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Statistical Computing 2016

Abstracts der 48. Arbeitstagung

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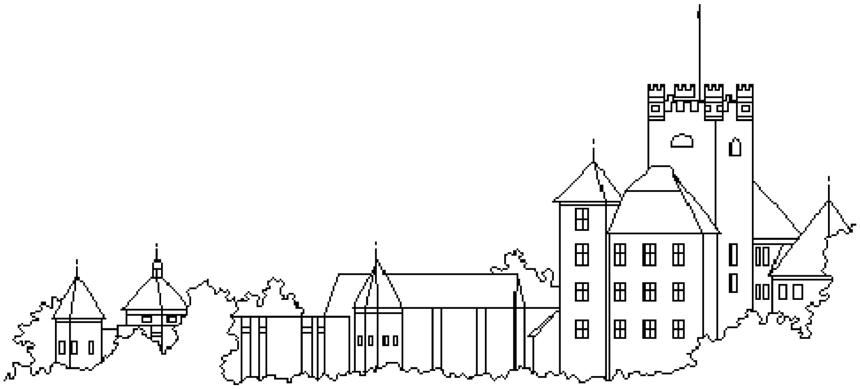
Statistical Computing 2016



48. Arbeitstagung

der Arbeitsgruppen Statistical Computing (GMDS/IBS-DR), Klassifikation und Datenanalyse in den Biowissenschaften (GfKl).

17.07. - 20.07.2016, Schloss Reisensburg (Günzburg)

Workshop Program

Sunday, July 17, 2016

18:00-20:00		**Dinner**
20:00-21:00		**Chair: H. A. Kestler**
20:00-21:00	Eyke Hüllermeier (Paderborn)	Superset learning and data imprecisiation

Monday, July 18, 2016

09:15-09:30		**Opening of the workshop: H. A. Kestler, M. Schmid**
09:30-10:30		**Chair: A. Groß**
09:30-09:50	Rainer Schuler (Ulm)	Counting the number of molecules of a single mRNA species
09:50-10:10	Jörn Lötsch (Frankfurt)	Process pharmacology: Using computational functional genomics knowledge to connect drugs with biological processes
10:10-10:30	Sebastian Krey (Köln)	Modeling and Calibration of robust Gas Sensors
10:30-11:00		**Coffee Break**
11:00-15:00		**Chair: M. Schmid**
11:00-12:00	Peter Chronz (Göttingen)	Introduction to Julia
12:00-13:30		**Lunch**
13:30-15:00	Tutorial: Peter Chronz (Göttingen)	Hands-on Introduction to Julia: Simplicity, Expressiveness, and Performance
15:00-15:30		**Coffee Break**
15:30-21:00	Social Program (Ulm)	Nabada (Schwörmontag)

Tuesday, July 19, 2016

09:30-10:30		**Chair: L. Lausser**
09:30-09:50	Janek Thomas (München)	Stability selection for boosted generalized additive models for location scale and shape
09:50-10:10	Tobias Hepp (Erlangen)	Assessing the significance of effects in boosted location and scale models
10:10-10:30	Andreas Mayr (Erlangen)	Boosting distributional regression models for multivariate responses
10:30-11:00		**Coffee Break**
11:00-12:00		**Chair: B. Bischl**
11:00-11:20	Sarah Friedrich (Ulm)	GFD: An R-package for the Analysis of General Factorial Designs - along with a Graphical User Interface
11:20-11:40	Thomas Welchowski (Bonn)	kernDeepStackNet: An R package for tuning kernel deep stacking networks
11:40-12:00	Julian Schwab (Ulm)	Implementation and Simulation of Boolean Networks on FPGAs
12:00-13:30		**Lunch**
13:30-15:00		**Chair: B. Lausen**
13:30-13:50	Moritz Hanke (Bremen)	A small REvolutioN and modified temporal centrality measures are needed for incomplete graph sequences of dynamic networks
13:50-14:10	Andre Burkovski (Ulm)	Performance of ordinal-scaled prototype-based classifiers on microarray datasets
14:10-14:30	Elisabeth Waldmann (Erlangen)	Boosting Joint Models for Longitudinal and Time-to-Event Data
14:30-15:00	Thomas Villmann (Mittweida)	Classification Certainty and Reject Options in Learning Vector Quantization
15:00-15:30		**Coffee Break**
15:30-16:50		**Chair: E. Sträng**
15:30-15:50	Bernd Bischl (München)	Multi-Objective Parameter Configuration of Machine Learning Algorithms using Model-Based Optimization
15:50-16:10	Philipp Probst (München)	On the Hyperparameter Settings of Random Forest
16:10-16:30	Lyn-Rouven Schirra (Ulm)	Feature selecting multi-class classification
16:30-16:50	Laura Beggel (München)	Anomaly Detection with Shapelet-Based Feature Learning for Time Series
17:00-18:00		Working group meeting on **Statistical Computing 2017** and other topics (all welcome)
18:00-20:00		**Dinner**

