Midterm meeting: Bachelor thesis of Robin Ender

Date: *2025-06-12*

Attendees: *Robin Ender, Asis Hallab, Eric Schumbera*

Current status of phase separation prediction

- Many Phase Separation Predictors have emerged, yet the performance is still not optimal
  - the best ones use scalar features (e.g. percentage of IDR)
- Problems are:
  - Lacking Training Data
  - Bias towards proteins containing IDRs
- Idea:
  - Using the sequence (block decomposition) to predict PS and try a newly published data set

Repetition - Block Decomposition

- The block decomposition algorithm takes a protein sequence and a mapping
- It outputs a list of blocks that all have a certain word balance (“uniformity”)
- Steps to use it for neural networks:
  - Adjusting the output
  - Finding relevant mappings

Adjusting the output of the block decomposition algorithm

The block decomposition algorithm was modified to yield an output that can be used in a neural network:

Old Output:
[(5, 14),(15, 22)…]

New Output:
[0,0,0,0,1,1,1,…,2,2,2…]

- The list of tuples was converted to one list representing the sequence.
- Labels were created, representing the most common group(s).

Finding meaningful mappings

Seven Mappings were found (in literature) that relate to phase separation or are generally meaningful:

Aliphatic - Aromatic - Positive - Negative
RG-Mappings (two separate)
IDR-Mapping
Most meaningful 5 mapping
PiPi-Mapping (two separate)

Those were used to generate one block decomposition for each mapping per protein.

Data sets I

For now two different data sets were used:

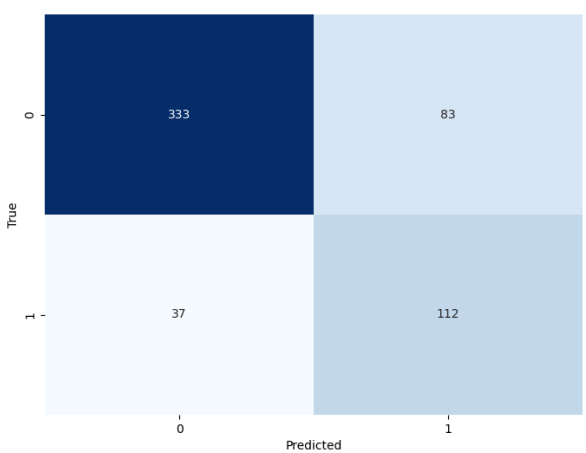
- PPMCLABs llps data set
  - created in an effort to create a dataset with an appropriate negative data set (many studies use RCSB Protein Data Bank, which are not guaranteed to be non phase separating)
  - contains 746 positive and 2077 negative entries

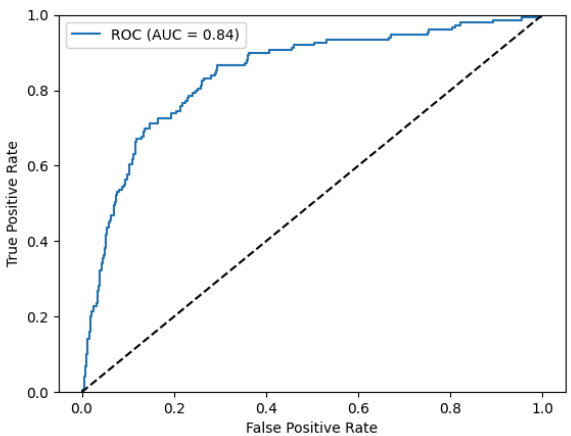
Data sets II

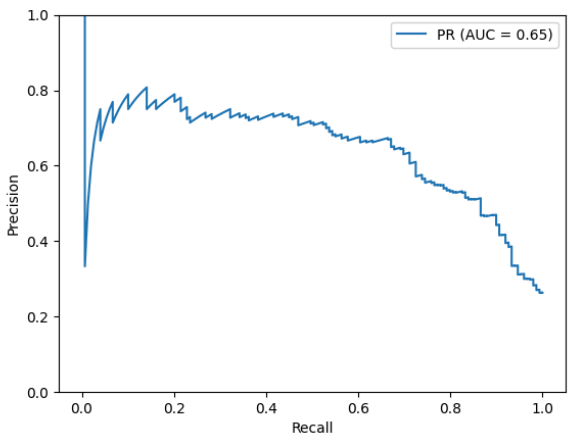
- PSPires data set
  - used to train PSPire, a recent well performing PS predictor addressing the difficulty of predicting phase separating proteins with no IDRs
  - contains 517 positive and around 10,000 negative entries

