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Statistical Computing 2019
Abstracts der 51. Arbeitstagung

HA Kestler, M Schmid, L Lausser,
A Fürstberger (eds)

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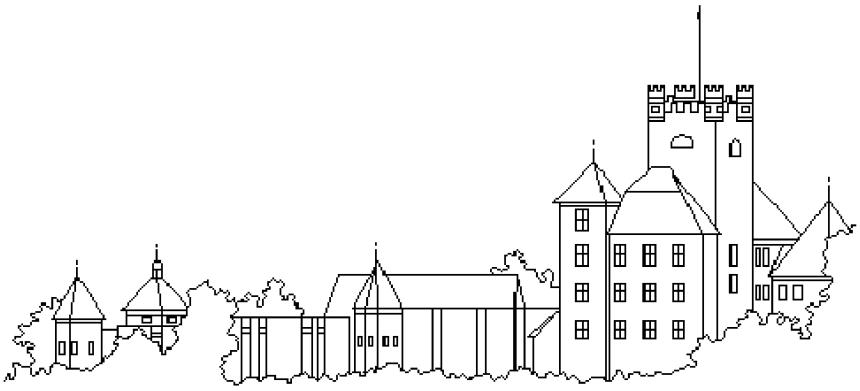
Statistical Computing 2019



51. Arbeitstagung

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

30.06. - 03.07.2019, Schloss Reisensburg (Günzburg)

Workshop Program

Sunday, June 30, 2019

		Introduction: H. A. Kestler
20:00 – 21:00	Joachim M. Buhmann (Zürich)	Can I believe what I see? - Information theoretic algorithm validation

Monday, July 01, 2019

08:50		**Opening of the workshop: H. A. Kestler**
09:00 – 10:20		**Chair: L. Lausser**
09:00 – 09:20	Alfred Ultsch (Marburg)	ESOM Sampling as a Tool for Detection of Needles in the Haystack of Big Data in Medical Diagnostic Technologies
09:20 – 09:40	Marcus Vollmer (Greifswald)	A Convolutional Neural Network for ECG Annotation as the Basis for the Classification of Cardiac Rhythms
09:40 – 10:00	Shekoufeh Gorgi Zadeh (Bonn)	Uncertainty-Guided Semi-Automated Editing of CNN-based Retinal Layer Segmentations in Optical Coherence Tomography
10:00 – 10:20	Dila Ram Bhandari (Kathmandu)	Big data: Challenges, Tools and Techniques in SAARC Region
10:20 – 10:50		**Coffee Break**
		Introduction: A. Mayr
10:50 – 11:30	Annika Hoyer (Düsseldorf)	A bivariate time-to-event model for the meta-analysis of full ROC curves
09:00 – 10:20		**Chair: A. Mayr**
11:30 – 11:50	Jan Feifel (Ulm)	Enough is as good as a feast: Comparing different subsampling designs for time-to-event data
12:00 – 13:30		**Lunch**
		Introduction: M. Vollmer
13:40 – 14:20	Nadja Klein (Berlin)	A Novel Spike-and-Slab Prior for Effect Selection in Distributional Regression Models
14:20 – 15:00		**Chair: M. Vollmer**
14:20 – 14:40	Jörn Lötsch (Frankfurt am Main)	Machine learning supported hypothesis and pattern finding in pain related phenotype data
14:40 – 15:00	Patrick Thiam (Ulm)	Pain Intensity Recognition via Deep Physiological Models
15:00 – 15:30		**Coffee Break**

Monday, July 01, 2019

15:30 – 16:30		**Chair: A. Ultsch**
15:30 – 15:50	Sebastian Krey (Köln)	Graphical User Interfaces for Surrogate Model-Based Optimization in Practice and Teaching
15:50 – 16:10	Robin Szekely (Ulm)	Correlation-based feature selection utilizing foreign classes
16:10 – 16:30	Roman Hornung (München)	Improved outcome prediction across data sources through robust parameter tuning
16:30 – 16:50		**Break**
16:50 – 17:50		Working group meeting on **Statistical Computing 2020**
18:00 – 20:00		**Dinner**

Tuesday, July 02, 2019

09:00 – 10:20		**Chair: J. Kraus**
09:00 – 09:20	Florian Pfisterer (München)	Towards Human-Centered AutoML
09:20 – 09:40	Christian Staerk (Bonn)	Boosting with random selection of weak learners for variable selection in high-dimensional models
09:40 – 10:00	Steffen Moritz (Köln)	imputeTS: Tidy Univariate Time Series Imputation
10:00 – 10:20	Colin Griesbach (Erlangen)	Joint Modelling approaches to survival analysis via likelihood-based boosting techniques
10:20 – 10:50		**Coffee Break**
		Introduction: M. Schmid
10:50 – 11:50	Christiane Fuchs (Bielefeld)	Tackling leukemia through computational statistics
12:00 – 13:30		**Lunch**

Tuesday, July 02, 2019

		Introduction: S. Krey
13:40 – 14:20	Nikolaus Umlauf (Innsbruck)	bamlss: A Lego toolbox for flexible regression models
14:20 – 15:00		**Chair: S. Krey**
14:20 – 14:40	Xudong Sun (München)	Automatic Machine Learning and (Deep) Reinforcement Learning with rlR package
14:40 – 15:30		**Poster teaser + session & Coffee break**
15:30 – 16:30		**Chair: A. Fürstberger**
15:30 – 15:50	Jörn Lötsch (Frankfurt an Main) Alfred Ultsch (Marburg)	Generative artificial intelligence based algorithm to increase the predictivity of preclinical studies while keeping sample sizes small
15:50 – 16:10	Hryhorii Chereda (Göttingen)	Utilizing molecular network information via Graph Convolutional Neural Networks to predict metastatic event in breast cancer
16:10 – 16:30	Lisa Schäfer (Ulm)	Extracting ordinal class sequences from high-dimensional datasets
16:30 – 16:50		**Break**
		Introduction: A. Fürstberger
16:50 – 17:50	Erin LeDell (California)	Scalable Automatic Machine Learning with H2O
18:00 – 20:00		**Dinner**
20:00 – 21:00	Erin LeDell (California)	Hands-on Tutorial: Scalable Automatic Machine Learning with H2O

Wednesday, July 03, 2019

09:00 – 10:20		**Chair: R. Schuler**
09:00 – 09:20	Tobias Hepp (Bonn)	Adaptive step-lengths in model-based gradient boosting algorithms for distributional regression
09:20 – 09:40	Sina Mews (Bielefeld)	A continuous-time capture-recapture model for the annual movement of bottlenose dolphins
09:40 – 10:00	Ralph Brinks (Düsseldorf)	Simulation of trajectories in the illness-death model for chronic diseases: discrete event simulation and Doob-Gillespie algorithm
10:00 – 10:20	Thomas Welchowski (Bonn)	A Classification Tree Approach for the Modeling of Competing Risks in Discrete Time
10:20 – 10:50		**Coffee Break**
10:50 – 11:50		**Chair: W. Adler**
10:50 – 11:10	Lea Siegle (Ulm)	Semantic feature selection for multi-class classifier systems
11:10 – 11:30	Carlo Maj (Bonn)	Modeling strategies to dissect the variable genetic architecture in the computation of polygenic risk score
11:30 – 11:50	Christoph Molnar (München)	Quantifying Interpretability of Arbitrary Machine Learning Models Through Functional Decomposition
12:00 – 13:30		**Lunch**
13:30		**Departure**