Wednesday, July 20, 2016

09:30-10:30		**Chair: J. Kraus**
09:30-09:50	Alexander Engelhardt (München)	Implementing an EM algorithm for partially dependent data
09:50-10:10	Pascal Schlosser (Freiburg)	Netboost: Boosting supported network analysis for highdimensional genomic datasets
10:10-10:30	Leonie Weinhold (Bonn)	A Statistical Model for the Analysis of Beta Values in DNA Methylation Studies
10:30-11:00		**Coffee Break**
11:00-12:00		**Chair: E. Hüllermeier**
11:00-11:20	Gunnar Völkel (Ulm)	Automated Design of Search Algorithms for Feature Set Ensembles
11:20-11:40	Werner Adler (Erlangen)	Ensemble Pruning for Glaucoma Detection
11:40-12:00	Berthold Lausen (Colchester)	Ensemble of selected classifiers
12:00-13:30		**Lunch**

Contents

Superset learning and data imprecisiation

Eyke Hüllermeier [1]

Superset learning is a generalization of standard supervised learning, in which training instances are labeled with a superset of the actual outcomes. Thus, superset learning can be seen as a specific type of weakly supervised learning, in which training examples are imprecise or ambiguous. We introduce a generic approach to superset learning, which is motivated by the idea of performing model identification and "data disambiguation" simultaneously. This idea is realized by means of a generalized risk minimization approach, using an extended loss function that compares precise predictions with set-valued observations. Building on this approach, we furthermore elaborate on the idea of "data imprecisiation": By deliberately turning precise training data into imprecise data, it becomes possible to modulate the influence of individual examples on the process of model induction. In other words, data imprecisiation offers an alternative way of instance weighting. Interestingly, several existing machine learning methods, such as support vector regression or semi-supervised support vector classification, are recovered as special cases of this approach. Besides, promising new methods can be derived in a natural way.

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Counting the number of molecules of a single mRNA species

Rainer Schuler[1]

Counting individual RNA or DNA molecules is a challenging task, because it is difficult to amplify quantitatively for detection. One approach is to mark the molecules with a *molecular barcode* i.e. a *unique molecular identifier* thereby making them unique. This method turns a quantitative problem of counting the number of molecules having the same sequence into a qualitative problem of detecting the number of different molecules.

The method includes four basic steps: 1) Isolate molecules of interest, 2) turn each molecule into a different molecular species (DMS), 3) amplify the DMS, 4) detect and count the number of DMS.
To implement the second step, oligonucleotides (tags) of a fixed length but with different sequences are used to label the molecules. Since hybridization of DNA molecules with identical sequences is competitive the tags are selected randomly. A collision occurs if two (or more) molecules are labeled with tags of the same sequence. We estimate the expected number of identical tags and consider the relationship between the observed number of different tag sequences (DMS) and the number of molecules.

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Process pharmacology: Using computational functional genomics knowledge to connect drugs with biological processes

Jörn Lötsch[1,2] and Alfred Ultsch[3]

Functional genomics investigates the biochemical, cellular, and/or physiological properties of each and every gene product [1] with the goal of understanding the relationship between genome and phenotype on a genome-wide scale. The acquired knowledge about the functions of gene products is provided in publicly accessible databases of which the current gold standard is the Gene Ontology (GO) database [2, 3]. The combination of this information with the acquired knowledge about the interaction of drugs with gene products is the basis of a recently introduced data science approach to pharmacology that links drugs directly with diseases [4]. This is regarded as the result of pathophysiological processes that are captured by the GO category “biological processes”.

A focus on biological processes [4] may provide a phenotypic approach to drug discovery and repurposing based on (i) selecting disease relevant biological processes as therapeutic targets of novel drugs and (ii) evaluating the utility of known drugs for new indications on the basis of their effects on disease-relevant biological processes. This requires a functional genomics based criterion of drug classification with equivalent performance of the genomics respectively drug target based criterion. Based on prior hints that the functional genomics based criterion provides reasonable drug classification accommodating current pharmacological concepts [4], the present analysis pursued the hypothesis that both criteria provide similarly correct drug classifications. In a comparative assessment using machine-learned techniques for computational drug classification, both criteria were compared in order to provide support for the utility of a functional genomics based criterion for drug development.

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Modeling and Calibration of robust Gas Sensors

Sebastian Krey[1], Margarita Alejandra Rebolledo Coy[1], Jörg Stork[1], Thomas Bartz-Beielstein[1]

In our society's pursuit to reduce air pollution and counteract global warming the reduction of carbon dioxide emission and other air pollutants is an important aim of all industrial sectors. Especially the automotive segment with its problems to reach the rising standards for carbon dioxide and nitrogen dioxide reduction has recently been in the news. To reach the ecological stricter standards the in-situ measurement of the different exhaust gas components gains importance. Based on these measurements a better control of combustion processes allows a more efficient and cleaner operation.

While the in-situ measurement of the oxygen percentage in exhaust gases is industrial standard, the development of long term durable sensors for the selective in-situ measurement of other gas components has been an unsolved problem. The usage of experimental design and linear models helped our industrial research partners to develop durable sensors with different sensitivities and optimize the sensor output for a higher signal quality. These sensors still measure only gas mixtures, but based on an array of different sensors individual readings for the different gas components can be calculated.

