# AmyloGram 2.0: MBO in the prediction of amyloid proteins

Dominik Rafacz* [1] Stefan Rödiger [2] Małgorzata Kotulska [3] Michał Burdukiewicz [1]

[1]Warsaw University of Technology [2]Brandenburg Technical University Cottbus-Senftenberg [3]Wrocław University of Science and Technology

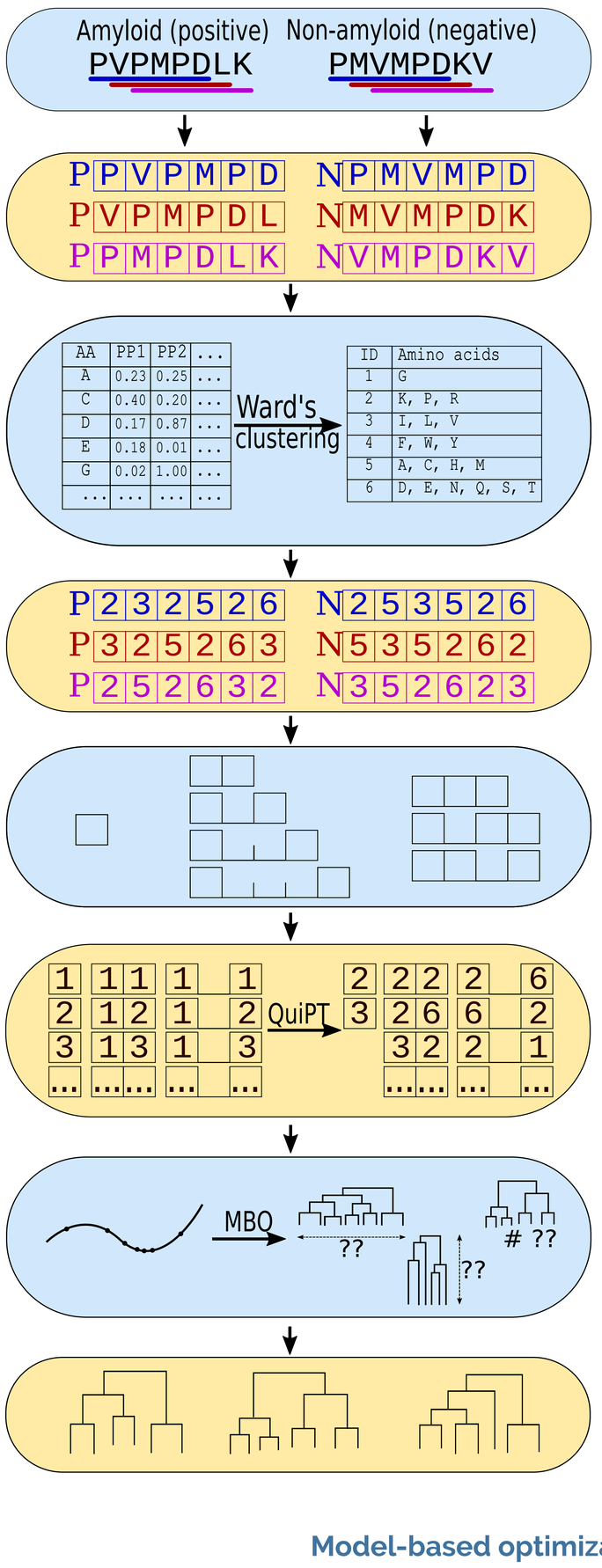
*dominikrafacz@gmail.com ♢ DominikRafacz@github.com

## Introduction

Amyloids are self-aggregating proteins associated with neurodegenerative disorders. The *in silico* identification of amyloid proteins is challenging because their amino acid composition can be extremely variable. Recently, we were able to identify motifs occurring in amyloid sequences and create a machine learning tool, AmyloGram [1], which has outperformed other predictors of amyloids. AmyloGram focuses on identifying amino acid motifs responsible for aggregation, thus providing researches with insights about structural sources of amyloidogenesis.

## AmyloGram workflow

AmyloGram 2.0 is an improved version of the AmyloGram. The improvement in the 2.0 version is the usege of Bayesian hyperparameter tuning.




Source data: peptides with known amyloidicity status. Overlapping hexamers are marked by horizontal lines.

Extraction of overlapping hexamers with ascribed the amyloid status taken from their source peptide (P-positive, N - negative).

Clusterization of amino acids into an encoding using a combination of various physicochemical properties (PP).

Reduction of the amino acid alphabet in hexamers.