Contents

Can I believe what I see? - Information theoretic algorithm validation

Joachim M. Buhmann[1]

Data Science promises us a methodology and algorithms to gain insights in ubiquitous Big Data. Sophisticated algorithmic techniques seek to identify and visualize non-accidental patterns that may be (causally) linked to mechanisms in the natural sciences, but also in the social sciences, medicine, technology, and governance. When we use machine learning algorithms to inspect the often high-dimensional, uncertain, and high-volume data to filter out and visualize relevant information, we aim to abstract from accidental factors in our experiments and thereby generalize over data fluctuations. Doing this, we often rely on highly nonlinear algorithms.
This talk presents arguments advocating an information theoretic framework for algorithm analysis, where an algorithm is characterized as a computational evolution of a posterior distribution on the output space with a quantitative stopping criterion. The method allows us to investigate complex data analysis pipelines, such as those found in computational neuroscience, neurology, and molecular biology. I will demonstrate this concept for the validation of algorithms using the example of a statistical analysis of diffusion tensor imaging data. In addition, on the example of gene expression data, I will demonstrate how different spectral clustering methods can be validated by showing their robustness to data fluctuations and yet sufficient sensitivity to changes in the data. All in all, an information-theoretical method is presented for validating data analysis algorithms, offering the potential of more trustful results in Visual Analytics.

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ESOM Sampling as a Tool for Detection of Needles in the Haystack of Big Data in Medical Diagnostic Technologies

Alfred Ultsch[1], Jörg Hoffman[2] and Cornelia Brendel[2]

In particular, within the context of molecular medical research data sets become larger and larger. High data volumes obtained with flow cytometric analyses of blood and tissue samples with real time multiparameter measurements were always a challenge for computer hard and software designers. Today, a regular Flow Cytometry [1] data sat for one single patient typically contains d ($10 < d < 100$) variables for $n > 1,000,000$ single blood cells (counts) [2]. A training period of many years is therefore prerequisite for biologists or physicians who perform the clinical data interpretation. It is, however, clear, that diagnostic structures in these files may be captured by an appropriate sampling procedure. In this work, we compare the advantages and disadvantages for three different sampling strategies producing a dataset consisting of $n_s < 5,000$ as a subset of the n original data: simple random [3], Learning Vector Quantization (LVQ) [4] and a novel proposal based on emergent self-organizing feature maps (ESOM) [5]. For a short overview on sampling strategies, see [3]. The approach is tested on different artificial and experimental datasets. Moreover, we validate our method by performing automated diagnosis of lymphomas employing diagnostic files from original flow cytometric patient lymphoma samples [6].

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A Convolutional Neural Network for ECG Annotation as the Basis for the Classification of Cardiac Rhythms

Marcus Vollmer[1,2], *Philipp Sodmann*[1,2] , *Neetika Nath* [1] *and Lars Kaderali*[1,2]

Objective: Electrocardiography is the most common tool to diagnose cardiovascular diseases. Annotation, segmentation and rhythm classification of ECGs are challenging tasks, especially in the presence of atrial fibrillation and other arrhythmias. Our aim was to increase the accuracy of heart rhythm classification by the use of extreme gradient boosting trees and the development of a deep convolutional neural network for ECG segmentation.

Methods: We trained a convolutional neural network with waveforms from PhysioNet databases to annotate QRS complexes, P waves, T waves, noise and interbeat ECG segments that characterize the essences of normal and irregular heart beats. We checked

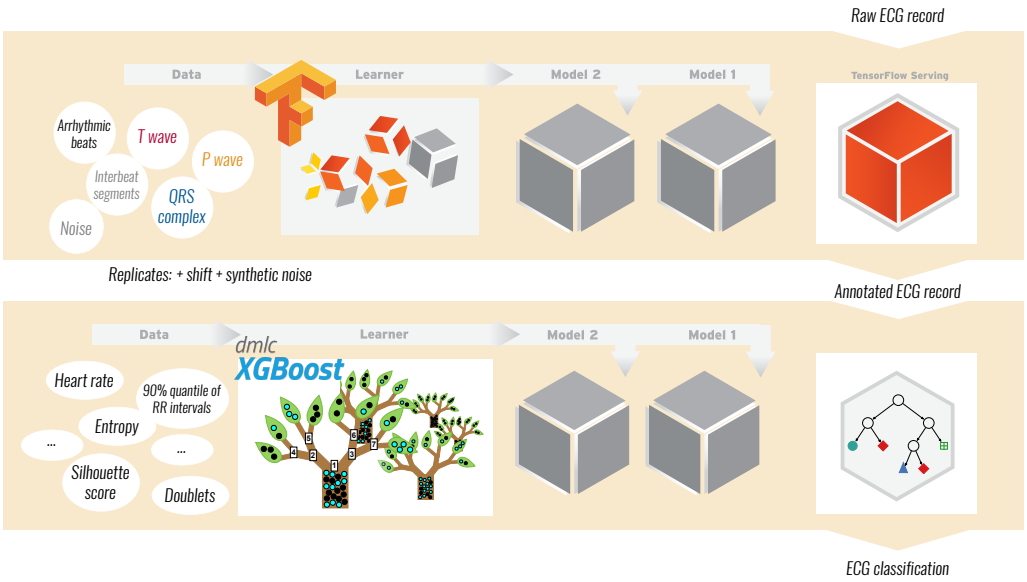

Figure 1: A schematic representation of our workflow. A CNN was trained with labeled 1.5 s ECG segments using TensorFlow. Features were extracted from the annotated ECG and eXtreme Gradient Boosting trees were used to classify the heart rhythm. TensorFlow logo by Wikimedia/FlorianCassayre (CC-BY-SA 4.0), TensorFlow serving chart adapted from www.tensorflow.org/serving/ (CC-BY-SA 3.0), random forest illustration adapted with permission from Sarah Chaudill and the American Physical Society from Figure 1 in [1]

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the segmentation performance by direct paired comparison to the reference annotations of the QT [2] and MIT-BIH P-wave databases [3]. True positive rates, positive predictive values and the mean absolute difference were calculated. Moreover, we compared the results with standard QRS detectors and Ecgpuwave. Extreme gradient boosting trees [4] were used to determine the heart rhythm based on hancrafted features. Essential features were computed from interval data, including heart rate analysis and noise estimation. Furthermore, we defined particular features based on ECG morphology, appearance of P waves and detection of irregular beats. We examined the feature importance and identified key features for normal sinus rhythm, atrial fibrillation, alternative rhythm and noisy recordings. The classification performance was evaluated externally using F1 scores by applying the algorithm to the hidden test set of the PhysioNet/CinC Challenge 2017 [5].

Results: The true positive rate of the convolutional neural network in detection of manually revised R peaks in the QT database was 98% and the positive predictive value was 99%. The detection of P and T waves reached a true positive rate of 92% and 88% respectively, given a 50 ms tolerance when comparing the reference to the test annotation set. The rhythm classification performance reached an overall F1 score of 0.82 when applying the algorithm to the hidden test set [6,7].