In this work we present how (frequentist and bayesian) linear models compare in this scenario with very noisy data against more computational intensive methods (Support Vector Regression, Kriging, Symbolic Regression using Genetic Programming) in modeling the sensors response as well as in creating a calibration model for the prediction of the different gas concentrations. Additionally we present a method to allow an easy and efficient recalibration of the measurement system if the working conditions change or to adapt the system to the effects of sensor aging.

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Hands-on Introduction to Julia: Simplicity, Expressiveness, and Performance

Peter Chronz [1]

This workshop introduces the open source programming language Julia for technical computing. Julia aims to offer a replacement for languages such as C, Fortran, Python, Matlab, and R for technical computing. Julia's development is motivated by the growing gap between processing requirements for data analysis and the capabilities of current programming languages and computing platforms. Currently, data processing is often performed with languages that roughly fall into two categories. The first category consists of languages, such as Fortran and C, that offer high performance but are tedious to program. The second category contains languages, such as Python and R, that offer convenient abstractions, but poor performance. Julia overcomes this dichotomy by merging convenient, high-level abstractions and high performance at the same time. This combination empowers programmers to quickly prototype and achieve excellent performance with the same code. To combine high-level abstraction and high performance, Julia's developers leverage the modern features of the LLVM compiler chain. One important feature leveraged by Julia is just-in-time compilation. Compiling code on the fly allows Julia to perform type inference at runtime and in effect to achieve high performance even if the code is dynamically typed. Concretely, Julia reaches nearly the performance of C for a set typical data processing algorithms. The workshop aims to teach the participants enough to start coding productively afterwards. The workshop covers the language fundamentals in 5 sections. First, basics, such as strings, functions, control flow, and multi-dimensional arrays are presented. Second, an introduction to plotting packages, which are similar to R's ggplot2 and Python's matplotlib, are introduced. Third, data management with DataFrames is covered. Fourth, Julia's package for generalized linear models is demonstrated. Finally, we will cover parallel programming with built-in methods. To learn as much as possible about Julia for productive use, the workshop offers exercises on all topics. The second phase of the workshop consists mostly of hands-on experience.

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Stability selection for boosted generalized additive models for location scale and shape

Janek Thomas[1]

In this project, a new algorithm to incorporate stability selection for boosting generalized additive models for location, scale and shape (GAMLSS) is presented. In one motivating application, a negative binomial hurdle model was fitted to handle excess zeros, overdispersion, non-linearity and spatiotemporal structures to investigate the abundance of the common eider in Massachusetts. The number of birds was estimated via boosting GAMLSS, allowing both mean and overdispersion to be regressed on covariates and incorporating variable selection.An increasingly popular way to obtain stable sets of covariates while controlling the false discovery rate (FDR) is stability selection. The model is fitted repeatedly to subsampled data and variables with high selection frequencies are extracted.Currently, this leads to a fundamental problem with boosted GAMLSS, where in every boosting iteration, the algorithm sequentially selects the best fitting effect for each distribution parameter. Thus, it is currently not possible to stop fitting individual parameters as soon as they are sufficiently modeled.In order to solve this problem, we developed a new approach to fit boosted GAMLSS. Instead of updating all distribution parameters in each iteration, only the update of the parameter which leads to the biggest reduction in loss is performed. With this modification, the stability selection framework can be applied. Furthermore, optimizing the tuning parameters of boosting is reduced from a multi-dimensional to a one-dimensional problem.The performance of the algorithm is evaluated in a simulation study and the application is demonstrated for the seabirds data, selecting stable predictors while controlling the FDR.

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Assessing the significance of effects in boosted location and scale models

Tobias Hepp[1], Matthias Schmid[2], Andreas Mayr[1,2]

While providing many advantages like automatic variable selection and feasibility in high-dimensional settings with more predictors than observations, the implicit regularization of gradient boosting algorithms that allows the shrinkage of effect estimates prevents the computation of standard errors As a result, the construction of confidence intervals or significance tests is problematic. To overcome this problem, Mayr et al.[1] proposed the use of permutation tests to derive p-values for the effect estimates of boosted location and scale models [2], which rely on the independence of the predictor of interest with all other covariates in the model.

In this talk, we therefore discuss the performance of two alternative approaches to extend the scope of possible application scenarios. In order to remove the correlations with other predictors, the first option is based on the replacement of the variable of interest with regression residuals, which can then be equally used for the permutation tests [2]. Another alternative is to draw new samples from the conditional distribution of the constrained model without the variable of interest. Then, the differences in the quality of fit between the full model and the constrained one are attributable only to the randomness of these parametric bootstrap samples and should be less distinctive than for the original data.

All models are fitted via the R add-on package `gamboostLSS`. In addition, the results are compared to the parametric Wald-type tests implemented in the `gamlss`-package [4].

