

HyPnOBrain

your homology based HPO neural network predictor

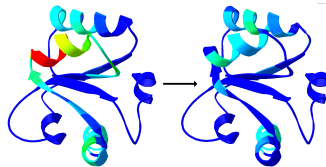
Jonathan Boidol, Rene Schoeffel, Yann Spöri

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Homology based function prediction

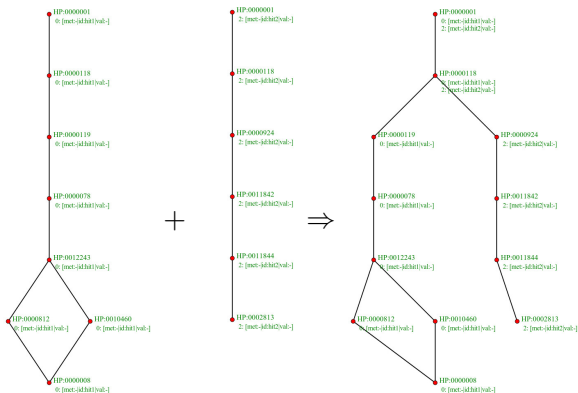
General approach:

- ▶ Search for annotated similar sequences (hits) and transfer annotations
- ▶ HPO is hierarchical: Merge found annotations from different hits
- ▶ Calculate confidence for every annotation from some distance measure to the hits



Preparations and Predictor input

- ▶ Prepare databases for annotated sequences
- ▶ Represent HPO Graph in predictor
- ▶ Merge trees corresponding to hits



Derived features

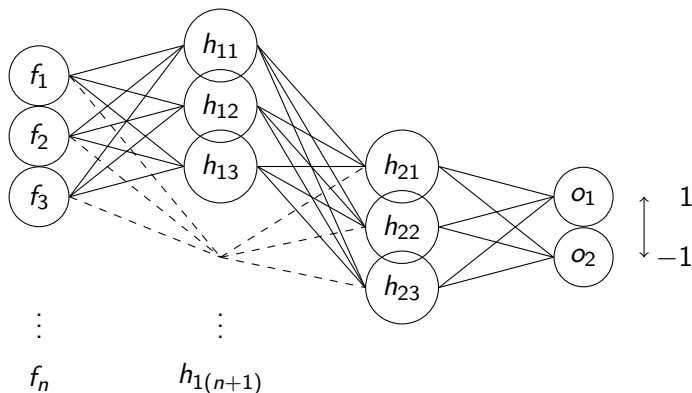
- ▶ each node is assigned 12 features derived from the merged tree

- ▶ length of query sequence
- ▶ number of hits
- ▶ longest hit
- ▶ avg. hit
- ▶ min. E-value
- ▶ avg. E-value
- ▶ product of E-values
- ▶ best E-value from blast or hhblits
- ▶ min. height in HPO-tree
- ▶ max. height in HPO-tree
- ▶ max. overlap of query and all hits
- ▶ length of best hit

[3, 0.0074, 0.45, 4.2e-7, 84, ...]

- ▶ use neural network to calculate confidence per node

Final network architecture

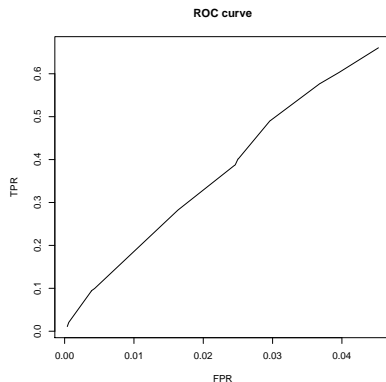
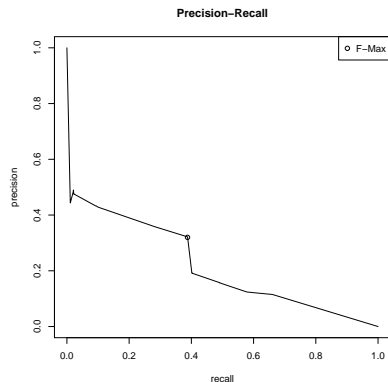


- ▶ different architectures evaluated
- ▶ fully connected net with two hidden layers
- ▶ two output nodes trained for the two possible predictions
- ▶ difference of predictions as confidence

Validation

- ▶ Inspection of the dataset shows: Most sequences have pairwise similarity $< 80\%$
 \Rightarrow no significant bias in the dataset caused by very close homologs
- ▶ 10-fold crossvalidation over 2815 sequences
- ▶ Calculate precision and recall per test sequence and average over all sequences
- ▶ Final model trained on all sequences

Results



- ▶ F-measure 0.35 ± 0.03 (at confidence level 0.34)
- ▶ Precision 0.32 ± 0.04 (at same confidence level)
- ▶ Recall 0.39 ± 0.10 (at same confidence level)

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Submit

Protein Sequence:

Either input your sequence to predict here:

```
>sp|Q03154|ACY1_HUMAN Aminoacylase-1 OS=Homo sapiens GN=ACY1 PE=1 SV=1
MTSKGPEEEHPSVTLFRQYLRI RTVQPKPDYGA AVAFEE TARQLGLGCQKVEVAPGYV
TVLTWPGTNP TLLSILLNSHTDVVPV FKEHWSHDPFEAFKDSEGYIYARGAQDMKCVSIQ
YLEAVRRLKVEGHRFPRTIHM TFPD EEVGGHQGMELFVQRPEFHALRAGFALDEGIANP
TDAFTVFYSESPWWVRVTSTGRPGHASRFMEDTAAEKLHKV VNSILAFREKEWQRLQSN
PHLKEGSVTSVNLTKLEGGVAYNVIPATMSASFDFRVAPD VDFKAFEEQLQSWCQAAGEG
VTLEFAQKWMHPQVTP TDDSNPWWAAFSRVCKDMNLTLEPEIMPAATDNRYIRAVGVPAL
GFSPMNRTPVLLHDHDERLHEAVFLRGVDIYTRLLPALASVPALPSD
```

or upload a fasta file: Keine ausgewählt

Settings:

Performe fast prediction: ☒ yes ☐ no

- ▶ <https://dataminer.informatik.tu-muenchen.de/~spoeri/>
- ▶ file or text field input
- ▶ option to speed prediction up by restricting hits to 6 best

Productive waste of time aka: Future Improvements

- ▶ Incorporate SVG output of results in webinterface
- ▶ Feature evaluation and improvement
- ▶ Investigate effect of homologs in dataset
- ▶ Different network architectures
- ▶ Other machine learning devices
- ▶ Data mining in other sources
- ▶ ...