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Uncertainty-Guided Semi-Automated Editing of CNN-based Retinal Layer Segmentations in Optical Coherence Tomography

Shekoufeh Gorgi Zadeh[1,2], Maximilian W. M. Wintergerst[3], and Thomas Schultz[4]

Convolutional neural networks (CNNs) have enabled dramatic improvements in the accuracy of automated medical image segmentation. Despite this, in many cases, results are still not reliable enough to be trusted "blindly". Consequently, a human rater is responsible to check correctness of the final result and needs to be able to correct any segmentation errors that he or she might notice. In [1], for a particular use case, segmentation of the retinal pigment epithelium (RPE) and bruch's membrane (BM from optical coherence tomography (OCT), we develop a system that makes this process more efficient by guiding the rater to segmentations that are most likely to require attention from a human expert, and by developing semi-automated tools for segmentation correction that exploit intermediate representations from the CNN. We demonstrate that our automated ranking of segmentation uncertainty correlates well with a manual assessment of segmentation quality, and with distance to a ground truth segmentation. We also show that, when used together, uncertainty guidance and our semi-automated editing tools decrease the time required for segmentation correction by more than a factor of three.

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Big data: Challenges, Tools and Techniques in SAARC Region

Dila Ram Bhandari[1]

Big data is a term for huge data sets having large, varied and complex structure with challenges, such as difficulties in data capture, data storage, data analysis and data visualizing for further processing for leading to an upsurge of research, as well as industry and government applications. Data is deemed a powerful raw material that can impact multidisciplinary research endeavors as well as government digital revolution and business performance. Exploitation of Big Data platforms and technologies requires both corporate strategies and government policies to be in place much before the results would start pouring in. Digitization also has a significant impact on job creation in the overall economy of big data. The goal of this paper is to describe, review and reflect on big data share the data analytics opinions and perspectives of the authors relating to the new opportunities and challenges brought forth by the big data movement. The irrelevance of statistical significance, the challenges of computational efficiency and the unique characteristics of big data discussed above highlight the need to develop new statistical techniques to gain insights from predictive models. The authors bring together diverse perspectives, coming from different geographical locations with different core research expertise and different affiliations and work experiences.

Keywords: Big data, Government policy, social welfare, Hadoop, Data Privacy

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A bivariate time-to-event model for the meta-analysis of full ROC curves

Annika Hoyer[1]

Meta-analysis and systematic reviews are the cornerstones of evidence-based medicine and are used to inform treatment, diagnosis or prevention of patients as well as policy decisions in health care. While meta-analytic methods for intervention trials are well-established today, those for diagnostic accuracy studies are still under development in recent years due to the increased complexity of the bivariate outcome of sensitivity and specificity. The situation becomes even more challenging when the single studies report full ROC curves with several pairs of sensitivity and specificity corresponding to different diagnostic thresholds. However, this information is frequently ignored and only a single pair of sensitivity and specificity per study is used to arrive at meta-analytic estimates. Although methods have been proposed which deal with the full information, these have still disadvantages as, for example, allowing only for the same numbers or values of thresholds across studies.

To overcome the disadvantages of previously suggested models, we propose a novel approach for the meta-analysis of full ROC curves using all available information based on bivariate time-to-event models for interval-censored data [1]. The model is illustrated by an example on population-based screening for type 2 diabetes mellitus, where the original reviews include only one pair of sensitivity and specificity from 38 single studies, but an intensified search yields 124 pairs of sensitivity and specificity for 26 different thresholds.

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Enough is as good as a feast: Comparing different subsampling designs for time-to-event data

Jan Feifel[1], Luis Pauler[1] and Jan Beyersmann[1]

Antimicrobial resistance is one of the major burdens not only for today's clinicians, especially in infections resistant to Carbapenem, an antibiotic of last resort. Often the outcome variable is the time to a specific event. Standard procedures like the Cox regression model require covariate information for all individuals within the cohort.
In time-to-event analyses, information on the actual event times is only provided by uncensored patients. If the outcome is rare or if interest lies in evaluating expensive covariates, sub-sampling designs are favorable due to efficient use of limited resources. In our situation, not the outcome is necessarily rare, but interest lies in the impact of a rare time-dependent exposure such as the occurrence of an infection caused by carbapenem-resistance or disease progression.
We introduce and compare two different subcohorting schemes: the nested exposure case-control design[1] and the exposure density sampling[2]. Both account for past time-dependent exposure status to reduce the number of individuals substantially. A simulation study will outlay that a smart utilization of the available information at each point in time can lead to more powerful and simultaneously less expensive designs. Furthermore, a discussion of their relative merits will give a recommendation on when each design is most auspicious.

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A Novel Spike-and-Slab Prior for Effect Selection in Distributional Regression Models

Nadja Klein[1]

We propose a novel spike and slab prior specification with scaled beta prime marginals for the importance parameters of regression coefficients to allow for general effect selection within the class of structured additive distributional regression. This enables us to model effects on all distributional parameters for arbitrary parametric distributions, and to consider various effect types such as non-linear or spatial effects as well as hierarchical regression structures. Our spike and slab prior relies on a parameter expansion that separates blocks of regression coefficients into overall scalar importance parameters and vectors of standardised coefficients. Hence, we can work with a scalar quantity for effect selection instead of a possibly high-dimensional effect vector, which yields improved shrinkage and sampling performance compared to the classical normal-inverse-gamma prior. We investigate the propriety of the posterior, show that the prior yields desirable shrinkage properties, propose a way of eliciting prior parameters and provide efficient Markov Chain Monte Carlo sampling. Using both simulated and three large-scale data sets, we show that our approach is applicable for data with a potentially large number of covariates, multilevel predictors accounting for hierarchically nested data and non-standard response distributions, such as bivariate normal or zero-inflated Poisson.

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Machine learning supported hypothesis and pattern finding in pain related phenotype data

Jörn Lötsch[1,2], Reetta Sipilä[3], and Eija Kalso[3]

Hypothesis generation in biomedical data can become challenging when a novel research topic is complex and incompletely understood. In the present analysis, we show the utility of a combination of unsupervised and supervised machine-learned techniques for data-driven assessment of pain-related phenotypes.
In a cohort of 1,000 women operated for breast cancer at the Helsinki University Hospital, psychological and sleep related parameters were acquired from a subgroup of n = 373 patients (complete data). In addition, pain intensity during the last week and the impact of pain on daily life activities (interference) were acquired. Unsupervised machine learning, implemented as emergent self-organizing feature map [1, 2], identified a structure in the data space of d = 17 psychological parameters indicating two-clusters. A "low pain but high interference" group was significantly overrepresented in the smaller cluster.
For the membership in this "low pain but high interference" group, feature selection based on fast and frugal tree (FFT [3, 4]) analysis identified d = 4 parameters as the most frequent size of the best performing trees during 1,000 runs on randomly resampled disjoint training and test data subsets. The derived decision rules obtained a balanced classification accuracy of 70% for the assignment to the "low pain but high interference" clinical group, versus all other clinical groups. The feature set was supported in its main parts, when repeating feature selection using random forests analysis followed by computed ABC analysis of the decrease in classification accuracy, when the respective feature was omitted from forest building [5].
The analysis shows, that complexity of clinical facets of persistent pain can be captured by combining unsupervised with supervised methods for of data exploration and analysis. Verifiable hypotheses can be found in complex data acquired with the expectation of interrelationships and subgroups but without clear pre-definitions of hypotheses.