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Boosting distributional regression models for multivariate responses

Andreas Mayr[1,2], Janek Thomas[3], Matthias Schmid[2], Nadja Klein[4]

Over the last few years, statistical modelling approaches that go beyond the classical regression of the conditional mean have gained more and more attention. One of the most popular approaches in this context are generalized additive models for location, scale and shape (GAMLSS, [1]). The main idea of GAMLSS is that each parameter of the conditional distribution – not only the expected value – is modelled by its own additive predictor.

We extend this approach towards multivariate responses [2] and present a statistical boosting algorithm that is able to estimate the unknown quantities of these complex models in potentially high-dimensional settings by circling through the different parameter and outcome dimensions [3].

Our approach will be illustrated by an epidemiological study where the factors influencing children's growth regarding their height and weight are analysed simultaneously in a longitudinal setting.

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GFD: An R-package for the Analysis of General Factorial Designs - along with a Graphical User Interface

Sarah Friedrich[1] *,Frank Konietschke*[2] *and Markus Pauly*[1]

Factorial designs are widely used tools for modeling statistical experiments in all kinds of disciplines, e.g., biology, psychology, econometrics and medicine. For testing null hypotheses formulated in terms of means, analysis-of-variance (ANOVA) methods are well known, and preferred for making statistical inference. ANOVA methods are implemented in R within the functions anova and lm in the R-package stats, along with clearly arranged ANOVA tables in the output. The corresponding F tests, however, are only valid for normally distributed data with equal variances, two assumptions which are often not met in practice. The R-package GFD provides implementation of the Wald-type statistic (WTS), the ANOVA-type statistic (ATS) and a studentized permutation version of the WTS as in [1]. Both the WTS and the permuted WTS do not require normally distributed data or variance homogeneity, whereas the ATS assumes normality. All methods are available for general crossed or nested designs and all main and interaction effects can be plotted. Additionally, the package is equipped with an optional graphical user interface to facilitate application for a wide range of users. We illustrate the implemented methods for a range of different designs.

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kernDeepStackNet: An R package for tuning kernel deep stacking networks

Thomas Welchowski[1] and Matthias Schmid[1]

Kernel deep stacking networks [1] (KDSNs) are a novel method for supervised learning in biomedical research and belong to the class of deep learning methods. Deep learning uses multiple layers of non-linear transformations to derive higher abstractions of the input features [2]. These can more efficiently represent complex dependencies of joint distributions [3]. Training of deep artificial neural networks is a non-convex optimization problem, which may result in local optima and slow convergence. Kernel deep stacking networks are an computational faster alternative, which are based on solving multiple convex optimization problems by combined kernel ridge regressions with random Fourier transformations.

Tuning of KDSNs is a challenging task, as there are multiple hyper parameters to tune. We propose a new data-driven tuning strategy for KDSNs using model based optimization (MBO) [4]. The performance criterion is RMSE on cross validation samples, and noisy Kriging is used as surrogate model. New design points are choosen by maximisation of the expected improvement criterion.

Numerical studies show, that the MBO approach is substantially faster than traditional grid search strategies. Further analysis of real data sets demonstrate, that tuned KDSNs are competetive to other state-of-art machine learning techniques in terms of prediction accuracy. The fitting and tuning procedures are implemented in the R package *kern-DeepStackNet.*

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Implementation and Simulation of Boolean Networks on FPGAs

Julian Schwab[1], Andre Burkovski[1], Johann M. Kraus[1], Hans A. Kestler[1]

In Systems Biology mathematical models are often used to gain insights into cellular pathways and regulatory networks. If only qualitative knowledge is available, Boolean networks can provide important insights into the dynamic behavior of complex regulatory systems.

Boolean network models are described as a set of Boolean variables $X = \{x_1, ..., x_n\}$ and a set of Boolean functions $F = \{f_1, ..., f_n\}$, one variable x_i and one corresponding Boolean function $f_i : \mathbb{B}^n \to \mathbb{B}$ for each regulatory factor and its interaction within the system. The successor state of a regulatory factor x_i at time t is determined by the function $x(t+1) = f_i(\mathbf{x}(t))$ with $\mathbf{x}(t) = (x_1(t), ..., x_n(t))$ [1]. In synchronous Boolean networks a state transition is performed by updating each regulatory factor at the same time.

State transitions from each state in the network eventually lead to a recurrent cycle of states. These stationary cycles are called attractors. Attractors describe the longterm behavior of Boolean networks and can often be linked to biological phenotypes [2].

To search a network for attractors exhaustively, the search algorithm has to be executed from each of the 2^n possible states in a network with n regulatory factors. This leads to an exponential growth $\mathcal{O}(2^n)$ of computation time and memory consumption for an exhaustive attractor search [3]. Due to this fact, exhaustive attractor search is limited to a comparatively small number of regulatory factors.

Aim of this work is to simulate Boolean networks on field programmable gate arrays (FPGAs). We use FPGAs, specialized hardware chips, to accelerate the attractor search. The integration of FPGAs makes attractor search faster and allows simulation of larger networks than in conventional software solutions. We developed an algorithm to search for attractors on FPGAs using VHDL, a hardware description language. The implementation on the FPGA has a modular design, which allows to adapt the design to new Boolean networks readily.