Test if a simple cnn model can learn from the data

To see if a cnn model was able to learn a basic 1 layer model was created and run on the PPMCLAB data set:

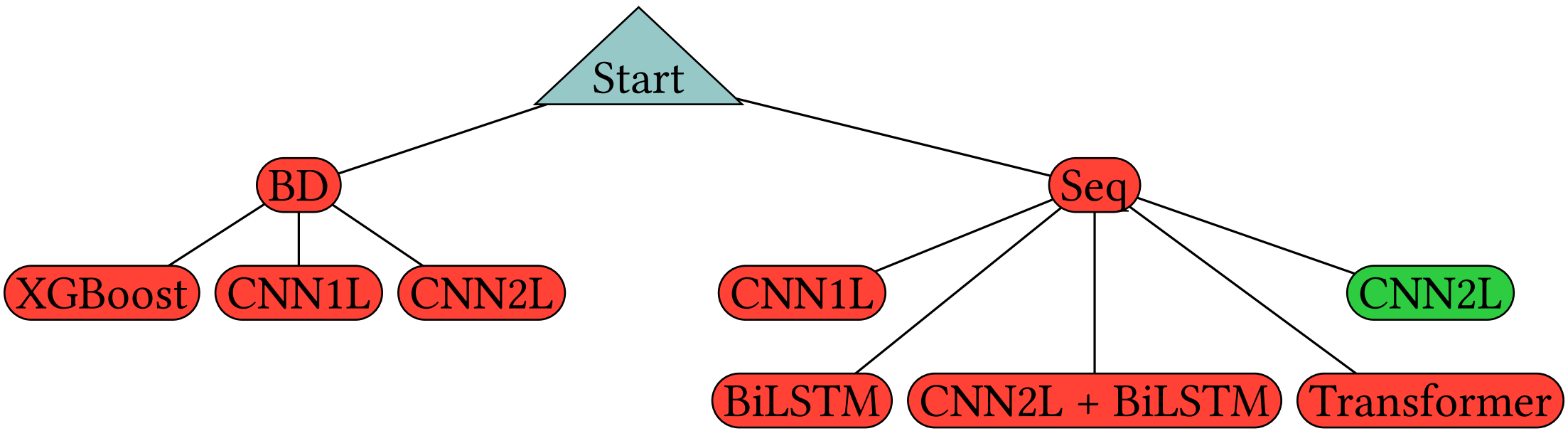