Acknowledgement
Landesoffensive zur Entwicklung wissenschaftlich-ökonomischer Exzellenz (LOEWE), LOEWE-Zentrum für Translationale Medizin und Pharmakologie (JL) and European Union Seventh Framework Programme (FP7/2013, grant agreement no. 602919, EK, JL, GLORIA).

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Pain Intensity Recognition via Deep Physiological Models

Patrick Thiam[1,2], Hans A. Kestler[1], and Friedhelm Schwenker[2]

The common inference model optimization process involves the design, assessment and selection of measurable descriptors based on some expert knowledge in the domain of application. The final inference model is subsequently trained, based on the set of selected descriptors. Recent works in the field of deep learning have shown that this whole process can be effectively and efficiently replaced by a neural network architecture that integrates feature engineering, feature selection and inference model optimization into a single learning process. Such approaches have been successfully applied in the domains of image and audio processing, with significantly improved overall performances in comparison to approaches based on traditional inference models such as support vector machines (SVMs) or decision trees.
In the following work, several deep learning approaches based on convolutional neural networks are designed and applied on measurable physiological channels in order to perform an accurate classification of different levels of artificially induced pain intensities. The aim of the current work is to achieve state-of-the-art pain intensity classification performances without the need of specific domain expert knowledge for the generation of relevant descriptors. The assessment of the designed classification architectures is based on the *BioVid Heat Pain Database (Part A)* and the conducted experimental validation demonstrates the relevance of the proposed approaches. Based on a *Leave-One-Subject-Out* (LOSO) cross-validation evaluation relative to the binary classification task consisting of the discrimination between the baseline and the pain tolerance level ($T_0 vs. T_4$), new state-of-the-art classification performances could be achieved, in particular with the electrodermal activity (EDA) and the designed deep fusion approach with respective classification rates of 85.03% and 84.74%.
Keywords: Pain Intensity Classification, Deep Neural Networks, Information Fusion, Signal Processing

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Graphical User Interfaces for Surrogate Model-Based Optimization in Practice and Teaching

Frederik Rehbach[1], Sebastian Krey[1] and Thomas Bartz-Beielstein[1]

State-of-the-art Surrogate Model-Based Optimization, Evolutionary algorithms and related search heuristics are well suited to solve complex industrial and scientific problems. Unfortunately, easy to use graphical user interfaces (GUI) are not available for many algorithms. Especially tools for the parallel computation of resource intensive methods often require long familiarisation phases. These difficulties prevent a wide adoption of these methods.

We claim that the availability of well-designed GUIs increases the interest for these technologies in industry and even for students without a background in optimization, statistics or computer science. In consequence they lead to a wider adoption in industrial practice.

The spotGUI R-package provides a GUI, based on Shiny, for the already well-established SPOT package. SPOT is a toolbox for model-based optimization, focusing on sequentially updated surrogate models for efficient optimization using state-of-the-art algorithms and modeling techniques that can be used without the requirement of optimization or programming knowledge. Additionally, it allows offloading computationally intensive tasks to an HPC cluster in a completely transparent way, allowing to easily solve extremely complex problems even for people who have never used an HPC system before.

We are successfully using the spotGUI for teaching design of experiments and statistical modeling to engineering students and for solving industrial optimization problems. One such problem is the electrostatic precipitator. It is a large scale electrical filtering/separation device, used to remove solid particles from gas streams, for example from the exhaust gases of coal-burning power plants. The configuration of these devices is a highly complex discrete optimization problem based on a computationally expensive computational fluid dynamics models of the exhaust gas system. In this work, we show how this optimization process can be controlled from a spotGUI interface and how the used methods improved the performance of the particle separation.

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Correlation-based feature selection utilizing foreign classes

Robin Szekely[1,2], Ludwig Lausser[1] and Hans A. Kestler[1]

Datasets obtained from high-throughput experiments are typically characterized by their extremely high dimensionality compared to a small amount of samples ($n \gg m$). Feature profiles usually comprise several thousand molecular markers where sample sets rarely contain more than a hundred samples. Obtaining more samples is difficult due to ethical and economical reasons. To cope with this high-dimensional setting, sparse classification models or the aqusition of additional data resources might become relevant.
In this work, we supplement samples of an original binary classification task by samples of foreign but related classes [1,2]. We assume that these additional classes occur in multi-class datasets collected for a common research question. To be specific, samples from foreign classes are utilized for feature selection. We use an indirect selection strategy between original and foreign classes based on the Pearson correlation.
The feature selection strategy is evaluated in classification experiments on multi-class microarray and RNA-Sequencing datasets using linear support vector machines, random forests and k nearest neighbour classifiers. All experiments are designed as 10×10 cross-validation experiments. Our results show that certain constellations including foreign classes imply a high quality measure for the original classification task. In our evaluations this strategy outperformed the original feature selection over all datasets in up to 48.42%.

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Improved outcome prediction across data sources through robust parameter tuning

Nicole Schueller[1], Anne-Laure Boulesteix[1], Bernd Bischl[2], Kristian Unger[3,4], Roman Hornung[1]

In many application areas, prediction rules trained based on high-dimensional data are subsequently applied to make predictions for observations from other sources, but they do not always perform well in this setting. This is because data sets from different sources can feature (slightly) differing distributions, even if they are, in principle, similar in terms of population and definitions of the variables. In the context of high-dimensional data and beyond, most prediction methods involve one or several tuning parameters. Their values are commonly chosen by maximizing the cross-validated prediction performance within the training data. This procedure, however, implicitly presumes that the data to which the prediction rule will be ultimately applied, follow the same distribution as the training data. If this is not the case, less complex prediction rules that slightly underfit the training data may be preferable. Indeed, a tuning parameter does not only control the degree of adjustment of a prediction rule to the training data, but also, more generally, the degree of adjustment to the *distribution of* the training data. On the basis of this idea, we compare various approaches including new procedures for choosing tuning parameter values that lead to better generalizing prediction rules than those obtained based on cross-validation. Most of these tuning approaches use an external validation data set. In our extensive comparison study based on a large collection of 15 transcriptomic real data sets, tuning on external data and robust tuning with tuned robustness parameter are the two approaches leading to better generalizing prediction rules.

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Scalable Automatic Machine Learning with H2O

Erin LeDell[1]*, Jo-fai Chow*[1]

Course Description:

H2O.ai will be presenting an overview of the H2O machine learning library with a focus on the AutoML (Automatic Machine Learning) functionality. This is an opportunity to learn about the field of Automatic Machine Learning and get hands-on with a popular, open source AutoML tool which can be used to speed-up and/or augment your machine learning modeling workflow. The tutorial will focus on the AutoML function inside the **h2o** R library, though equivalent materials will also be available for the **h2o** Python module. The H2O platform provides fast, scalable implementations of a variety of popular machine learning algorithms. No prior knowledge of H2O is required, though a familiarity with the basic concepts of supervised machine learning will be helpful.

