

Part 1- Impact of the different model parameters and network characteristics in the prediction performance using BMRF.

Using human and yeast data, we choose values for the different model parameters (Appendix I, tables 1-3). Then, using chicken data, we defined a network for this species. The conclusions were as follows:

(i) Using human data

- Using domain information increases the overall performance considerably (0.043 higher AUC). Thus, domain information will be used
- The filters of number of GO terms does not seem to have an effect. However, this may be the case only in those cases in which the number of GO terms remains high.
- Increasing the number of folds in the k-validation from 2 to 5 or 10 leads to an improvement of AUC of 0.026 and 0.037, respectively. K:10 will be used whenever possible.
- Due to time constraints, we will apply the filterminGOsize:20 and maxGOsize:0.1. However, the analysis could be extended to GO terms withminGOsize>9.

(ii) Using yeast data

- The GO-size filters affect the overall prediction performance. We observed that as the filter form minGOsize becomes more strict and the filter for maxGOsize becomes less strict, the overall prediction performance increases.
- the GO-size filter seems to cause some alterations at the level of individual GO terms. In line with this, the prediction of one GO term are not entirely independent of the other GO terms considered in the analysis.
- We will perform the analysis with 20 replicates
- **Subsetting...**

(iii) Using chicken data

- A Pearson correlation of 0.35 will be considered

(iv) Other conclusions.

- Non-validated data seem to be more reliable for yeast than for humans.

Then, we investigated which characteristics in the network data have a larger impact of the prediction performance. For this, we used data from different species, since the network data differs considerably between these (Tables 7-9 in Appendix I). For a more detailed description of the differences in data between the species, as well as the data sources, see Tables 4-7 and Illustrations 1-3 in Appendix I.

The main conclusions from part 1b are:

- epp/tpepp seem to be the network parameter with a larger impact in the prediction performance.
- The epp/tpepp standard error is very similar for the species considered.
- Reducing Epn increases the performance
- Approaches like Positive-Unlabelled learning can improve these parameters.

Part 2 – BMRF results

	yeast_ppi	yeast_co	humans	Chicken_07	Chicken_035	Chicken_035_filter8
# GO terms	1,073	1,104	1,982	9	142	347
mean AUC	0.734	0.775	0.712	0.728	0.762	0.754
sd AUC	0.090	0.080	0.083	0.062	0.077	0.093
median AUC	0.736	0.775	0.717	0.718	0.771	0.765

Table 1: Overall prediction performance for the different species using BMRF

The across replicates for a given GO term was around 0.015

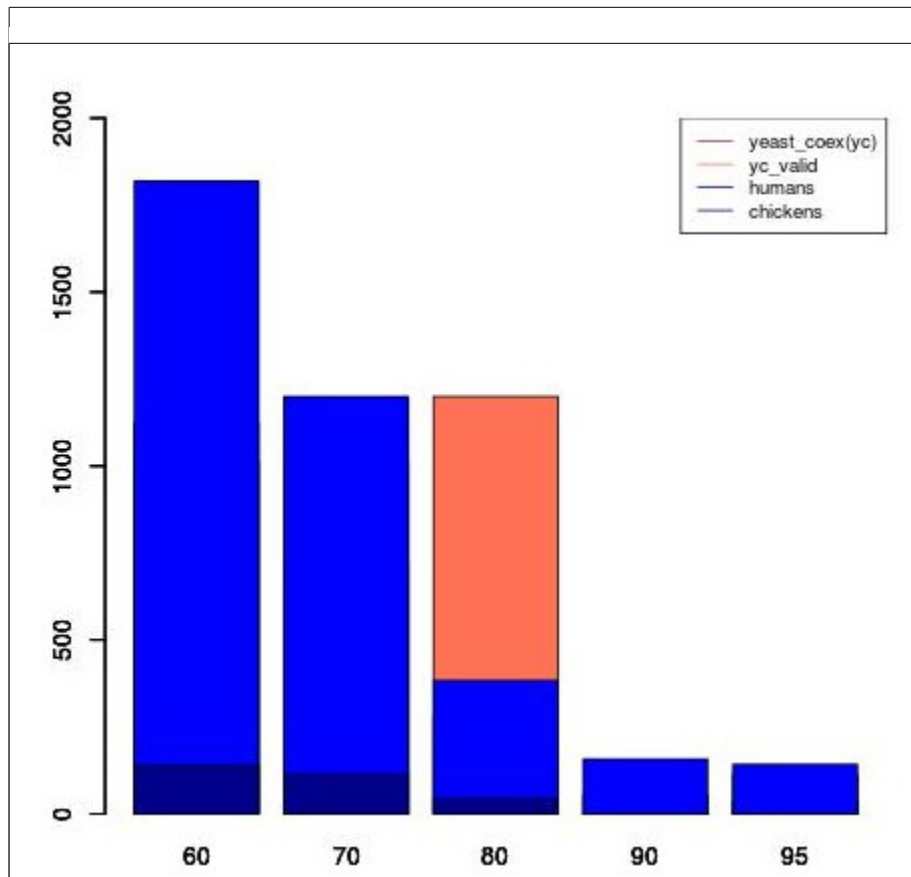


Illustration 1: Number of GO terms with AUC above a certain value, for the different species

Part 3- Results using PU.

