A. MODEL SUMMARY

A1. Background on you/your team

Competition Name: leash-BELKA
(https://www.kaggle.com/competitions/leash-BELKA)
Team Name: mamba1-one-fold-lb0.432
Private Leaderboard Score: 0.28557
Private Leaderboard Place: rank 5th

A2. Background on you/your team

What is your academic/professional background?
I am a contract computer vision and deep learning algorithm engineer. My job includes discovering fracture in x-ray images and implementing visual slam for robotic navigation. Recenting I am helping companies to finetune LLM models for their applications.

Did you have any prior experience that helped you succeed in this competition?
I am familiar deep learning and build deep models in my work. I also have experiences in making models for medicine and molecular appications from previous Kaggle competitions (Bristol-Myers Squibb – Molecular Translation, OpenVaccine: COVID-19 mRNA Vaccine Degradation Prediction)

What made you decide to enter this competition?
The problem of virtual screening in DNA encoded libraries is interesting. I can learn from other kagglers about the latest AI methods and insights in this area.

How much time did you spend on the competition?
About 5 hours per day, over two months.

A3. Summary

In this competition, our task is to predict the binding affinity of small molecules to specific protein targets – a critical step in drug discovery. Since there are only 3 target proteins, we can treat this as a multi-label classification problem, i,e bind verus non-bind for a protein, given an input molecule.

One issue in the kaggle competition is that a large part of the test molecules are synthesized from different building blocks used in the train molecules. To mitigate the effects of OOD (out-of-domain) distribution, we use an ensemble of different sequence models of 3-fold conv1d, 2-fold transformer and single-fold mamba SSM (selective state machines) nets shown in Figure.1.

All models are build with python and pytorch deep learning framework. In order to handle 98 millions of training molecules efficiently, we use customized cuda kernel from open source flash attention[1] and mamba SSM[2] libaries.

Training takes about 12 hours for one net for each one fold, using Nvidia Ada A6000 Ampere GPU with memory 48 GB.

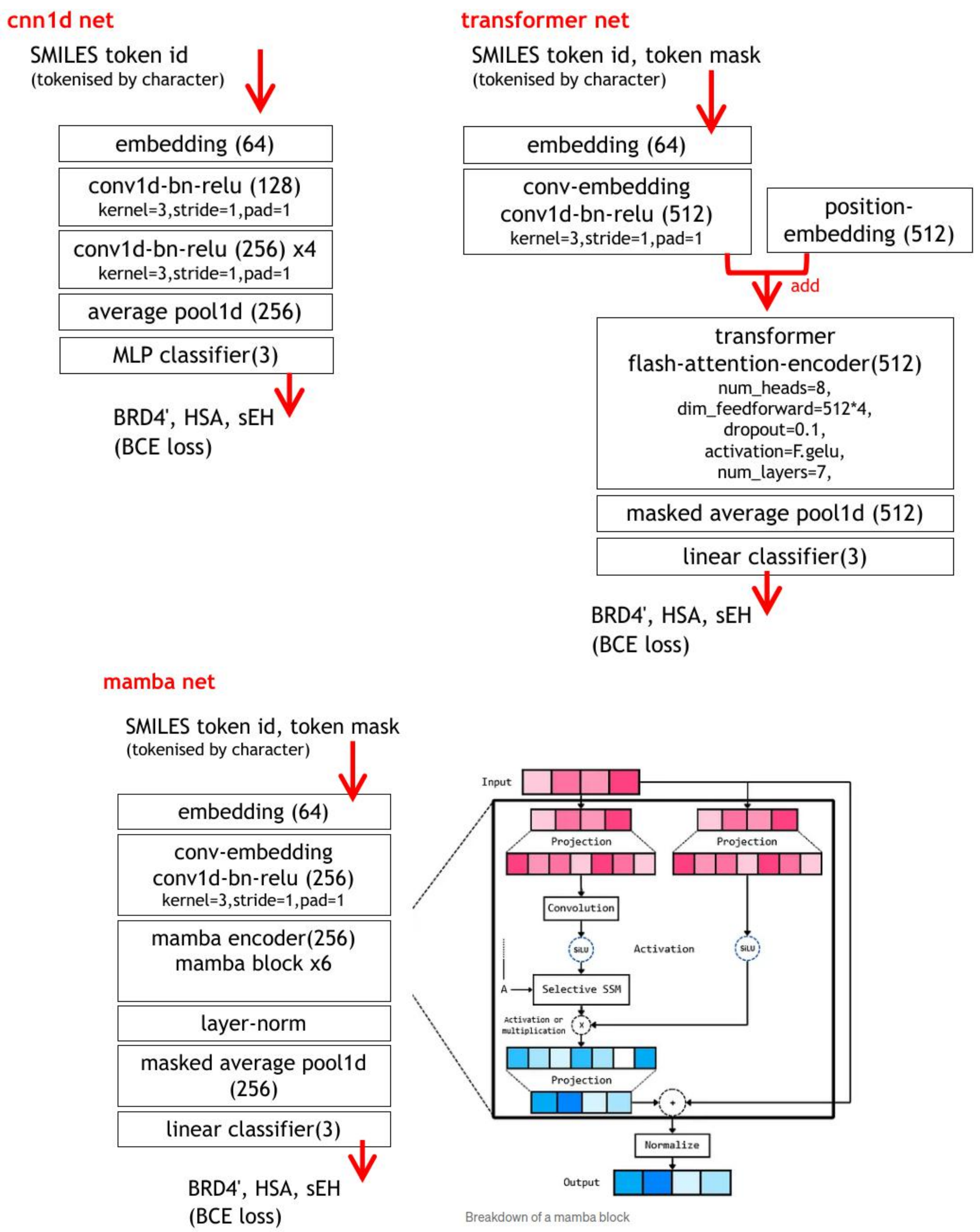
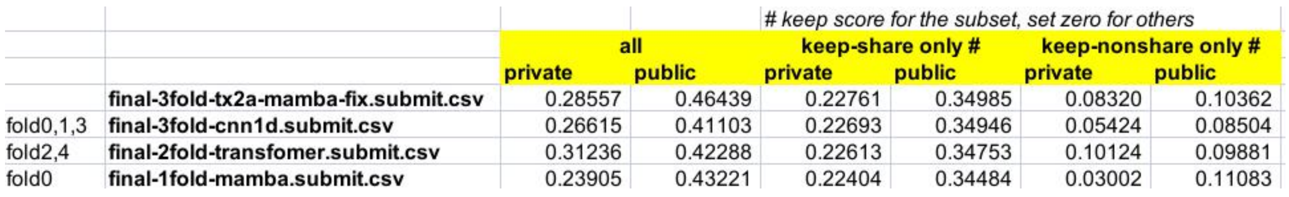