In recent years, the demand for machine learning experts has outpaced the supply, despite the surge in people entering the field. To address this gap, there have been big strides in the development of user-friendly software for AI that can be used by non-experts. Although these tools have made it easier for non-experts to experiment with machine learning, there is still a fair bit of experience that is required to produce high-performing, production-ready machine learning models. A user of these tools must understand which algorithms to use under what circumstances, as well as how to tune the models to get good results on any particular dataset. A nascent subfield of AI called Automatic Machine Learning or simply, "AutoML" is rapidly growing to address this issue.

This tutorial will provide a history and overview of the field of Automatic Machine Learning and introduce H2O's approach to AutoML. The presentation will be followed by a hands-on demonstration of how to use H2O's open source AutoML software. R and Python code will be provided so that attendees can walk away with a practical understanding of how to automatically train and tune production-ready machine learning models in a single line of code or with press of a button on their own datasets.

Required Hardware / Software:

- Attendees will need their **laptops**.
- H2O R or Python package.
- Java JRE or JDK installed (requirement of H2O).
- Code will be on GitHub (thus internet access is required).

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Towards Human-Centered AutoML

Florian Pfisterer [1], Janek Thomas [1], Bernd Bischl [1]

Building models from data is an integral part of the majority of data science work flows. While data scientists are often forced to spend the majority of the time available for a given project on data cleaning and exploratory analysis, the time available to practitioners to build actual models from data is often rather short due to time constraints for a given project. AutoML systems such as *auto-sklearn* [2] are currently rising in popularity, as they can build powerful models without human oversight and knowledge. We propose to modify the AutoML process in two ways by 1) allowing to incorporate multiple criteria in the AutoML workflow, and 2) opening up systems to allow for human intervention and adaption during the search process.

In the scientific community, those systems are compared in several AutoML challenges[3] organized at top machine-learning conferences. These challenges focus solely on the predictive performance of models built by the AutoML systems, mainly because it is easy to compare and rank the systems in this way. The humans role in current AutoML processes is to choose data sets, validation protocols, performance measures to optimize and to define the pipeline search space, i.e., which preprocessing and modeling steps to consider. After that, the systems usually do not require human intervention and returns an optimal model after a prespecified amount of time. This often drastically speeds up the process of obtaining well working models as technical optimization is left to the machine and has not to be dealt with in a manual trial-and-error process. Furthermore, this process can be scaled up to run on massively parallel systems.

Besides predictive performance, we consider sparseness, model size, prediction speed and interpretability, as well as other measures such as fairness and robustness important criteria we might want to integrate in the AutoML process. All those criteria and their respective importance vary between projects and have inherent trade-offs, meaning that not all of them can be optimized equally well. We want to point out some criteria that are currently ignored in many AutoML systems, and showcase an implementation based on [4], that allows for the selection and tuning of models according to user-defined preferences. While some of the criteria mentioned can not be easily assessed in an automatic manner, others can already be integrated in existing AutoML frameworks. This problem can be circumvented by either finding working proxies that allow to assess models wrt. some criteria, such as fairness, or by allowing humans to rate whether models suit their choice and incorporating this feedback in the process. The latter can be achieved by getting the human-in-the-loop. This does not only increase adaptivity of the system, but would also help to increase trust in those systems because parts of the process is driven by the data scientist. Thus, systems should make intermediate results available to

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the practitioner, which can then be evaluated and played back to the AutoML system. An important approach to making this complex process more accessible to humans was proposed in ATMSeer[1]. This can especially help in situations, where user preferences are not easily quantifyable, or where relevant criteria are not known a-priori. The field of AutoML promises great enhancements to the current data science workflow, but to harness its full potential, it needs to be extended to be more accommodating towards multiple criteria and human intervention.

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Boosting with random selection of weak learners for variable selection in high-dimensional models

Christian Staerk[1] *and Andreas Mayr*[1]

Statistical boosting is a promising alternative to popular regularization methods such as the Lasso [1] for fitting high-dimensional models with many possible explanatory variables: early stopping of the algorithm leads to implicit regularization and variable selection, enhancing the interpretability of the final models. Traditionally, the class of possible weak learners is fixed for all iterations of Boosting and usually consists of simple learners including only one explanatory variable at a time. Furthermore, the choice of the number of Boosting iterations is typically guided by optimizing the predictive performance of the resulting models, leading to final models which often include unnecessarily large numbers of noise variables with small effects.

We propose modifications of L_2Boost [2] for variable selection in high-dimensional linear models which aim at addressing the potential issues described above. The modifications are based on an adaptive random selection of different classes of weak learners in each Boosting iteration, where the adaptation of the weak learners is motivated by the recently proposed Adaptive Subspace (AdaSub) method [3, 4]. The considered classes include weak learners with several variables so that multiple coefficients can be updated at a single iteration. Furthermore, the proposed modifications of L_2Boost can impose an automatic stopping of the algorithm, leading to a reduced number of selected noise variables. The performance of the new approach is investigated in a simulation study, comparing it with the original version of L_2Boost as well as with other approaches such as Stability Selection for Boosting [5], which also aim at controlling the number of falsely selected variables.

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imputeTS: Tidy Univariate Time Series Imputation

Steffen Moritz[1]*, Thomas Bartz-Beielstein*[1]

While nowadays more and more time series data are generated, missing values quite naturally remain a pervasive problem. Those missing values can compromise subsequent processes, thus replacing missing values (imputation) often benefits the quality of further data analysis.
Univariate time series imputation thereby is a special sub-field. Imputation techniques for cross-sectional data, time series cross-sectional data or multivariate time series altogether at least partially rely on inter-variable correlations to estimate the missing data. In comparison, univariate time series imputation solely can employ inter-temporal correlations.
We present **imputeTS**, an R package for time series imputation [1]. It provides several different state-of-the-art imputation and visualization functions for univariate, equispaced time series, $X = \{x_1, x_2, ..., x_n\}$. Additionally, the package works seamlessly with current tidy data workflows.
Favorable use cases hereby do not only include originally univariate time series. Univariate time series imputation is also helpful for multivariate time series with only uncorrelated variables. Another use case are multivariate time series, where whole observations at some points in time are completely missing. Especially the latter case is quite common for sensor data, if the data recording or transmission fails it often does for all variables at once. Meaning no inter-variable correlations can be employed for these points in time.

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Joint Modelling approaches to survival analysis via likelihood-based boosting techniques.

Colin Griesbach[1], *Andreas Groll*[2], *Elisabeth Waldmann*[1]

When analyzing data where event-times are recorded alongside a longitudinal outcome, one commonly used approach in practice is separate modelling of the two outcomes without considering any interaction effects. Especially in survival analysis one main interest is incorporating time-varying covariates into the model. This however is quite a challenge, since popular methods like the extended cox regression produce biased results. Joint modelling on the other hand combines a longitudinal and a survival submodel in one single joint likelihood and thus accounts for interactions like time-varying covariates measured with error, which can be often found in follow-up studies. Previous works proposed algorithms to fit joint models via component-wise gradient boosting techniques which focus on minimizing the predictive risk, offer advantages like variable selection and also work with high dimensional data. However, gradient boosting leads to problems in the survival part of the model, since effects of time-varying covariates can not be estimated so easily. Likelihood-based boosting approaches on the other hand are, as verified in various literature, capable of handling time-dependent covariates in survival analysis, since likelihood-based boosting directly optimizes the likelihood by using newton algorithms with a component-wise updating procedure.

