25th Anniversary Symposium of the Section for Clinical Biometrics

Thursday, April 14, 2016, 9-13h
Medical University of Vienna
Jugendstilhörsaal BT88.02
Spitalgasse 23, 1090 Wien

On the occasion of its 25th anniversary, the Section for Clinical Biometrics cordially invites you to its Silver Jubilee Symposium taking place on April 14, 2016, 9 a.m. – 1 p.m., in the Jugendstilhörsaal, BT88. The Section has always been intrinsically tied to the person of Professor Michael Schemper, who retired by November 2015. Therefore, we are pleased to announce invited talks of six of Michael Schemper’s international collaborators, including:

- Robin Henderson, Newcastle, UK
- Samo Wakounig, Klagenfurt, A
- Alessandra Nardi, Rome, I
- Stefan Michiels, Villejuif, F
- Stephan Lehr, Vienna, A, and
- Janez Stare, Ljubljana, SLO.

Registration and opening of the symposium will take place at 9 am. The Symposium will be followed by a buffet at 1pm, a hiking tour in the Vienna woods starting at approx. 2 p.m., and dinner at a Heurigen at Grinzing (typical Viennese vineyard) at approx. 6 p.m. (service charge ca. 30€, payable on site).

We ask for online reservation at [http://tinyurl.com/25years-of-biometrics](http://tinyurl.com/25years-of-biometrics) for the symposium until April 11th; registration for the hike and/or the Heurigen was closed on April 4th.
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Programme

9.00 – 9.20  Registration and Get Together

9.20 – 9.30  Georg Heinze  Welcome Address

9.30 – 10.00  Robin Henderson  Influence and Survival Time Summaries

10.00 – 10.25  Samo Wakounig  Motivational Orientation Development of High Achieving Students at a Secondary Technical School

10.25 – 10.55  Alessandra Nardi  Outliers Matter (in Survival Analysis)

10.55 – 11.25  Coffee Break

11.25 – 11.55  Stefan Michiels  Gene Signatures in Clinical Trials in Oncology

11.55 – 12.20  Stephan Lehr  Overfitting

12.20 – 12.50  Janez Stare  Michael Schenper’s Influence on Biostatistics in Ljubljana

13.00 – 14.00  Buffet
Abstracts

9.30 – 10.00

Influence Measures and Survival Time Summaries

Robin Henderson
Newcastle University, UK

The performance of different treatment centres sometimes need to be compared, usually on the basis of simple summary statistics. In this talk we look at how to compare centres generating time-to-event (survival) data. We look at robustness, sensitivity and fitness-for-purpose of a variety of standard and non-standard statistics. We compare influence functions for each, as a measure of how the statistics are affected by inclusion or exclusion of a small number of unusual observations. We derive also a perturbation influence function which measures the effect of small changes in values rather than addition/removal. We conclude that of the measures considered the average hazard ratio (Schemper, 2009) possesses what seem to be the best characteristics in terms of simplicity and robustness.

Robin Henderson is former Professor of Biostatistics at Lancaster University and current Head of Mathematics and Statistics at Newcastle University. Research interests include survival and event history methodology, longitudinal data analysis, missing data, and adaptive treatment and robust control. He first collaborated with Michael Schemper in the late 1990s on measures of predictive accuracy for survival data.

Robin is ’Henderson’ of the famous ’Schemper-Henderson’ measure for explained variation in survival analysis. He is still willing to support us with his invaluable advice about predictive modeling.

Robin’s collaboration with the Section for Clinical Biometrics:


Robin serves as scientific advisor of our FWF-funded research project ‘Predicting rare events more accurately (PREMA)’.
Motivational Orientation Development of High Achieving Students at a Secondary Technical School

Samo Wakounig
Alpen-Adria-Universität Klagenfurt, A

The development of excellent performance levels in schools is based on multiple influencing factors like giftedness, environmental and personal characteristics. In an evaluation study the motivational orientation development of high achieving students at a secondary technical school (HTL) has been followed for 5 years. In the talk, I will present first descriptive results of this evaluation study, nostalgically looking back to my previous work at the Section of Clinical Biometrics.

Samo Wakounig is Senior Scientist at the Institute of Education at the University of Klagenfurt – Celovec. He studied Mathematics and Slovene at the University of Klagenfurt holds a PhD in Mathematics (Statistics) from the University of Klagenfurt (supervisor Michael Schemper). His previous positions include the Austrian Research Centers Seibersdorf, Medical University of Vienna, Section for Clinical Biometrics, teacher at several secondary schools and teacher training at University of Klagenfurt. His favourite hobbies are mountaineering, hiking and singing at Danica choir.

After Samo has left our Section, we definitely had to start a collaboration with Slovenian statisticians to compensate the loss.

Samo’s footprint on the Section’s publication list:


10.25 – 10.55

Outliers Matter (in Survival Analysis)

Alessandra Nardi
Università degli Studi di Roma „Tor Vergata“, I

Methods to identify anomalous observations are well developed in the General Linear Model but they have received much less attention in survival analysis. In this talk I will describe the contribution given in this area by Michael Schemper. I will focus on the definition of outlier for survival data and on the role these observations can play. The idea of developing a suitable “measure of surprise” will be explained and the way to extend this measure to censored data illustrated. Applications to real studies will be presented.

Alessandra Nardi is Associate Professor of Medical Statistics at the Department of Mathematics, University of Rome „Tor Vergata“. Her research aims at deriving novel methodologies for modelling life-time-data, centering on assessing the goodness of fit of survival models via residual analysis, estimating time-dependent effects in the Cox model, describing complex data through mixture models. She also explores potentialities of the Bayesian approach with the purpose of developing predictive models. Alessandra Nardi has spent two post-doctoral fellowships in Vienna, both supervised by Michael Schemper, in 1996 and in 1999-2000.