Our first results showed that, due to the acceleration of the FPGA, we achieved a reduction of computation time in orders of magnitude.

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A small REvolutioN and modified temporal centrality measures are needed for incomplete graph sequences of dynamic networks

Moritz Hanke[1], Ronja Foraita[1]

Statistical analysis of networks is gaining importance in areas like social, computer and life sciences. Different centrality measures (e.g. betweenness, closeness) exist for static networks to capture different aspects of a single vertex' importance within the network. However, in reality many processes defined on networks are rather dynamic than as static (e.g. spread of disease, gene cell regulation). Most approaches represent such dynamic networks as sequences of static graphs (so called graph snapshots). Based on these snapshots, for example Tang et al. [1] and Kim and Anderson [2] extended classical vertice centrality measures to take the network dynamics over time into account. For this purpose they assumed to have complete information about the dynamic network, i.e. that the sequence of snapshots is containing all dynamics within the network over time. In real world applications this assumption could often be untenable due to limited access to raw network data which might bias the observed centrality values.

To account for this incompleteness we propose the idea of adding extra snapshots to the observed graph sequence. Based on this idea we extended two of the original temporal centrality metrics of Kim and Anderson [2] by cloning observed snapshots as a first and easy implementation. We show for different simulated scenarios of incomplete graph sequences that our approach increases the accuracy of detecting important vertices in dynamic networks compared to the original methods. Furthermore, by proposing a new algorithm called REvolutioN (Reversed Evolution Network) we address the challenging calculation of temporal centrality measures which depends on the number of vertices, the edge density and the number of snapshots. Due to our algorithms linear computational effort regarding the number of snapshots it makes both feasible, the calculation of the original methods over long snapshot sequences as well as the calculation of methods based on extra snapshots. Additionally, the algorithm benefits from sparse or very dense temporal networks and can be parallelized up to the number of vertices. To illustrate our method we use an age-related gene expression data set from the human brain, consisting of 1128 genes and 55 samples [3].

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Performance of ordinal-scaled prototype-based classifiers on microarray datasets

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Comparative microarray studies provide whole genome expression profiles for different phenotypes. These phenotypes, assuming a suitable correspondence between phenotype and gene expression, can be represented by a prototypical gene expression pattern or signature. Such a signature can then be determined via feature selection techniques and be further used to create suitable classification models. Here, prototype-based classification is of special interest as they allow a direct biological interpretation.

However, the measurements of gene expression levels can be noisy and the training on real-valued profiles might be misguided by potential outliers. In order to reduce these effects, we propose to operate on ordinal scaled signatures. These signatures are known to be invariant to a wide range of data transformations. Standard prototype-based classifiers can be adapted for processing the ordinal-scaled data in various ways. Both instance-based and centroid-based classifiers can rely on distances developed for rankings, i.e. ordinal data, and rank-aggregation procedures in order to compute centroids.

In this study we analyse and compare the performance of ordinal-scaled prototype-based classifiers against their real-valued counterparts. They are examined in experiments with different feature selection methods on a number of publicly available microarray datasets. We show that the performance of ordinal-scaled prototype-based classifiers in some cases can improve the classification performance and therefore should be incorporated in classification experiments with microarrays.

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Boosting Joint Models for Longitudinal and Time-to-Event Data

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Joint Models for longitudinal and time-to-event data have gained a lot of attention in the last few years as they are a helpful technique to approach a data structure very common in life sciences. The two outcomes are modeled by predictors which are composed of individual as well as shared sub predictors. The shared sub predictor is scaled by a so called association parameter which quantifies the relationship between the two parts of the model. Commonly Joint Models are estimated in likelihood based expectation maximization approaches or in a Bayesian framework[1]. The main drawbacks of the classical estimation procedures for joint model for modern biomedical settings is (i) the lack of a clear variable selection strategy and (ii) that they are unfeasible in high-dimensional data situations where the number of candidate variables p exceeds the number of observations n. In this work we propose a new inference scheme for joint model based on gradient boosting [2] that was particular designed to overcome these issues.

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Classification Certainty and Reject Options in Learning Vector Quantization

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Classification learning by means of prototype-based classifiers like learning vector quantization (LVQ, [1]) or support vector machines (SVM, [2]) is one of the most successful paradigms in machine learning. The prototypes in SVM are the support vectors, which are data vectors determining the class borders. The aim of LVQ is distribute a preselected number of prototypes such that the classes are represented. After training it realizes a nearest prototype classifier (NPC) based on (differentiable) distances or dissimilarities. An energy function based variant of LVQ was proposed in [3] denoted as generalized LVQ (GLVQ). The main idea is to use a classifier function