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Tackling leukemia through computational statistics

Christiane Fuchs[1,2,3], *Lisa Amrhein*[2,3]

Acute Myeloid Leukemia (AML) is the most common acute leukemia affecting adults. Even after complete remission, leukemic cells likely remain in numbers below detection limit. Without further postremission or consolidation therapy, most AML patients will eventually relapse and die. An essential step towards successful treatment of AML is to understand the evolution of the genetic, epigenetic, and functional properties of clonally growing tumor cells.

The advent of single-cell RNA sequencing technologies holds enormous potential for research into this field. In recent years, technological advances have led to the development of large complex data. However, this data encounters uncertainty on both experimental and biological levels. Despite several breakthrough, measured values are still affected by substantial noise and missing values. Even under identical experimental conditions, data from different runs suffer from systematic differences including natural biological variation within and between individuals, especially regarding diseases like AML. In addition, AML patients frequently carry mixtures of different cancer cell types, so-called subclones, which evolve over time, so that the mixture at relapse is different from the one at diagnosis. Understanding clonal evolution and identifying rare subclones is still an open challenge.

In this talk, we will present computational modeling and estimation techniques that can contribute to the understanding of evolutionary processes in AML: the derivation of appropriate probability distributions to describe single-cell mRNA counts [1]; the identification of differently regulated cells from heterogeneous populations using mixture models [2]; and the modeling of time-continuous evolutions of clonal compositions.

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bamlss: A Lego toolbox for flexible regression models

Nikolaus Umlauf[1]

During the last decades there has been an increasing interest in distributional regression models that allow to model all distributional parameters, such as location, scale and shape and thereby the entire data distribution conditional on covariates. In particular, the framework of structured additive distributional regression models enables to specify different types of effects such as linear, non-linear or interaction effects on all the distribution parameters hence providing a very flexible and generic framework suited for many complex real data problems. However, the implementation of new models is usually time-consuming and complex, especially using Bayesian estimation algorithms. We propose an unified modeling architecture that makes it possible to embed many different approaches suggested in literature and software. We show that implementing (new) algorithms, or the integration of already existing software, is relatively straightforward in this setting. An implementation is provided in the R package bamlss (https://cran.r-project.org/package=bamlss). We illustrate the usefulness of the approach by implementing neural network distributional regression models and evaluate the performance on simulated data and an application in survival analysis.

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Automatic Machine Learning and (Deep) Reinforcement Learning with rlR package

Xudong Sun[1] *,Jiali Lin*[1]*,Bernd Bischl*[1]

Reinforcement Learning especially Deep Reinforcement Learning has gained increasing attention recently. Deep reinforcement learning has gained great attention in the past years with its rapid advances in solving complex scenarios like Atari Games, the game of Go and continous robotic control, etc. The idea of using deep neural network as a general function approximator is relatively new to both the Computer Science and Statistics field. The R package rlR https://github.com/smilesun/rlR is developed to bridge the reinforcement learning with statistics by incorporating several state of art deep reinforcement learning algorithms into the package. Algorithms like Frozen Target Deep Q learning, Actor Critic Method, Deep Deterministic Policy Gradient, Trust Region Policy Optimization, Soft Q learning and Stein Variational Inference will be covered. The talk will cover the basic usage of rlR, and how it can be extended for Automatic Machine Learning (AutoML) with Bayesian Optimization. The new algorithm is called ReinBo. Its mechanism will be explained and Benchmarks with state of art AutoML softwares will be presented which showed a considerable improvement.

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Additional sparsity and enhanced variable selection for statistical boosting algorithms

Annika Strömer[1,2], Jan Speller[1], Christian Staerk[1] and Andreas Mayr[1]

An alternative approach for fitting linear models is component-wise gradient boosting. It is very flexible and useful for fitting high-dimensional data. Furthermore, statistical boosting includes variable selection, which is controlled by the main tuning parameter the number of boosting iterations [1,2].

While being very flexible and also relatively easy to extend, in some practical applications the algorithm shows the tendency towards selecting too many variables, including false positives. This seems to take place particularly for rather low-dimensional data ($p < n$) when one can generally observe a slower overfitting behavior. Due to the slow overfitting, the resulting stopping iteration (m_{stop}), tuned with cross-validation, gets larger and more variables are effectively included in the model. In practice, many of the false positives are incorporated with very small coefficients as the estimates are heavily shrinked towards zero. They hence do not have a larger impact on prediction accuracy, but lead to larger models with difficult interpretation.

We try to fix this problem by giving the algorithm the chance to de-select those variables that have (i) either been updated in very few iterations or have (ii) been estimated with very small coefficients. We analyze the impact of these fixes on both variable selection and prediction accuracy while comparing them to other methods for enhanced variable selection in the context of boosting.

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Adaptive robust boosting for high-dimensional regression models

Jan Speller[1], Christian Staerk[1] and Andreas Mayr[1]

A promising, application-oriented alternative to the already established methods for computing regression models is statistical boosting [1,2]. This approach is particularly helpful for high-dimensional data incorporating implicit variable selection via an iterative gradient-based descent in function space. The basic idea is to minimize the empirical risk by fitting simple base-learners (these are regression type functions in case of statistical boosting) to the negative gradient of the loss function. For the classical L_2 loss, this basically leads to re-fitting the residuals from the previous iteration.

While the classical mean regression via the L_2 loss is quite sensitive to extreme observations or outliers, optimizing the L_1 loss leads to the more robust median regression. We analyse the Huber loss [3,4] as a robust mixture between L_1 and L_2 and propose an adaptive approach via a self-regulating quantile-based parameter which ensures that the same amount of observations are incorporated in both parts of the loss in all boosting iterations. Therefore, we investigate in simulation and an application whether setting this quantile-based self-regulating parameter has an effect on the robustness of the final model.

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Correlation between quality of life and gait parameters in Parkinson's Disease

Isabelle Kaiser[1], Heiko Gassner[2], Jochen Klucken[2] and Werner Adler[1]

Gait deficits are common symptoms in Parkinson's disease (PD) [1], which leads to the restriction of mobility and thus the quality of life. A wearable sensor-based gait analysis system enables to objectively assess gait parameters without the need of having a specialized gait laboratory [2]. The correlation between the quality of life, which is represented by the widely used and standardized health survey SF-12 [3], and gait parameters is analyzed in this work.
Our study population consists of 163 Patients with Parkinson's disease visiting the movement disorder outpatient center at the University Hospital Erlangen, Germany, as wells as 95 controls. After an examination of pairwise correlations, we analyze the ability of gait parameters and common clinical variables like age and sex to predict quality of life with several different regression models, e.g. multiple linear regression, support vector machine [4] and random forest [5]. The performances of these models are estimated via cross-validation.
Results show that there are several significant correlations between gait parameters and the physical component of the quality of life. Nevertheless, reliable prediction of quality of life using only variables available in our study is not possible.

