

AmyloGram: a novel predictor of amyloidogenicity

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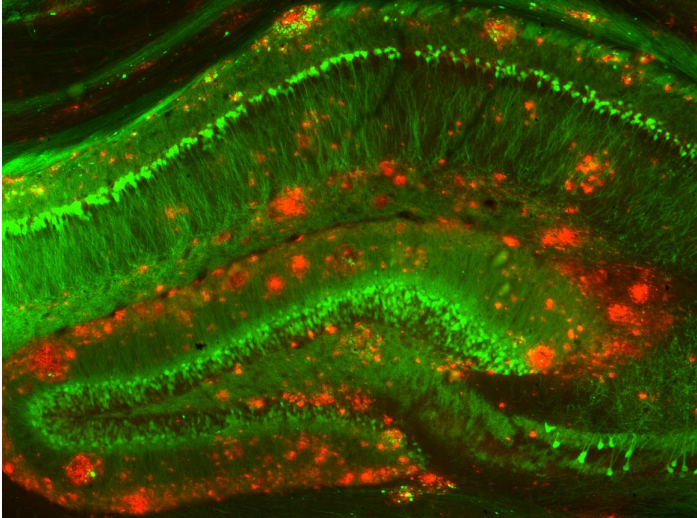
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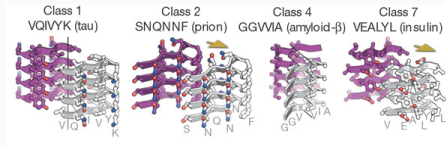
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Amyloids

Proteins associated with various neurodegenerative disorders (e.g., Alzheimer's, Parkinson's, Creutzfeldt-Jakob's diseases) creating harmful aggregates.



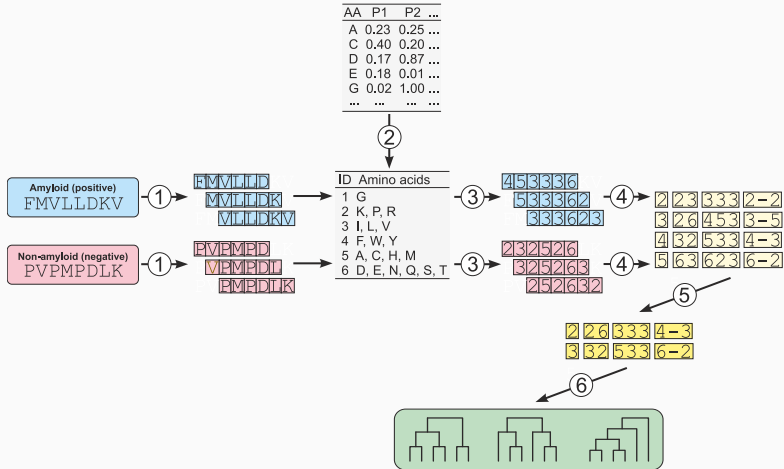
The aggregation of amyloids is initiated by 6- to 15-residue segments called hot spots, diverse subsequences that form unique zipper-like β -structures.



Sawaya et al. (2007)

Analyze structure of hot spots and create a novel predictor of amyloids.

Learning framework



Reduced amino acid alphabets

- 17 measures handpicked from AAIndex database
 - size of residues,
 - hydrophobicity,
 - solvent surface area,
 - frequency in β -sheets,
 - contactivity
- 524 284 amino acid reduced alphabets with different level of amino acid alphabet reduction (three to six amino acid groups).

Quick Permutation Test

Informative n-grams are usually selected using permutation tests.

During a permutation test we shuffle randomly class labels and compute a defined statistic (e.g. information gain). Values of statistic for permuted data are compared with the value of statistic for original data.

$$\text{p-value} = \frac{N_{T_P > T_R}}{N}$$

$N_{T_P > T_R}$: number of cases, where T_P (permuted test statistic) has more extreme values than T_R (test statistic for original data).

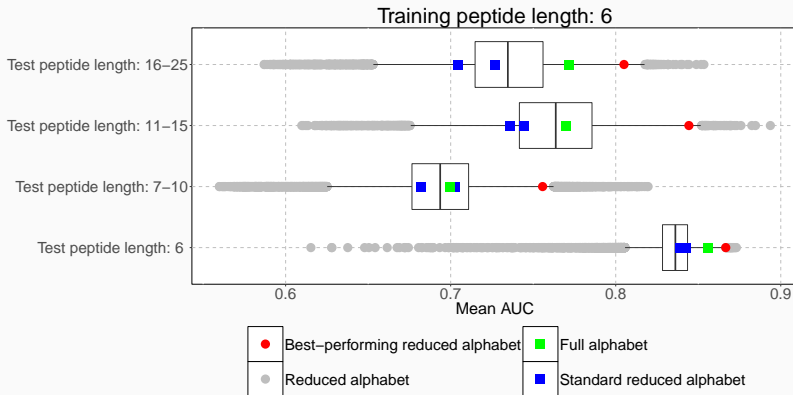
N : number of permutations.