$$\mu\left(\mathbf{v}\right)=\frac{d\left(\mathbf{v},\mathbf{w}^{+}\left(\mathbf{v}\right)\right)-d\left(\mathbf{v},\mathbf{w}^{-}\left(\mathbf{v}\right)\right)}{d\left(\mathbf{v},\mathbf{w}^{+}\left(\mathbf{v}\right)\right)+d\left(\mathbf{v},\mathbf{w}^{-}\left(\mathbf{v}\right)\right)} \tag{1}$$

in this energy function, where $\mathbf{w}^{+}\left(\mathbf{v}\right)$ and $\mathbf{w}^{-}\left(\mathbf{v}\right)$ are the nearest prototypes with correct and incorrect class, respectively, regarding a presented data vector $\mathbf{v}$ depending on the dissimilarity measure d in use.[3] Hence, the classifier function $\mu\left(\mathbf{v}\right)\in\left[-1,1\right]$ becomes negative, iff $\mathbf{v}$ correctly classified. The respective energy function $E=\sum_{\mathbf{v}}\mu\left(\mathbf{v}\right)$ to be minimized approximates the classification error and is optimized by stochastic gradient descent learning [6]. However, as it is shown in [7], classification combined with data representation requires additional constraints to achieve class representative prototypes. These constraints can be realized in GLVQ by an additional penalty term based on the mean squared error [8].

One challenging problem in classification learning is the so-called classification certainty, i.e. the estimation of the evidence of a classification decision for an unknown data object. For SVM, a quantity related to secure classification decisions is the separation margin, which is maximized during the model learning. For GLVQ, the hypothesis margin

$$m_{h}\left(\mathbf{v}\right)=d\left(\mathbf{w}^{-}\left(\mathbf{v}\right),\mathbf{w}^{+}\left(\mathbf{v}\right)\right) \tag{2}$$

is optimized describing the robustness of the GLVQ regarding model shifts [9]. Yet, these quantities cannot be used to judge the decision certainty for unknown data. For NPC-classifiers the distance relation between best matching prototypes for each class can be used to estimate class assignment probabilities [10].

If classification decisions are related to costs, those classifiers come into play, which optimize Bayes decisions regarding optimum costs [11]. The performance of these classifiers can be further improved, reject options are incorporated [12], i.e. objects can be

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[3] For a dissimilarity measure d we require at least $d\left(\mathbf{v},\mathbf{v}\right)=0$ and $d\left(\mathbf{v},\mathbf{w}\right)\geq 0$ [4, 5]. For stochastic gradient learning in GLVQ we further suppose the differentiability in the second argument.

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rejected to push the classification performance but paying additional reject cost. Alternatively, the model can be used to indicate insecure classification decisions. Yet, the methods require the precise determination of the class distributions, which might be difficult [13]. GLVQ provides a robust model approach to estimate class distributions and, hence, it may serve as an approximated Bayes classifier with reject option in the working phase [14]. Recently, a GLVQ variant was proposed, which takes into account this knowledge about reject options in recall already during learning, i.e. the prototype learning is influenced by the perspective reject options in the application phase [15]. In this approach, cost dependent (geometric) dissimilarity thresholds are considered indicating a reject decision. Analogously, a similar approach can be derived, if costs for outlier detection are introduced [16]. After model adaptation, insecure data at the class borders or outlier can be rejected or indicated as decisions with high uncertainty. Both concepts of reject option are explained in detail during the conference presentation.

Additionally to these models, we provide an alternative outlier detection strategy for GLVQ, which takes explicitly the hypothesis margin m_h from (2) into account. According to this idea, a prototype rejects a data vector $\mathbf{v}$ because of uncertainty, if the distance value $d\left(\mathbf{v}, \mathbf{w}\left(\mathbf{v}\right)\right)$ is greater than the hypothesis margin $m_h\left(\mathbf{v}\right)$. In this way, classification certainty knowledge determines the dissimilarity range for secure classification decisions. We denote this strategy as an exploration horizon based outlier reject option (EHBORO). Particulalrly, we show that the knowledge about this post-learning reject option can be integrated into GLVQ adaptation to obtain an respectively optimized model. As before, this EHBORO can also be used to indicate classification decisions with high uncertainty.

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Multi-Objective Parameter Configuration of Machine Learning Algorithms using Model-Based Optimization

Daniel Horn[1],Bernd Bischl [2]

The performance of many classification algorithms heavily depends on the setting of their respective hyperparameters. Many different tuning approaches exist, from simple grid or random search approaches to evolutionary algorithms and sequential model-based optimizers. Often, these algorithm are used to optimize only a single performance criterion. However, in some practical situations a single criterion may not be sufficient to adequately characterize the behaviour of the machine learning method under consideration and the Pareto front of multiple criteria has to be considered. We propose to use multi-objective model-based optimization to efficiently approximate these Pareto fronts.

Furthermore, the parameter sets of many classifiers do not only consist of numeric, but also categorical and integer parameters. Moreover, the ultimate goal in parameter tuning is the automatic selection of the best classifier. Instead of tuning each classifier individually, one after the other, our method operates on the joint space of all considered machine learning algorithms. Therefore a control parameter that selects the currently active base classifier is introduced. All other parameters of the machine learning algorithms are made dependent / subordinate on this model choice parameter. Our model-based optimization approach can efficiently handle these hierarchical, mixed parameter spaces in a multi-objective setting.