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Generative artificial intelligence based algorithm to increase the predictivity of preclinical studies while keeping sample sizes small

Jörn Lötsch[1,2], and Alfred Ultsch[3]

The translation of basic science into new clinical effective compounds seems to be often unsatisfactory. This has been attributed to inappropriate data quality standards and to the often small sample sizes. As solutions of this problem, combinations of several studies or otherwise-increased sample sizes have been proposed to obtain adequate statistical power, facilitating the validity of the results and their predictivity of clinical drug effects. We propose the development of an artificial intelligence (AI) -based method, which can generate valid, i.e. which have the same structure and properties, additional data from available data sets. If the data is acquired only in small numbers, the sample size for data analysis is enhanced, without increasing the number of laboratory animals included in the preclinical experiments. Specifically, generative models (GM) will be used that try to solve the problem of generating valid data from a nontrivial, possibly high dimensional distributions, that are either unknown or can be hardly described analytically. In the case of success, GM can solve the problems of sparse data, rare cases or small sample sizes. Several statistical models for GM have been proposed, including rejection sampling, the Metropolis-Hasting algorithm and the so-called inverse transform method. More recent developments include Generative Adversarial Networks (GAN), which have the advantage that a comparison of the distribution of generated data with the targeted non-trivial distribution can be obtained by means of a learned classifier implemented as a supervised neuronal network. GAN proofed as particularly useful in image processing and related tasks.

An alternative structure detecting neuronal network based algorithm is provided by emergent self-organizing maps (ESOM), which have the advantage of a vast body of successful applications on non-image related biomedical data, both experimental and clinical. Using the so-called "U-matrix" it can be judged whether or not structure in the data exists [1-5]. Based on the valid data structure detection by means of the ESOM/U-matrix artificial intelligence, generative neuronal networks offer the possibility to generate valid synthetic examples in the data space. Following investigation of the structure of data acquired in small samples or small subgroups, the probability matrix ("P-matrix") can be obtained that represents the joint distribution p(x,c), where x is a feature vector of a data example and c the label of a subgroup [6]. Using both, the structure detection properties of the SOM algorithm and the probability matrix of the data, new data can

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be generated that artificially increase the sample size.
Thus, to increase the predictive power of preclinical studies, rather than an increase in the number of cases, directly or indirectly via merging multiple studies, we propose an innovative, AI-based, valid, and probabilistic generation of experimental data that, together with the original data, provides the high data density necessary to draw valid conclusions from preclinical experiments. First proof-of-concept data will be presented; a working implementation into preclinical model derived data is subject of ongoing and future research.

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Utilizing molecular network information via Graph Convolutional Neural Networks to predict metastatic event in breast cancer

Hryhorii Chereda[1], Annalen Bleckmann[1, 2], Frank Kramer[3], Andreas Leha[1], and Tim Beissbarth[1]

Gene expression data is commonly available in cancer research and provides a snapshot of the molecular status of a specific tumor tissue. This high-dimensional data can be analyzed for diagnoses, prognoses, and to suggest treatment options. Machine learning based methods are widely used for such analysis.
In recent years deep learning was applied to a wide range of problems in various areas. Deep learning methods are aimed at the automatic learning of data representations (features) needed for machine learning task. These methods demonstrated state-of-the-art performance in visual object recognition, object detection, speech recognition as well as other domains such as drug discovery and genomics [1]. One of the most popular methods of deep learning are Convolutional Neural Networks (CNN). They show cutting edge results for data that are spatially structured. The main property of CNNs is a capability of capturing local spatial patterns in natural signals and merging them into high-level abstractions. Nowadays, deep learning is extending to Non-Euclidean domains. Essentially such an extension is based on generalization of CNNs [2] to graphs. Molecular networks are commonly represented as graphs detailing interactions between molecules. Gene expression data can be assigned to the vertices of these graphs, and the edges can depict interactions, regulations and signal flow. In other words, gene expression data can be structured by utilizing molecular network information as prior knowledge.
Here, we applied graph CNN to gene expression data of breast cancer patients to predict the occurrence of metastatic events. To structure the data we utilized a protein-protein interaction network. We show that the graph CNN exploiting the prior knowledge is able to provide classification improvements for the prediction of metastatic events compared to existing methods.

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Extracting ordinal class sequences from high-dimensional datasets

Lisa M. Schäfer[1,2], Ludwig Lausser[1] and Hans A. Kestler[1]

Ordinal classifier cascades have been shown to be suitable for detecting embeddings of total ordinal relations in high-dimensional feature spaces [1]. The performance of these classifier cascades depends on the assumed class order. A performance drop indicates that an assumed order is not reflected within the analysed feature representation. By screening through all possible class permutations it is possible to distinguish between reflected and not reflected classes.
However, the assumption of one total order comprising all class labels might not be valid. We therefore extended this screening procedure to ordinal relations in any subgroups of classes.

Within an explorative analysis we applied the extended screening procedure to various datasets. We analysed the best performing longest cascades, as those imply the most and accurate information about a dataset. Furthermore, we observed that the found cascades often allow for a compact assignment of the remaining classes.
The screening procedure does not only allow the confirmation of known ordinal relations in alternative feature representations, but also to reveal new relations and thereby to get more insight about the neighbourhood structure of classes.

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Adaptive step-lengths in model-based gradient boosting algorithms for distributional regression

Tobias Hepp[1,3],Boyao Zhang[2],Andreas Mayr[1],Elisabeth Waldmann[3]

Gradient boosting methods are iterative updating schemes, in which the gradient of the loss-function in the current step is fitted to the data. The best fitting variable is then selected and updated by a fracture ν of the parameter suggested. Technically speaking, this means that the algorithm must be tuned with two parameters: the overall number of iterations and this fracture, also called step-length, but current practice is to fix the latter at $\nu = 0.1$. While this has been shown to work well in a variety of scenarios, those findings are based on models with only one gradient [1]. However, using gradient boosting algorithms for more complex model classes such as generalized additive models for location, shape and scale involves fitting multiple gradients derived from a single global loss function [2]. Depending on the updating scheme in the iterations, using the same step-length for all base-leaners may result in unfair comparisons in the selection process. Balancing the step-lengths with the potential contribution of the corresponding base-learners to the global loss function might therefore help to improve the performance of the algorithm regarding variable selection accuracy and overall model sparsity.

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A continuous-time capture-recapture model for the annual movement of bottlenose dolphins

Sina Mews[1],Roland Langrock[1],Ruth King[2],Nicola Quick[3]

Our modelling approach is motivated by individual sighting histories of bottlenose dolphins off the east coast of Scotland. Due to ongoing offshore development, conservation managers seek to better understand the temporal movement patterns of the dolphin population between different sites. Typically, the Arnason-Schwarz model is fitted to such multi-state capture-recapture data[1], assuming a first-order Markov chain in discrete time for the state process, which here corresponds to the location (site) of a given individual (in addition to alive and dead). In our case, however, the capture occasions are not regularly spaced in time, leading to the problem that standard capture-recapture methods are not readily applicable as they address the more commonly found regular sampling protocols. Therefore, we consider a continuous-time model formulation instead.

