ALTeGraD Data Challenge

Final Presentation

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Protein graph dataset

- 4888/1223 protein graphs in the training/test set
  $\rightarrow$ We took 500 proteins to make a validation set
- Task : Classify the protein graphs into 18 different classes
- Nodes as well as edges have features

Discrepancies in the dataset

Figure: Distribution of the classes in the dataset

Discrepancies in the dataset

	Min	0.25-quantile	Median	Mean	0.75-quantile	Max
Nodes	9	129	221	257	340.5	989
Edges	55	2187	3996	4721	6491	20417

Table: Statistics on the number of nodes and edges of the protein graphs.

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First approach

Graph convolutional networks on the default features from the dataset.

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Same for the aggregation part: the mean is the best.

Adding extra features

- From the literature:
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Adding extra features

- From the literature:
  - Local Degree Profile (5)
  - Laplacian Positional Embedding (3)
- Custom features:
  - Torsion angle (2)
  - Distance to the center of mass (1)
  - Position in the sequence (1)

Adding extra features

	Node features	
	default	default + extra features
Number of features	83	95
Validation loss	1.77	**1.62**

Table: Performance of the same GCN model using extra node features.

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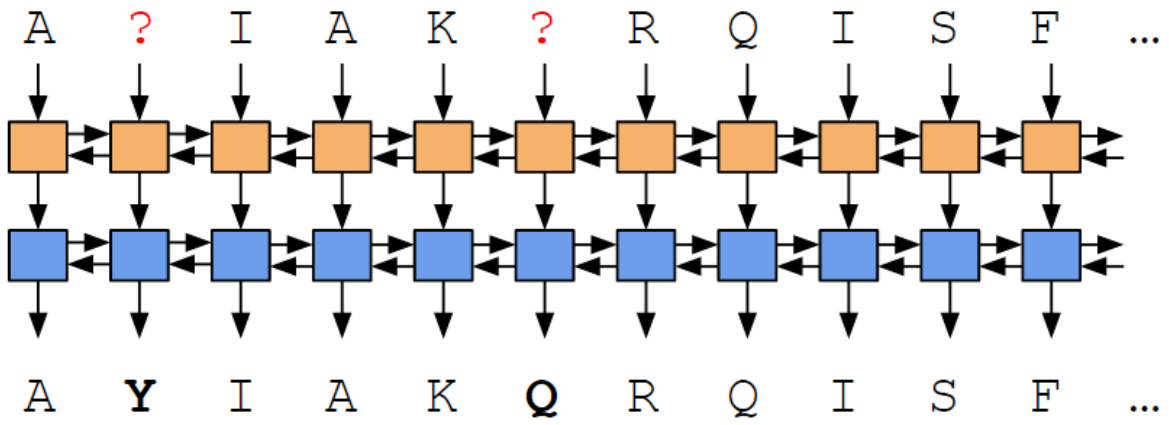
Masked language modelling with Bidirectional LSTM

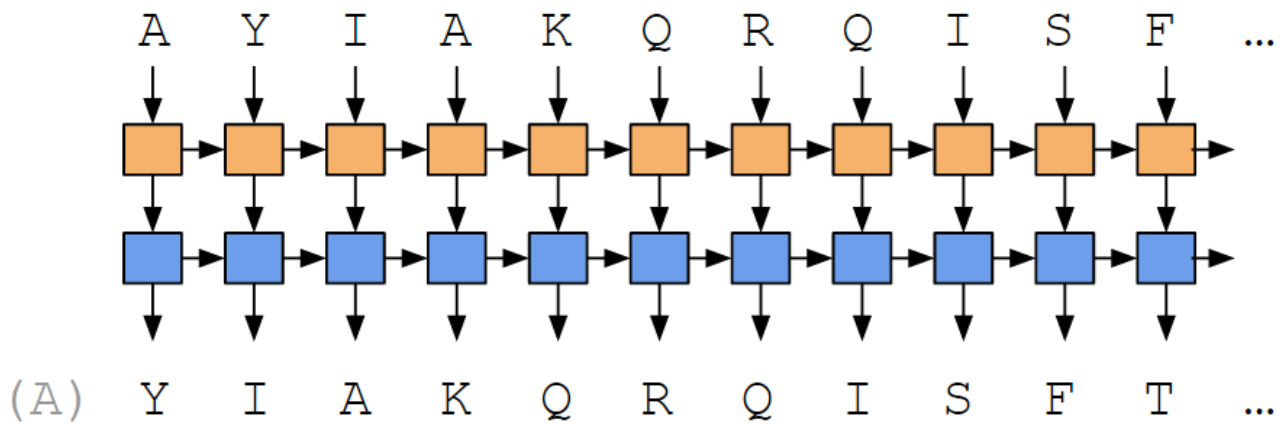
Pretraining task: masked language modelling