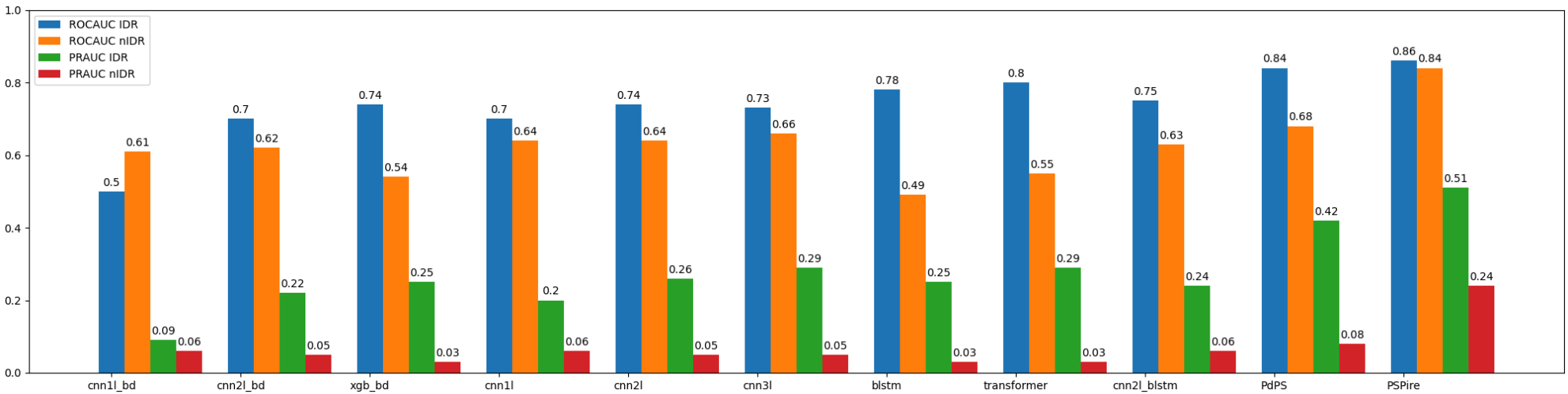


Testing different models

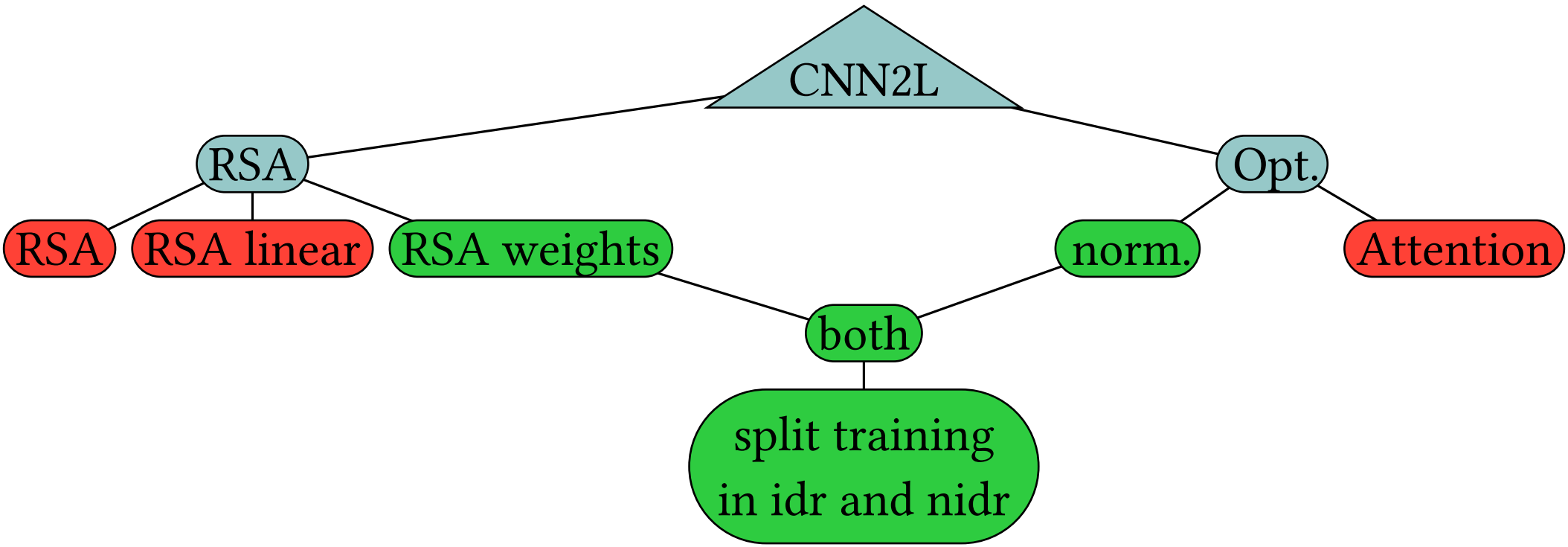
As the CNN2l model performed relatively good and was relatively quick in training it was used for further tests:



