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

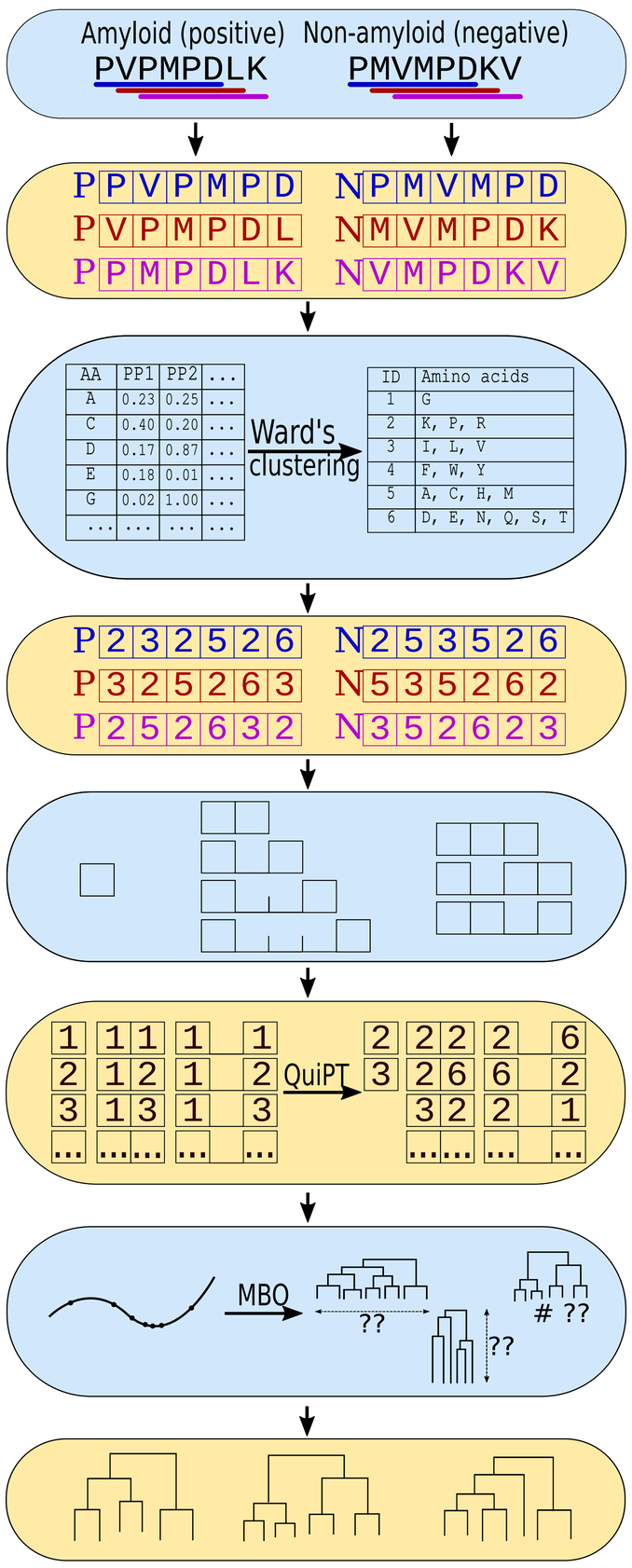
*dominikrafacz@gmail.com ♢ DominikRafacz@github.com

Introduction

Amyloids are proteins that tends to aggregate. Their aggregates are causes of neurodegenerative disorders. The in silico identification of amyloids 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, 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. Its principle of operation is very similar - a novelty is the use of 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

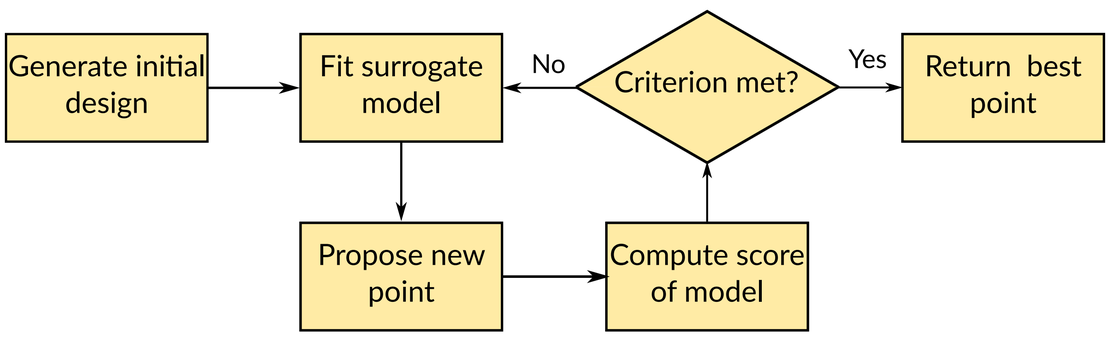
Model-based optimization method is one of possible techniques of discovering optimal hyperparameters for a model in machine learning. Here we treat model as a function from space of hyperparameters into space of possible model performance values. Computing model performance in numerous points of hyperparameters space is too expensive, so we are trying to estimate the model performance function using so-called surrogate model. It seeks for regions of space where optimal results are more probable to occur basing on previous computations.