#RN	AUC PU.BMRF	sd AUC PU.BMRF	AUC BMRF	sd AUC BMRF
2000	0.677	0.033	0.642	0.032
4000	0.677	0.034	0.63	0.032
6000	0.655	0.033	0.624	0.028
8000	0.641	0.033	0.617	0.03

Table 2: Comparison accuracy of prediction BMRF vs PU-BMRF

We observed a correlation of 0.67 between the number of labels of the GO-term and the increase in accuracy when PU-bMRF was used instead of BMRF, indicating that PU is more effective when the number of known associations is large.

Accuracy in the extraction of RN:

Average value of tolerance (sd)			
tol_AUC85	tol_AUC90	tol_AUC95	tol_AUC1
0.885(0.088)	0.96(0.15)	1.2(0.346)	1.42(0.438)

Table 3: Values of "tolerance" that were required for different values of AUC in the process of extraction.

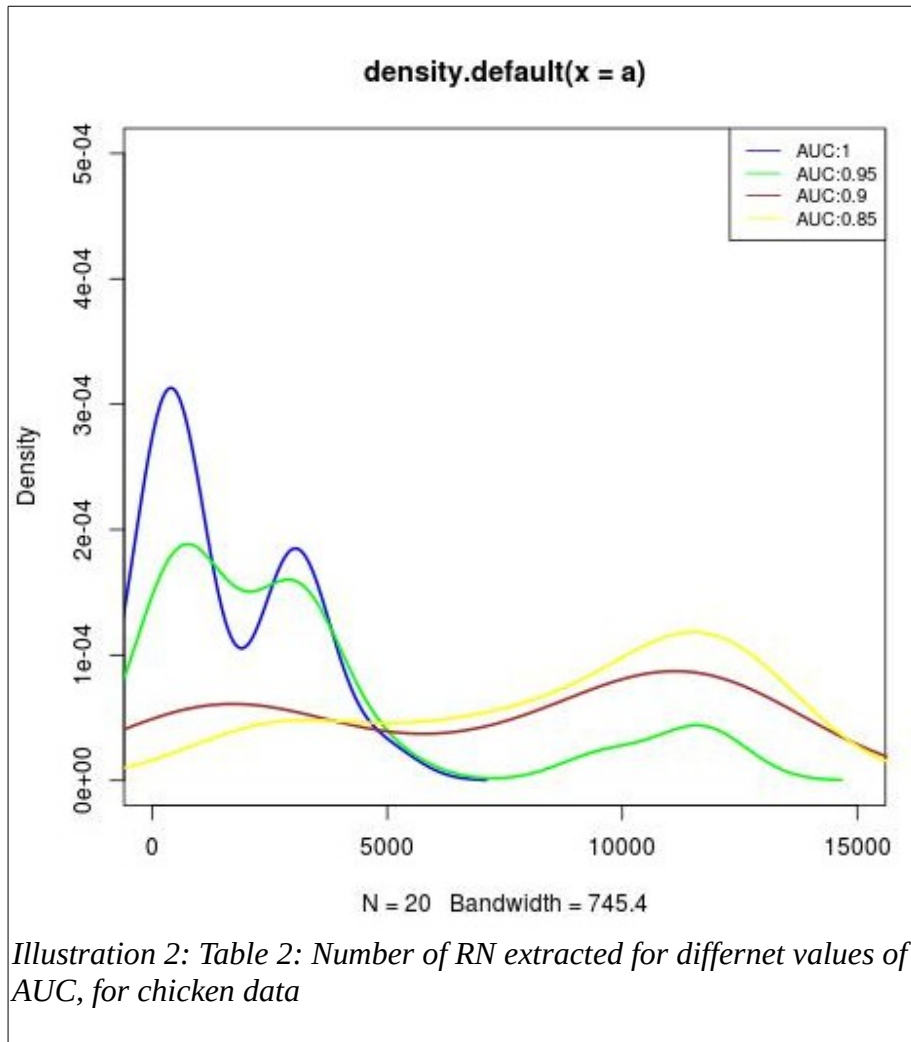


Illustration 2, shows the distribution of the number of RN that were extracted for different values of AUC in the process of extraction. As expected the number of extracted RN becomes lower and more stable as we become more strict (higher value of AUC).

Part 4- Biological support of the approach

	Average	
	50% less general GO-terms	50% more general GO-terms
betweness		
closeness		
transitivity		

	Average	
	Network of genes that are only on the 50% less general GO- terms	Network of genes that are only on 50% more general GO-terms
betweness		
closeness		
transitivity		