The capture-recapture setting can be regarded as a special case of a (partially) hidden Markov model (HMM), with the observed capture history of an individual as the state-dependent process and an underlying, partially observed state process related to the movement of the individual between different sites. In particular, we can exploit the convenient and efficient HMM-based forward algorithm for evaluating the likelihood and hence for parameter estimation[2]. Further inferential tools that become applicable by embedding the capture-recapture setting in the HMM framework include the Viterbi algorithm and the forward-backward algorithm, which can be used to decode the underlying states (sites).

The main aim of the present analysis was to investigate how the dolphins' movement rates

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between two sites, expressed as state transition intensities in our model, depend on the time of year. However, incorporating such time-varying covariates into the continuous-time Markov state process is rather challenging as the corresponding likelihood function then becomes intractable. We suggest an approximation using piecewise constant state transition intensities, which renders the likelihood evaluation feasible[3]. The approximation can be made arbitrarily accurate by using an increasingly fine resolution of the approximating step function.

The suggested approach is applied to investigate the annual movement of bottlenose dolphins between their main sites on the east coast of Scotland, revealing seasonal patterns which can help to inform conservation management. Our modelling approach can easily be transferred to other scenarios and is hence a general method for irregularly sampled capture-recapture data subject to switches in underlying states.

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Simulation of trajectories in the illness-death model for chronic diseases: discrete event simulation and Doob-Gillespie algorithm

Ralph Brinks[1], *Annika Hoyer*[1]

This work is about simulation of populations transiting through the stages of the illness-death model for chronic diseases. First, we compare the commonly used discrete event simulation [1] with the Doob-Gillespie algorithm [2,3] in terms of computational speed. The comparison is accomplished in a test example motivated from diabetes in the German population [4]. It turns out that the current implementation of the discrete event simulation is slower than the Doob-Gillespie algorithm by a factor of about 75. Second, we use the Doob-Gillespie algorithm to explore the coverage probability of the 95% Wald confidence intervals of the binomial distribution for different population sizes (n) and success probabilities (p). The success probabilities p in the illness-death model corresponds to the prevalences of the chronic disease. Coverage is examined by 5000 simulation runs for population sizes from n = 50 to n = 500,000 and prevalences from p = 1% to p = 35%. The prevalences p are obtained from the solving an ordinary differential equation that is closely related to the illness-death model [5]. Irrespective of the tested simulation settings, the coverage probability of the 95% Wald confidence intervals is at least 94.3% and reaches up to 97.4%. Thus, in the tested settings the Wald confidence interval is a reasonable approximation to the 95% confidence interval of the binomial distribution .

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A Classification Tree Approach for the Modeling of Competing Risks in Discrete Time

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Cause-specific hazard models are a popular tool for the analysis of competing risks data. The classical modeling approach in discrete time consists of fitting parametric multinomial logit models. A drawback of this method is that the focus is on main effects only, and that higher order interactions are hard to handle. Moreover, the resulting models contain a large number of parameters, which may cause numerical problems when estimating coefficients. To overcome these problems, a tree-based model is proposed that extends the survival tree methodology developed previously for time-to-event models with one single type of event. The performance of the method, compared with several competitors, is investigated in simulations. The usefulness of the proposed approach is demonstrated by an analysis of age-related macular degeneration among elderly people that were monitored by annual study visits.

Keywords: Discrete time-to-event data, Competing Risks, Recursive Partitioning, Cause-Specific Hazards, Regression modeling

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Semantic multi-class classifier systems in precision medicine

Lea Siegle[1], Ludwig Lausser[1], Hans A. Kestler[1]

Molecular high-throughput technologies have made the aggregation of large collections of bio-markers possible. The downside: the size of these collections prohibit the direct analysis by human experts. Intermediate representations such as classification models are required for the evaluation of these high-dimensional datasets, be it in diagnostics (for personalised medicine) or in sciences (to create new hypotheses). However, the patterns used to classify samples are often as unintererepretable as the data itself. We developed a new technique named "Semantic multi-class classifier system" (SM-CCS) to train biologically meaningful classifiers and to increase model interpretability. SMCCSs combine (knowledge-based) semantic feature selection (SFS) on the basis of established vocabularies (e.g. GO and KEGG) with a multi-class classification (MCC) method [1]. Here, we test two types of SFS on the well known one-against-one (OaO) and one-against-all (OaA) MCCs [2]: In both strategies features are selected individually for each base classifier. In the first strategy (type I), however, only one of the selected terms is chosen (either the least well, the mean or the best term, called MMM selection) and provided to all of the base classifiers, whereas in the second strategy (type II), each base classifier is trained in their own selected term. The four combinations (with all different MMM selections) are evaluated on a 4-classed breast cancer as well as on a 5-classed liposarcoma dataset and characterised by their accuracy and feature selection stability. We additionally provide evidence on the selected semantic terms. Interestingly, support can even be found for terms selected for individual twoclass comparisons.

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Modeling strategies to dissect the variable genetic architecture in the computation of polygenic risk score

Carlo Maj[1], Oleg Borisov[1], Christian Staerk[2], Andreas Mayr[2], Peter Krawitz[1]

Many complex (i.e., not monogenic) phenotypes are characterized by a relatively high heritability (e.g., height, common disease susceptibility [1]). However, only a little proportion of the phenotypic variance can be explained by significantly associated genetic variants identified by means of genome-wide association studies [2]. The genetic contribution of these traits can be due to the small effect of several variants leading to an overall genetic load according to an additive model [3]. Such a genetic load is known in the genetic field as "polygenic risk score" and indeed several works revealed strong polygenetic associations for many traits using linear models with quantitative traits (e.g., height [4], weight [5]) or logistic models for binary traits (e.g., case/control status for many disease [6]). The integration of polygenic risk score with other influencing factors proved to improve the performance of phenotype prediction model [7]. However, the overall applicability of these scores in clinical practice is still under investigation due to issues in the modeling of the genetic architecture [8]. In particular, genetic correlation across variants (i.e., linkage disequilibrium) and different allele frequencies across populations (i.e., population stratification) can strongly influence polygenic risk score hampering the generability of these scores across different datasets [9]. In the present work, we analyze different strategies to model linkage disequilibrium and population stratification in order to have more generalizable genetic risk models.

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Quantifying Interpretability of Arbitrary Machine Learning Models Through Functional Decomposition

Christoph Molnar[1], *Giuseppe Casalicchio*[1], *Bernd Bischl*[1]

To obtain interpretable machine learning models, either interpretable models are constructed from the outset – e.g. shallow decision trees, rule lists, or sparse generalized linear models – or post-hoc interpretation methods – e.g. partial dependence or ALE plots – are employed. Both approaches have disadvantages. While the former can restrict the hypothesis space too conservatively, leading to potentially suboptimal solutions, the latter can produce too verbose or misleading results if the resulting model is too complex, especially w.r.t. feature interactions. We propose to make the compromise between predictive power and interpretability explicit by quantifying the complexity / interpretability of machine learning models. Based on functional decomposition, we propose measures of number of features used, interaction strength and main effect complexity. We show that post-hoc interpretation of models that minimize the three measures becomes more reliable and compact. Furthermore, we demonstrate the application of such measures in a multi-objective optimization approach which considers predictive power and interpretability at the same time.

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