Our optimization method is readily available as part of the mlrMBO R package on Github. We compare its performance against the TunePareto package and regular random search in a pure numerical setting of SVM parameter tuning and a hierarchical, mixed setting where we optimize over multiple model spaces at once.

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On the Hyperparameter Settings of Random Forest

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Due to their good predictive performance, simple applicability and flexibility, random forests are getting increasingly popular for building prediction rules. Unfortunately, not much knowledge is available about the ideal hyperparameter settings of random forests. Some important hyperparameters are the number of trees, the number of randomly drawn features at each split, the number of randomly drawn samples in each tree and the minimal number of samples in a node. Common modern strategies for tuning are grid search, random search iterated F-racing or bayesian optimization. This can be too complicated for users without expertise on random forests, computationally costly or even infeasible in case of too big datasets.

In our empirical study, we study the influence of a diverse range of hyperparameter settings of random forest algorithms / implementations of many different R packages on more than 200 different regression and classification problems from the OpenML platform. We use out-of-bag predictions and different performance measures for evaluation, and simple meta-learning to relate the performance results to data set characteristics.

Our results yield valuable insights into a) parameter sensitivity for different performance measures b) optimal default settings, to be applied without further tuning c) tuning starting points and ranges for less time-consuming model building.

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Feature selecting multi-class classification

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Gene expression profiles are a valuable resource for gaining insight into molecular processes in cells and tissues. The analysis of these profiles gives the opportunity of understanding the development of certain diseases on a cellular level. Nevertheless, interpretation of this data is quite challenging due to their high dimensionality. For instance, although support vector machines achieve fairly good classification performances the resulting classification models are barely interpretable and obscuring possible insight in the molecular processes.

Feature selection methods have proven to be a useful approach handling the high dimensionality of gene expression data [1]. By selecting small subsets of highly informative features, they can provide starting points for new biological hypotheses and experiments. The elementary strategies are using purely data driven filters, selecting features on the basis of scores, which is calculated feature-wise.

Another demanding challenge appears with the introduction of finer grained diagnostic classes. While most of the classifiers and the feature selection methods are designed to be applied to binary classification tasks, we are increasingly facing scenarios with multiple classes. One basic approach is to divide the whole dataset into two-class subsets by choosing every possible pair of classes (One-against-One). Another strategy picks each class in turn as the positive class and subsume the remaining classes as the negative class (One-against-All).

In this study we examined the interaction between four data-driven feature selection methods and the aforementioned multi-class classification strategies and their impact on the accuracy of the classification as well as on the classwise sensitivities and specifities.

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Anomaly Detection with Shapelet-Based Feature Learning for Time Series

Laura Beggel[1,2], Bernhard X. Kausler[1], Martin Schiegg[1] and Bernd Bischl[2]

The detection of anomalous behavior in temporal data is a very diverse area of research. The concrete applications have focused on detecting anomalous behavior within time series, but the classification of entire time series into normal and anomalous has not received much attention yet. Previous works addressing the latter task typically utilize standard features or require features hand-crafted by an expert with domain knowledge. In response, we propose a novel method based on one-class Support Vector Data Description [1] which jointly detects anomalous time series in a set of sequences and learns features that are highly discriminative for this task. Our algorithm minimizes a learning objective that considers 1.) the quality for anomaly detection of the data representation using shape-based features [2] and 2.) the compactness of the (normal) data under the given feature representation. This objective function is optimized using a block-coordinate descent procedure.
By jointly learning the features and a decision boundary for anomaly detection, our method is able to extract explicit characteristics for domain-specific normal behavior without the requirement of expert domain knowledge. These learned features are thus highly discriminative for the detection of anomalous observations in test data. We demonstrate the effectiveness of our approach on multiple data sets.

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Implementing an EM algorithm for partially dependent data

Alexander Engelhardt [1]

The expectation-maximization algorithm (EM algorithm) is a popular method for finding maximum likelihood estimates in the presence of latent variables. We implemented an EM algorithm for a family study of colorectal cancer (CRC), where the data consisted of pedigrees of families, the dependent variable being the age at the onset of CRC. We assume a latent variable Z denoting the presence of an unknown genetic risk factor that increases the hazard ratio for the onset of CRC by a factor alpha. The unobservable proportion p1 of carriers of this risk factor as well as the risk increase alpha were then estimated with the EM algorithm. Genetic inheritance of this risk factor implies dependence within families, which led to computational difficulties for large families. We also show methods to minimize memory usage and computation time of this algorithm.

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Netboost: Boosting supported network analysis for highdimensional genomic datasets

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Sequencing and array technologies develop rapidly, even exceeding development in computer science. Thereby, the computational challenge in analysing highdimensional genomic datasets is increasing and a need to identify networks within these large datasets is eminent. Weighted Gene Co-expression Network Analysis (WGCNA) is a versatile framework to do this[1]. But when combining multiple measurement types to interrogate their relations the data has many independent components and we reach computational limits.