Figure.1 : Different nets used in ensemble solution



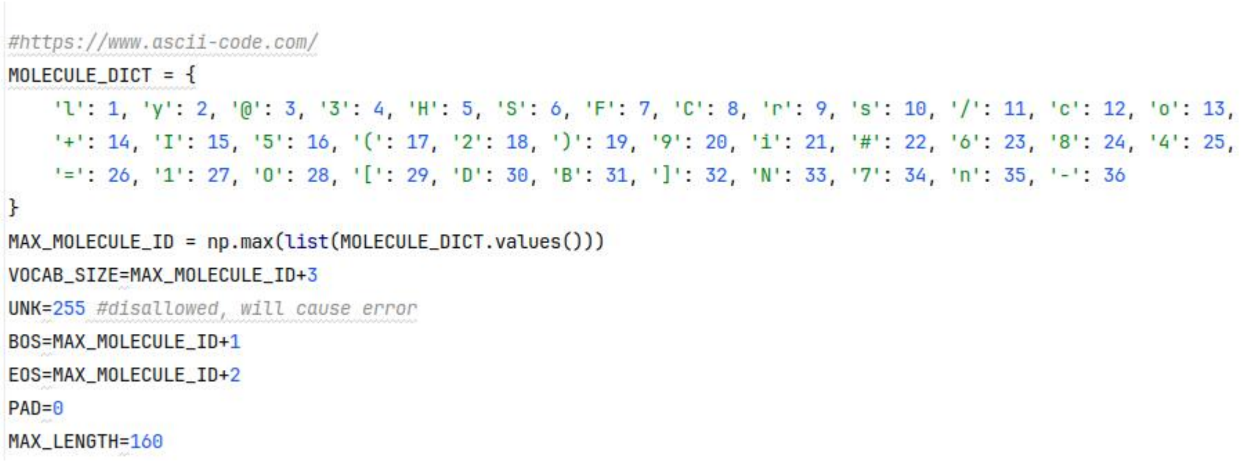
				# keep score for the subset, set zero for others			
		all		keep-share only #		keep-nonshare only #	
		private	public	private	public	private	public
	final-3fold-tx2a-mamba-fix.submit.csv	0.28557	0.46439	0.22761	0.34985	0.08320	0.10362
fold0,1,3	final-3fold-cnn1d.submit.csv	0.26615	0.41103	0.22693	0.34946	0.05424	0.08504
fold2,4	final-2fold-transfomer.submit.csv	0.31236	0.42288	0.22613	0.34753	0.10124	0.09881
fold0	final-1fold-mamba.submit.csv	0.23905	0.43221	0.22404	0.34484	0.03002	0.11083