After initialising surrogate model $\hat{f}$, the following steps are repeated until some of stoping criterions are met:

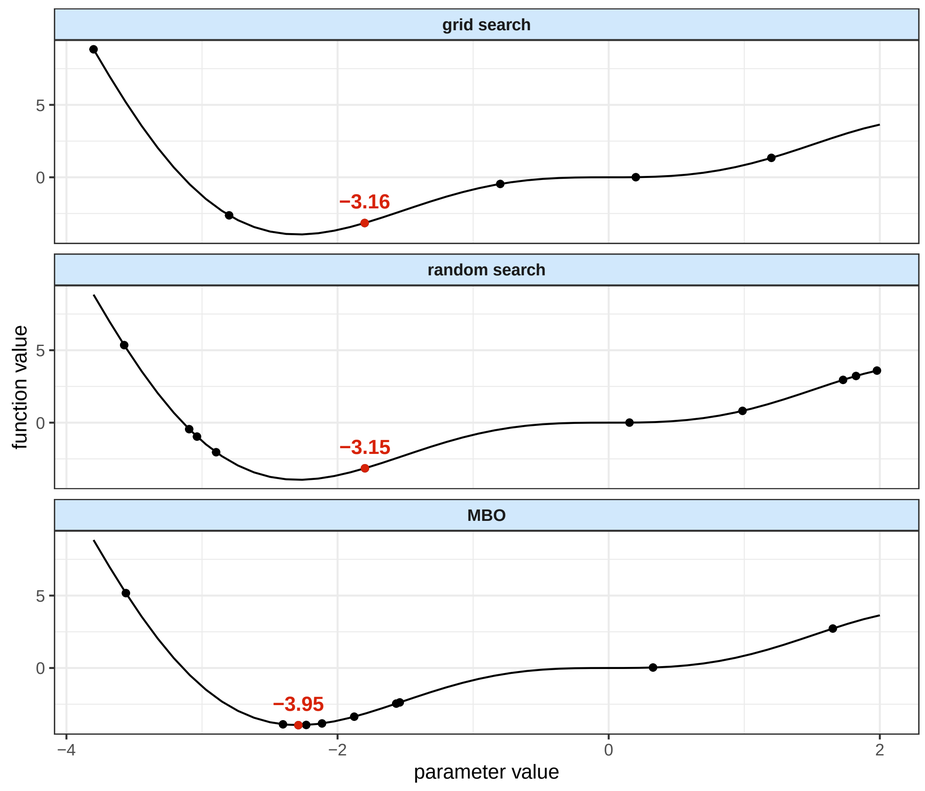
1. A set of points $\mathbf{x}^{(\mathbf{i})}$ in the hyperparameters space is proosed basing on values of $\hat{f}$.
2. Value of performance of destination model f is calculated in proposed points $\mathbf{x}^{(\mathbf{i})}$ (model is fit with given set of hyperparameters).
3. Points $\mathbf{x}^{(\mathbf{i})}$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

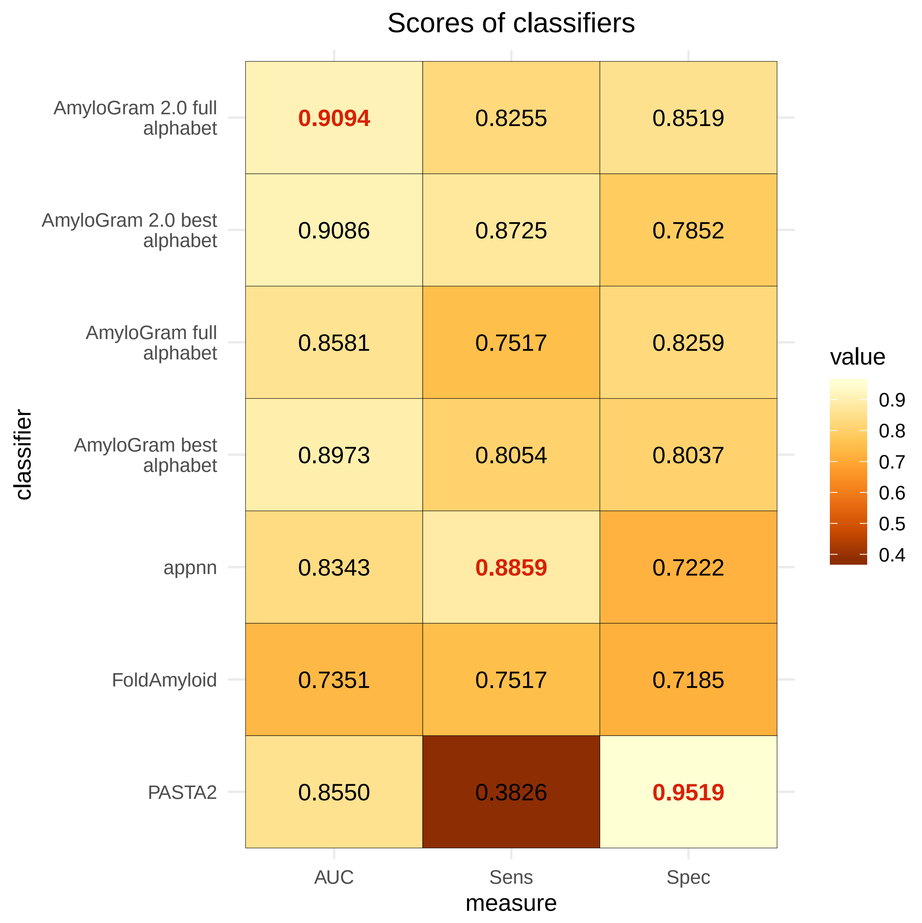


Comparison of methods of hyperparameters tuning



Grid search method seeks for optimal value of hyperparameter only in equally-spaced points that are defined by user. Random search method relies on randomization of points that are being tested and is empirically better than the previous one. Model-based optimization is the one method that actually decides how to change the parameter basing on the previous results.

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 is able to 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