→ Quite bad...

Language modelling with LSTM

Pretraining task: language modelling



→ Already much better!

Performance with pretrained LSTM

Figure: Loss and accuracy during training with and without using a pretrained 2-layer LSTM for the node embeddings, before a GCN.

Combining different features

	Node features			
	default	default + extra features	LSTM	LSTM + extra features
Number of features	83	95	512	524
Validation loss	1.77	1.62	1.57	**1.49**

Table: Performance of the same GCN model using different node features. The default features from the dataset can be improved with additional features, while replacing them with a pretrained LSTM is even better.

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What is ESM-2?

- Transformer protein language model
  - Introduced by FAIR in 2019
  - Unsupervised pre-training on 250 millions protein sequences
- Main task is (atomic resolution) structure prediciton, SOTA model
- Trained with MLM objective

ESM-2 as a feature extractor

- One could just fine-tune the model with a classification head : quick overfitting
- Works better : train a model on the transformed dataset
  - Combinations of the hidden states as embeddings
  - Different sizes of ESM-2: 8M, 35M, 150M, 650M, 3B
- Different models :
  1. MLP
  2. GNN
  3. Multi Head Attention

Influence of the size of ESM-2

Figure: Loss and accuracy during training with respect to the size of ESM-2.

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Preventing overfitting

- Dropout (20%)

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Label smoothing

Extreme case: output probabilities are 0 or 1 (before label smoothing)
Test accuracy $= 85\%$, label smoothing $= 0.05$, 18 classes

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$$\Rightarrow \quad \mathcal{L}_{\text{test}} \approx -0.85 \log(1 - 0.05) - (1 - 0.85) \log \frac{0.05}{18 - 1}$$
$$\approx 0.92$$

