This substantially decreased the training time from approx 3.5 hours per epoch to 50 minutes per epoch. In total, the model was trained for 18 epochs.

2.6 Validation

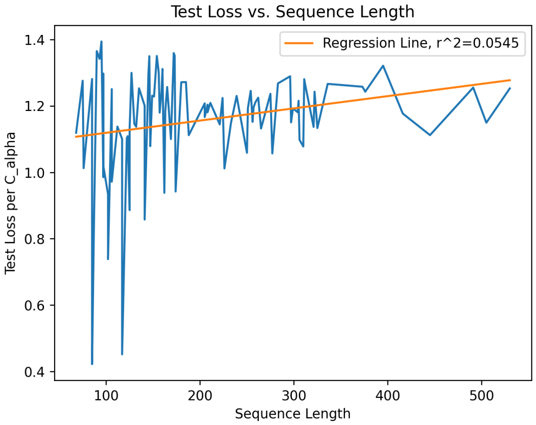
Validation was run after each epoch, and the model was stopped if the validation loss was greater than the 5-epoch rolling mean of previous validation losses.

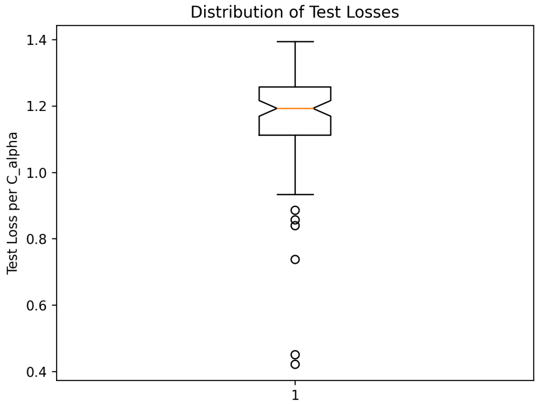
3 Results

3.1 Test Loss

Because each sequence are different lengths, the testing loss is reported as loss per sequence divided by sequence length $\longrightarrow$ loss per C_α.
The calculated average test loss was 0.00700787 per C_α.

Below are a couple of plots detailing a few more statistics with the test loss:





From the plots above, it appears that the average loss per C_α does not have a significant correlation with sequence length - the least squares regression line has a r^2 value of 0.0545

4 Visualization

The predicted and true protein structures were visualized by plotting the coordinates of the C_α atoms in 3D-space.

Below are three sequences that were chosen based on their average loss per C_α (the maximum, median, and minimum average loss sequences).

4.1 Best Prediction

Average loss per C_α: 0.

4.2 Average Prediction

Average loss per C_α: 0.

4.3 Poor Prediction

Average loss per C_α: 0.

5 Conclusion