**Predicting gene expression using millions of random promoter sequences by mt**

***Abstract***

I developed an end-to-end procedure to predict the expression of genes using random promoters. My approach uses Recurrent (GRU) and Convolution Neural Networks to regress the strength of the targeted promoters using information encoded in the forward and reverse DNA strands. The starting point of my model, two bi-bidirectional GRUs, have been recently used in a machine learning competition at Kaggle to predict the stability of RNA vaccines (https://arxiv.org/abs/2110.07531). In this work, I expanded on this architecture and found that the addition of convolutions and fully connected layers can efficiently extract features from DNA sequences and predict gene expression.

**1. Description of data usage**

The DNA forward and reverse strands were one-hot encoded using the canonical four bases (A, T, C, G) plus two special tokens; one token for the bases that were miss-sequenced sequence (N) and one token for the padding (P). The sequences that are shorter than the longest sequence in the dataset (n=142) were padded. The padding was applied at the 5’ of the forward strand. The one-hot encoded sequences were stacked together to create an input of 142 columns (the longest sequence in the dataset) x 12 rows (6 for the forward plus 6 for the reverse DNA strands). A custom data generator was developed to train the sequences. The data generator takes care of grabbing the promoter sequences from a pandas data frame. The padding, reverse-complement computation, one-hot encoding and stacking of the forward and reverse strands happen at the batch level in the data loader. The model was trained with the whole dataset minus ten thousand promoters (randomly chosen) used for validation.

**2. Description of the model**

I used TensorFlow and Keras to develop a model with one branch. The model passes the inputs to two bi-bidirectional GRUs followed by three convolutions and max pooling operations. At the end of the convolutions, the data is flattened and fed to two fully connected layers. The model was trained without dropouts.

**3. Training procedure**

The training of this model uses the BinaryCrossentropy loss coupled with the sigmoid activation of the output layer. The model scores are recorded after each epoch and recorded in the jupyter notebook present in the GitHub repo. The epoch chosen for submission is 11. I’m choosing to stop training the first time the Pearson validation metric stops improving, +1 epoch. This strategy, supported by leaderboard probing, seems successful for this architecture.

**4. Other important features**

* I was not able to find a combination of train \ test split, dropout or more complex architecture that would make this model overfit. On the contrary, the model slightly underfits, with testing metrics always slightly better than the training metrics.
* The addition of dropouts at any level of the chosen architecture makes the model train slower with less competitive results. For this reason, the model was trained without dropouts.
* Until two weeks before the competition deadline, the model was very unstable, with nans appearing randomly in the evaluation metric during training. I figured out that the problem was the loss. The Keras MeanSquaredError or MeanAbsoluteError losses coupled with a liner activation of the output layer make the model unstable. The only way to train the model end-to-end is to use the Binary Crossentropy loss coupled with the sigmoid activation. For this reason, it seemed logical to me to scale the target values between 0 and 1. For the same reason, the model has been trained one epoch at a time, so I could re-start training from the last successful epoch in the case of nans. This is not necessary anymore, but I didn't change the training procedures anyway.

**5. Contributions and Acknowledgement**

**5.1 Contributions**

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**5.2 Acknowledgement**

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**7. Feedback (optional)**

I want to thank the organizer for setting up this interesting competition. It has been a very pleasant journey, with a lot of experience gained. Thanks especially to Abdul, that has been extremely helpful in the discussion forum.

I want also to report two decisions that I didn’t like. 1) I don’t think it was a good idea to decrease the number of submissions on the last day on such short notice. 2) I believe it was unfair to let people have more days to decide which model to submit by extending the submission deadline, even if it was a prediction already submitted. The final leaderboard should remove any submission made after the stated competition deadline.

Finally, I believe that future competitions might benefit from 1) Make public the leaderboard test set, given the substantial difference between the train and test set. 3) Make the models run in colab, so that it is easier to share and experiment with the code.