Quick Permutation Test is a fast alternative to permutation tests for n-gram data. It also allows precise estimation of p-value.

QuiPT is available as part of the **biogram** R package.

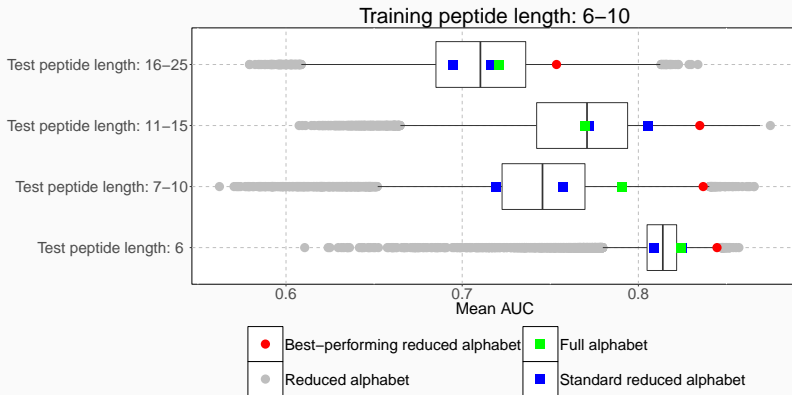
Results

Cross-validation



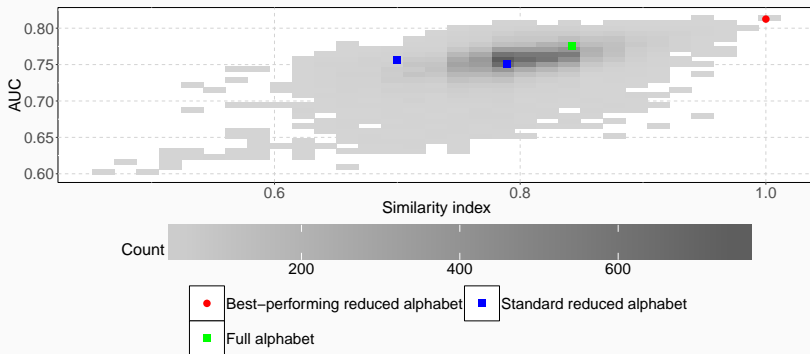
Hinges of boxes correspond to the 0.25 and 0.75 quartiles. The bar inside the box represents the median. The gray circles correspond to the reduced alphabets with the AUC outside the 0.95 confidence interval.

Cross-validation



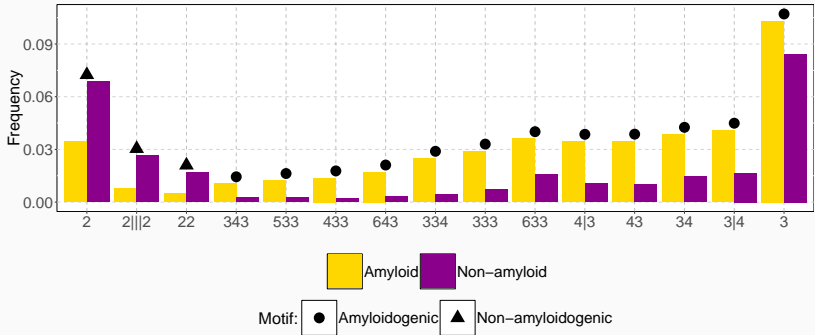
Hinges of boxes correspond to the 0.25 and 0.75 quartiles. The bar inside the box represents the median. The gray circles correspond to the reduced alphabets with the AUC outside the 0.95 confidence interval.

Similarity index



Similarity index (Stephenson and Freeland, 2013) measures the similarity between two reduced alphabets (1 - identical, 0, totally dissimilar).

Informative n-grams



Dots and triangles denote n-grams occurring in motifs found in respectively amyloidogenic and non-amyloidogenic sequences (Paz and Serrano, 2004).

Benchmark results

Classifier	AUC	MCC
AmyloGram	0.8972	0.6307
PASTA 2.0(Walsh et al., 2014)	0.8550	0.4291
FoldAmyloid (Garbuzynskiy et al., 2010)	0.7351	0.4526
APPNN (Família et al., 2015)	0.8343	0.5823

The predictor based on the best-performing alphabet, called AmyloGram, was benchmarked against the most popular tools for the detection of amyloid peptides using an external data set *pep424*.

Our software is available as a web-server:
`smorfland.uni.wroc.pl/amylogram`.

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References

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