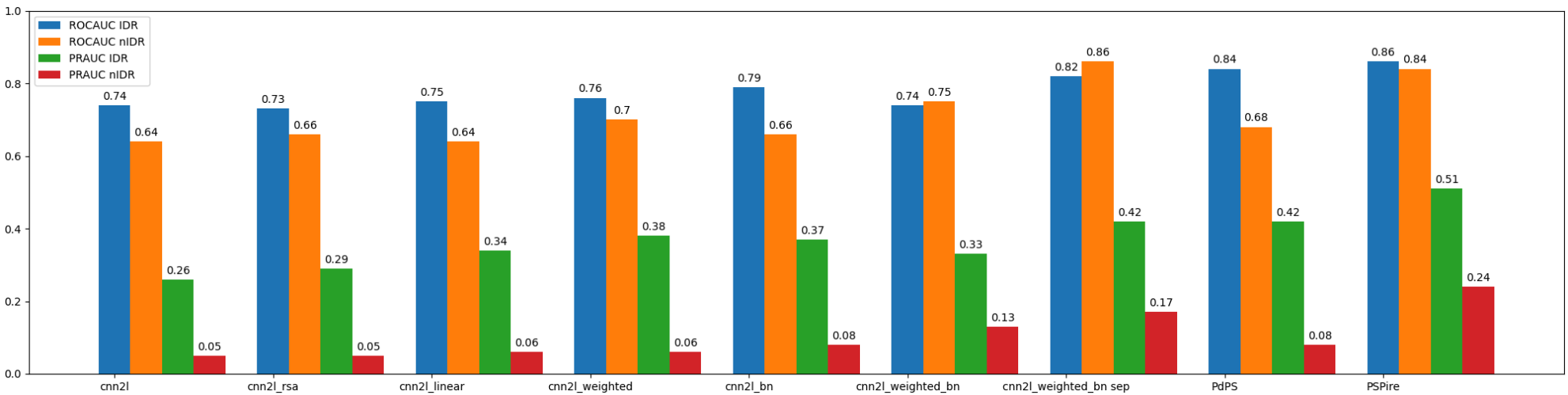
Performance of the initial models on PSPire data



Enhancing the CNN2L models



Performance of the new models



Performance on MLO data sets

PSPs	Dataset	Parameter	My model	PdPS	PSPire
noID-PSPs	G3BP1	ROCAUC	0.92	0.81	**0.93**
		PRAUC	0.36	0.18	**0.66**
	DACT1	ROCAUC	0.91	0.81	**0.93**
		PRAUC	0.43	0.18	**0.60**
	RNAGranule	ROCAUC	0.80	0.68	**0.90**
		PRAUC	0.11	0.08	**0.28**
	PhaSep	ROCAUC	**0.87**	0.65	0.80
		PRAUC	**0.71**	0.47	**0.71**
	DRLLPS	ROCAUC	**0.87**	0.68	0.85
		PRAUC	**0.76**	0.45	0.74

Performance on MLO data sets

PSPs	Dataset		My model	PdPS	PSPire
ID-PSPs	G3BP1	ROCAUC	0.76	0.86	**0.91**
		PRAUC	0.33	0.41	**0.58**
	DACT1	ROCAUC	0.72	0.85	**0.88**
		PRAUC	0.21	0.33	**0.35**
	RNAGranule	ROCAUC	0.82	0.82	**0.84**
		PRAUC	0.44	0.42	**0.48**
	PhaSep	ROCAUC	0.72	**0.74**	0.72
		PRAUC	0.72	**0.80**	0.79
	DRLLPS	ROCAUC	0.70	**0.76**	0.75
		PRAUC	0.72	0.77	**0.78**

Results in context of the initial idea of this work

- block decomposition can be used to predict phase separation
- but using the raw sequence yields better results
- therefore the focus has shifted to using the sequence and additional data to build a good phase separation predictor

Visualizing the results

- ROC AUC and PR AUC
- Confusion Matrix
- F1 Scores, Accuracy etc.
- bar plots / tables for comparison with other tools

What can / should be done in the remaining time?

- Add post translational modification data
- Cross validation of the final model
- Comparison of PSPire and my tool on the PPMCLAB data
- If there is time left, check for Driver and Client differences

Structure of the thesis

- Introduction
  - Block decomposition of protein sequences
  - Machine Learning in Bioinformatics
    - CNN
  - Liquid-Liquid Phase Separation
  - Current predictors and the difficulties
- Material
  - Data (explain and visualize data sets)
- Methods
  - Tools

- data preparation
- model architectures

- Results
- Discussion