Extraction of n-grams. From each hexamer, we extracted continuous and discontinous n-grams with the length n = 1, 2 or 3.

Selection of informative n-grams with Quick Permutation Test (QuiPT).

Seeking for optimal hyperparameters for a classifier using model based optimization (MBO).

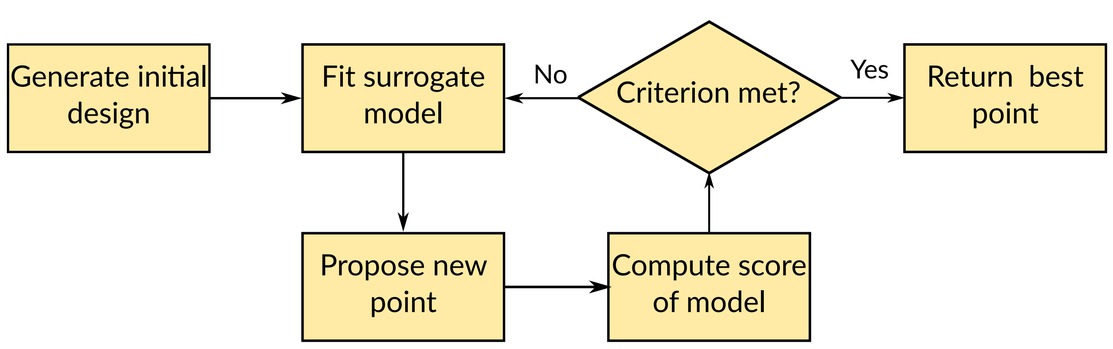
Training of a random forest classifier using the parameters determined in the previous step.

## Model-based optimization

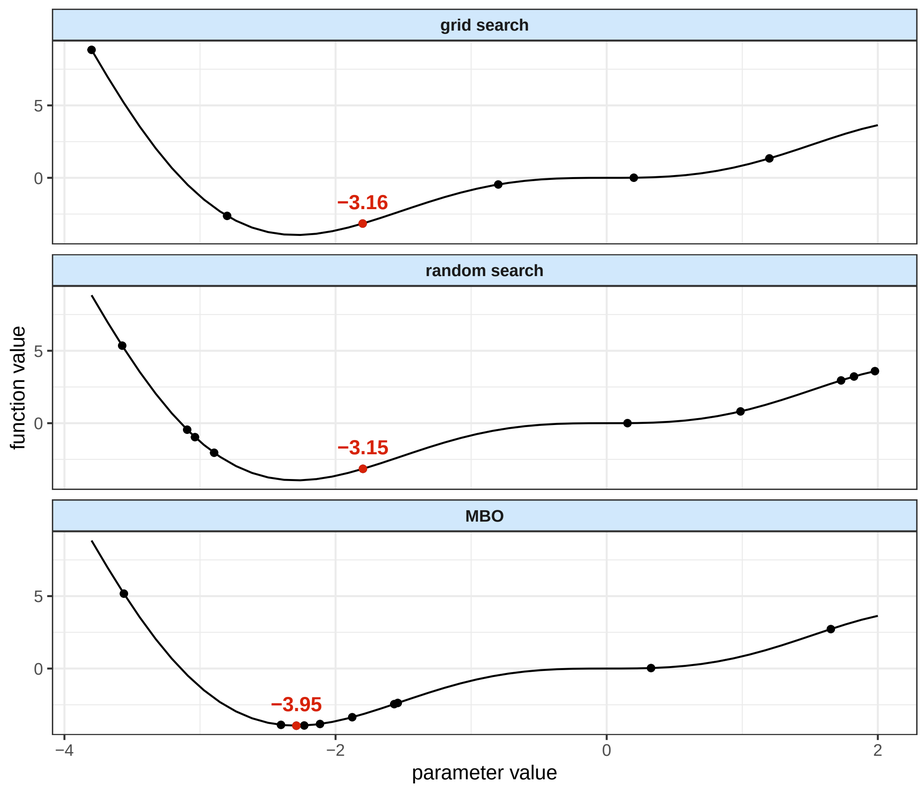
The model-based optimization method is one of the possible techniques of discovering optimal hyperparameters for a model in machine learning. Here we treat the model as a function from space of hyperparameters into space of possible model performance values. After initializing surrogate model $\hat{f}$, the following steps are repeated until some of stopping criterions are met:

1. A set of points $\mathbf{x}^{(\mathbf{i})}$ in the hyperparameters space is proosed basing on values of $\hat{f}$.
2. Value of performance of destination model $f$ is calculated in proposed points $\mathbf{x}^{(\mathbf{i})}$ (model is fit with given set of hyperparameters).
3. Points $\mathbf{x}^{(\mathbf{i})}$ with corresponding values $\mathbf{y}^{(\mathbf{i})}$ of model $f$ are used to fit surrogate model $\hat{f}$

After reaching certain stoping criterion, the best point $\mathbf{x}^{(\mathbf{i})}$ is returned.
MBO framework used by us is `mlrMBO` [2].