Figure.2 : Permenace of different nets in the leaderboard

A4. Features Selection / Engineering

1. Tokenization

We need compvert SMILES string to tokens as input to our sequence models. We tried several methods like character based, sentence piece, byte-pair-encoding (BPE), atom/smiles notation aware to break the SMILES strings. Surprisingly, the simplest character based tokenization, see Figure.3, perform the best across different net architecture.



```
#https://www.ascii-code.com/
MOLECULE_DICT = {
    'l': 1, 'y': 2, '@': 3, '3': 4, 'H': 5, 'S': 6, 'F': 7, 'C': 8, 'r': 9, 's': 10, '/': 11, 'c': 12, 'o': 13,
    '+': 14, 'I': 15, '5': 16, '(': 17, '2': 18, ')': 19, '9': 20, 'i': 21, '#': 22, '6': 23, '8': 24, '4': 25,
    '=': 26, '1': 27, 'O': 28, '[': 29, 'D': 30, 'B': 31, ']': 32, 'N': 33, '7': 34, 'n': 35, '-': 36
}
MAX_MOLECULE_ID = np.max(list(MOLECULE_DICT.values()))
VOCAB_SIZE=MAX_MOLECULE_ID+3
UNK=255 #disallowed, will cause error
BOS=MAX_MOLECULE_ID+1
EOS=MAX_MOLECULE_ID+2
PAD=0
MAX_LENGTH=160
```

Figure.3 : character-based tokenization

We further add a conv layer of kernel size=3, stride=1 to learned combinations of consecutive tokens (bigrams, trigrams) before passing the tokens into transformer or mamba.

2. Batch normalisation

We find that the model performance is sensitive to batch normalisaton. We think this is because:
- in-distribution and out-distribution samples have different feature values.
- class is imbalance (postive class is less than 1%), positive and negative samples also have different feature values.

We use high eps=5e-3 and low momentum=0.2 for cnn1d net.

A5. Training Method(s)

To train the sequence models, we use binary cross entropy loss. We perform back propagation with ADAM optimizer. The important hyper-parameters are:
- step learning rate of 1e-3,1e-4,1e-5 for 6-12 epoches.
- large batch size of 2000,2500,5000

Interesting, the best way to handle class imbalance is to do nothing (no upsampling or undersanding of the class). We think this could be because of the large batch size we used.

A6. Interesting findings

What was the most important trick you used?
From Figure.2, transformer has exception performance in the leaderboard score. We think the use of character-based tokenization and conv embedding to learn meaningful bigrams, trigrams are important tricks to make transformer robust to OOD.

What do you think set you apart from others in the competition?
We have very powerful GPU cards. The two Nvidia Ada A6000 /48GB Ampere GPUs make our training fast. To use large batch size of 2500 in transformer, we spend efforts to write memory-efficient code. In particular, we discard pytorch dataloader which uses multi-process that can led to growing memory usage in cpu RAM. This is because as the loader fetches the batch to queue, memory is not released until the epoach ends.

A7. Simple Features and Methods

Many customers are happy to trade off model performance for simplicity. With this in mind:
Is there a subset of features that would get 90-95% of your final performance?

From Figure.2, it is sufficient just to use transformer net.

A8. Model Execution Time

How long does it take to train your model?
Training takes 12 hours for one net for each one fold, using Nvidia Ada A6000 Ampere GPU with memory 48 GB.

How long does it take to generate predictions using your model?
The test data has about 880,000 molecules. It take less than 5 minutes for each net to process them.

How long does it take to train the simplified model (referenced in section A7)?
I expect a reduction of more than 50% in time.

How long does it take to generate predictions from the simplified model?
I expect a reduction of more than 50% in time.

A9. References

[1] “FlashAttention: Fast and Memory-Efficient Exact Attention with IO-Awareness” - Tri Dao
https://github.com/Dao-AILab/flash-attention

[2] “Mamba: Linear-Time Sequence Modeling with Selective State Spaces” - Albert Gu, Tri Dao
https://github.com/state-spaces/mamba