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- Tuning the learning rate

Tuning the learning rate

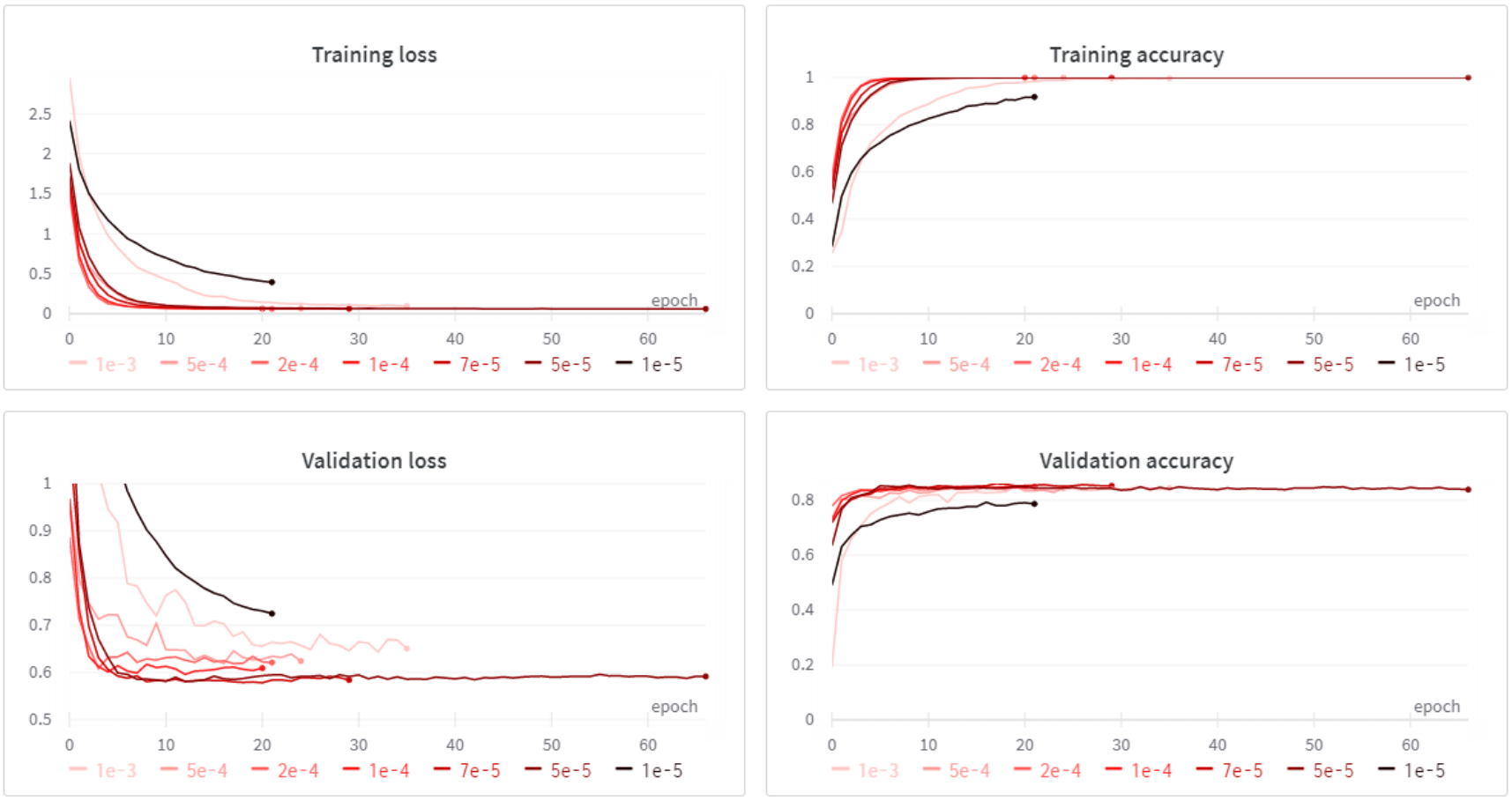

Figure: Loss and accuracy during training with respect to the learning rate, for train and validation data (same model, using ESM-2 3B).

Preventing overfitting

- Dropout (20%)
- Label smoothing (0.05)
- Reducing the embedding dimension (PCA or learned)
- Tuning the learning rate
- Averaging predictions of multiple models

Improvements with averaging

	Number of models			
	1	4	25	336
Average	0.684	0.638	0.628	**0.625**
Median	0.684	0.659	0.635	0.631

Table: Public score on Kaggle after aggregating the predictions of multiple models using ESM-2 650M, either with the average or the median.

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Scores of the models developed

	Sequence Baseline	GCN	GCN + LSTM	ESM-2 + MLP	ESM-2 + GNN	ESM-2 + MHA
Validation Loss	1.45	1.33	1.30	1.00	0.9	**0.4**
Validation Accuracy	$\lesssim 0.5$	0. 51	0.55	0.65	0.6	$\gtrsim$ **0.85**
Kaggle private score	1.68	1.51	1.55	1.18	1.21	**0.59**

Table: Best scores obtained for each method

- Best method : ESM-2 + MHA
- 1^{st} place on the leaderboard !

Tuning of the final solution : ESM-2 + MHA

ESM-2 embeddings with naive self attention layer is not enough. It scores only $\simeq 1.2$ of public score. In decreasing order, here is a list of hyper parameters with the greatest impact:

1. Size of the model : 3B
2. Number of models used for prediction (averaging) : 113
3. Combination of the hidden layers of ESM-2: (2, 13, 24, 35)
4. Label smoothing, dropout, initial learning rate: 0.5, 0.2, 7e-5
5. Hidden dimension, Number of queries, Number of heads : 128, 20, 4

Thank you!

Any question?