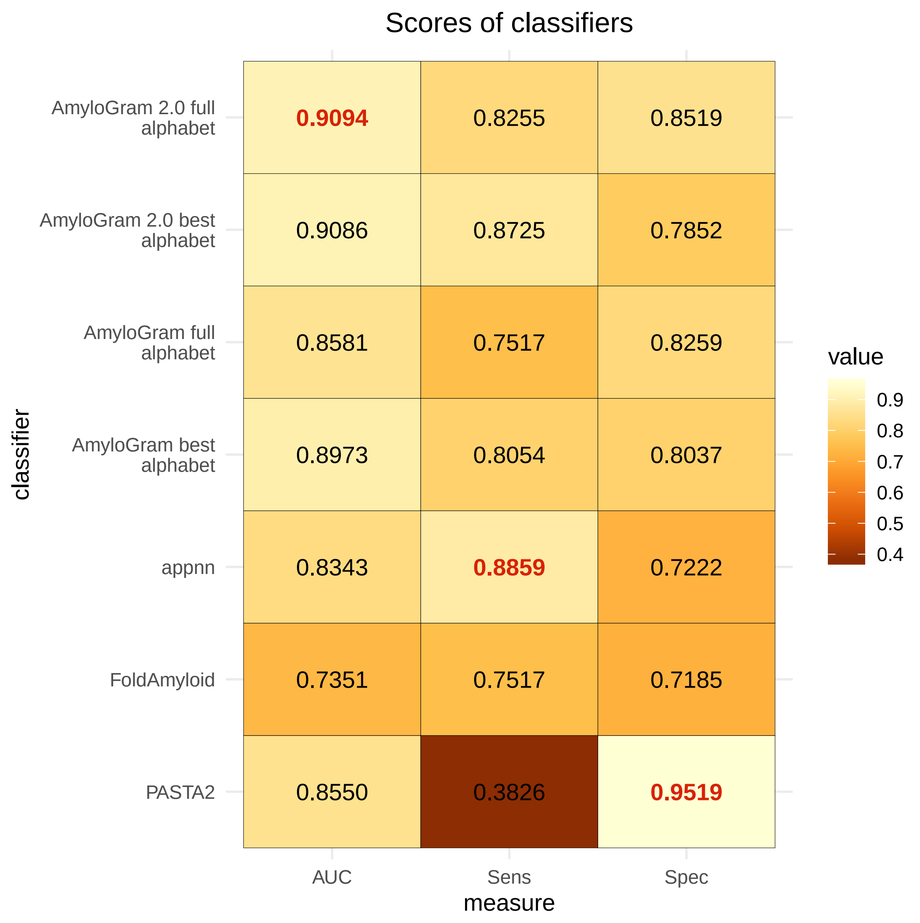



## Comparison of methods of hyperparameters tuning




Grid search method seeks for the optimal value of hyperparameter only in equally-spaced points that are defined by the user. Random search method relies on randomly chosen points in parameter space and is empirically better than the previous one. The model-based optimization seeks for improvement of prediction performance using results of its previous iterations.

## AmyloGram 2.0 performance




## Results and discussion

Thanks to the usage of MBO, on the pep424 dataset AmyloGram 2.0 reached AUC 0.91. Moreover, the new version of AmyloGram can detect aggregation-prone regions in proteins and explain which amino acid motifs are contributing to the amyloidogenicity. We cross-validate motifs and protein regions detected by our tool with experimental data.

AmyloGram is available primarily as the web server (http://www.smorfland.uni.wroc.pl/shiny/AmyloGram/) but can be also accessed as standalone software and the R package.

## Acknowledgements

## Bibliography

[1] Michał Burdukiewicz, Piotr Sobczyk, Stefan Rödiger, Anna Duda-Madej, Paweł Mackiewicz, and Małgorzata Kotulska. Amyloidogenic motifs revealed by n-gram analysis. *Scientific Reports*, 7(1):12961, October 2017.

[2] Bernd Bischl, Jakob Richter, Jakob Bossek, Daniel Horn, Janek Thomas, and Michel Lang. mlrMBO: A Modular Framework for Model-Based Optimization of Expensive Black-Box Functions. March 2017.