We propose to implement a boosting based filtering step to improve the signal-to-noise ratio and obtain sustainable computational requirements. For each feature j likelihood based boosting is applied, using all other features as covariates. The inter-feature distances, defined by the topological overlap measure of convex transformations of the correlations, are then calculated for selected features (i, j). The sparse distances matrix is then hierarchically clustered by MC-UPGMA[2] and the resulting dendrogram separated into modules by DynamicTreeCut[3].

We apply Netboost on The Cancer Genome Atlas data from 192 acute myeloid leukemia patients. Together these methylation and expression arrays cover more than 532,000 features in the human genome. The subset of chromosome 18 features is small enough to apply WGCNA as well. Netboost results in smaller and fewer modules by extracting the most prominent effects. The analysis of the whole genome data comparing Netboost and a scalable adaptation of WGCNA is ongoing. The resulting modules will be benchmarked by their association to the clinical endpoints.

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A Statistical Model for the Analysis of Beta Values in DNA Methylation Studies

Leonie Weinhold[1], Simone Wahl[2], Per Hoffmann[3] and Matthias Schmid[1]

The analysis of DNA methylation is a key component in the development of personalized treatment approaches. A common way to measure DNA methylation is the calculation of beta values, which are bounded variables of the form $M/(M+U)$ that are generated by Illumina's 450k BeadChip array. The statistical analysis of beta values is considered to be challenging, as traditional methods for the analysis of bounded variables, such as M-value regression and beta regression, are based on regularity assumptions that are often too strong to adequately describe the distribution of beta values. We develop a statistical model for the analysis of beta values that is derived from a bivariate gamma distribution for the signal intensities M and U. By allowing for possible correlations between M and U, the proposed model explicitly takes into account the data-generating process underlying the calculation of beta values. Using simulated data and a real sample of DNA methylation data from the Heinz Nixdorf Recall cohort study, we demonstrate that the proposed model fits our data significantly better than beta regression and M-value regression. In addition, the proposed model improves the identification of associations between beta values and covariates such as clinical variables and lifestyle factors.

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Automated Design of Search Algorithms for Feature Set Ensembles

Gunnar Völkel[1], Ludwig Lausser[1], Hans A. Kestler[1]

Feature selection is one of the most important methods for generating interpretable decision rules for high-dimensional profiles. Selecting valuable biomarkers, these techniques point at potential hypotheses on the molecular background of a phenotype or disease. Nevertheless, in the context of low sample sizes these hypotheses will not be unique. Often, several suitable biomarker combinations and explanations exist.

In this work, we present an ensemble feature selection technique aiming at the parallel construction of sparsely overlapping marker combinations. The technique evolves a population of marker combinations using a genetic algorithm with diversity preserving methods. The marker combinations are rated by a correlation-based measure. From the final population, the subset consisting of the best marker combinations is aggregated to a multi-classifier system.

Metaheuristics like the genetic algorithm allow a large degree of customisation. Suitable operators or parameter values are typically not evident. In this situation tuning methods are preferable to manual selection. We utilize the irace tuning package [1] to find good parameter and operator choices for the genetic algorithm. To find a configuration for the genetic algorithm that achieves a good performance for the general marker selection problem, the tuning is carried out on multiple datasets. The tuning is parallelised on remote computation servers via the Sputnik library [2].

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Ensemble Pruning for Glaucoma Detection.

Werner Adler[1], *Olaf Gefeller*[1], *Asma Gul*[2], *Folkert K. Horn*[3], *Zardad Khan*[4], *Berthold Lausen*[5]

Glaucoma is a neurodegenerative eye disease leading to blindness when not treated in time. The Heidelberg Retina Tomograph (HRT) is a non-invasive device producing topographical features of the eye-background suitable for glaucoma detection. A Random forest (RF) (Breiman, 2001) is an ensemble of classification trees that has shown to perform very well in detecting glaucoma based on HRT parameters (Adler et al., 2008). A typical RF consists of several hundred trees. To minimize the computational cost, several ensemble pruning techniques have been proposed that reduce the number of trees in the ensemble without loss of classification performance (Tsoumakas et al., 2009). We examine the performance of ensemble pruning based on the Double-Fault similarity and the classification performance of single trees in the field of glaucoma classification using a data set consisting of 309 observations of 102 topographical features. To validate our findings based on this data set, and to examine the influence of the prevalence of glaucoma in the data, we additionally perform a simulation study. Sensitivities, specificities, and the AUCs are reported and the performances of the examined pruning strategies are discussed.

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Ensemble of selected classifiers

Berthold Lausen [1]

I discuss recent proposals to improve classification based on data with high dimensional feature space. For example after preprocessing microarray data with 500 000 probes and 22125 features (probesets) which represent genes, I use our proposal to improve feature selection of microarray data based on a proportional overlapping score[1]. Using benchmark data sets I compare random forests and our recent proposals of new classification methods based on ensembles of selected k-nearest neighbours and tree classifiers [2].

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