At these occasions, she introduced us to Bayesian statistics and revolutionised the Section’s coffee drinking habits.

Alessandra’s footprint on the Section’s publication list:


Gene Signatures in Clinical Trials in Oncology

Stefan Michiels
Institute Gustave Roussy and University Paris-Sud, Villejuif, F

The derivation of gene signatures using -omics technologies is increasingly integrated in clinical trials in oncology and even in clinical practice. They are expected to provide valuable information for prognosis assessment and for therapeutic decision-making. In this talk, I will investigate some approaches to develop a gene signature in Cox regression model using main effects (prognosis) or using treatment by gene interactions (treatment modifiers). Using some contemporary data we show that the added value in prognostication as compared to clinicopathological factors is often small. For prognosis, we propose different extensions to the lasso penalty in Cox models to reduce the false positive rate in variable selection. For treatment modifiers, we propose to apply a permutation procedure in a survival model based on c-statistics that controls the family-wise error rate at a pre-specified alpha level. A gene signature can be developed for predicting the treatment effect with a crossvalidation scheme. We present simulations under null and alternative scenarios, and illustrate the methods with gene expression data from early breast cancer.

Stefan Michiels is Director of the Oncostat Team, INSERM U1018, University Paris-Saclay, University Paris-Sud, and Head of Methodology in the Department of Biostatistics and Epidemiology at Gustave Roussy, Villejuif, France. His areas of expertise are statistical analysis of biomarker and genomic data, prognostic models, clinical trials, Independent Data Monitoring Committees and meta-analyses in oncology. His previous positions include the Université Libre de Bruxelles- Institut Jules Bordet (FNRS researcher), the National Cancer Institute (France) and the University of Leuven (Belgium).

Very recently we have renewed our collaboration with Stefan by mutually co-supervising our PhD students.

Stefan’s collaboration with the Section for Clinical Biometrics:


Building a prediction model, the statistician is tempted to fit a model with too many degrees of freedom. Degrees of freedom are easily spent by selecting among a set of putative predictor variables, categorization of continuous predictors, the inclusion of interaction terms, or the consideration of non-linear relationships. Overfitting leads to optimistic model performance for the data at hand, but to disappointment in the prediction for new external subjects. The presentation gives a personal tour on the subject of overfitting, from student life to non-proportional hazards, from the genomics era to the strict regulatory environment.

**Stephan Lehr** is a statistical assessor at the Austrian Medicines and Medical Devices Agency. He started his endeavours as an applied statistician at the (Medical) University of Vienna, was involved in different phases of drug development in the pharmaceutical industry, and finally decided to join the regulatory environment. Michael Schemper was Stephan's dissertation advisor when he was studying over-fit in the analysis of time-dependent effects.

*Stephan is the incoming president of the Vienna Biometric Section.*

Stephan's footprint on the Section's publication list:

Michael Schemper's support to me, advice for me, and collaboration with me, were essential for development of (serious) medical statistics in Ljubljana. If I were to sum up what I learned from Michael Schemper in one sentence, I would say: having an idea is the most important thing, and intuitive understanding is more important (deeper) than understanding of the theory. In the first part of my talk I will tell a short story about my acquaintance with Michael, and illustrate the sentence above. In the second part, I will show how misunderstanding of explained variation, the subject at the core of my collaboration with Michael, still persists, and has even led to a potentially dangerously wrong conclusion in a highly esteemed journal.

Janez Stare graduated from the Faculty of Mathematics, University of Ljubljana, then held a Master Degree and Ph.D. in Biostatistics from the Faculty of Medicine, University of Ljubljana. He is currently full Professor of Biostatistics at the Faculty of Medicine, Ljubljana, and Head of the Institute of Biostatistics and Medical Informatics, Faculty of Medicine, Ljubljana. His research interests are explained variation in survival analysis, linear models in survival analysis, predictive ability of regression models in survival analysis, frailties, random effects in survival models, relative survival. He spent fellowships at the Section for Clinical Biometrics in 1992 and 1994.

And of course he never missed the chance for a stop-by in Vienna.

Janez' collaboration with the Section for Clinical Biometrics:


Janez also serves as scientific advisor of our FWF-funded research project ‘Predicting rare events more accurately (PREMA)’. 
The Section for Clinical Biometrics supports clinical research by biostatistical advice, develops innovative methodology for biostatistical applications and teaches undergraduate and PhD students in statistical methodology. Methodological research topics include regression modelling, explained variation, analysis of high-dimensional (-omics) data, small sample analysis, missing covariate values, clinical trials, and uncertainty assessment. Collaboration with various clinics and departments of the Medical University is documented by numerous joint publications each year.

The current members of the Section, from left to right: Harald Heinzl, Michael Kammer, Christine Wallisch, Martina Mittlböck, Georg Heinze, Ilona Hofbauer, Angelika Geroldinger, Michael Schemper (retired 2015), Daniela Dunkler, Alexandra Kaider, Maria Haller, Andreas Gleiß

Former employees of our Section were Wolfgang Draxler, Viktoria Fryskak, Eva Graber (†), Milan Hronsky, Renate Klebinger, Maria Kohl, Stephan Lehr, Alessandra Nardi, Petra Ofner, Sigrid Pete, Meinhard Ploner, Ingrid Rauch, Albert Rosenberger, Terry Smith, Janez Stare, Klaudia Steiner, Ursula Taborsky, and Samo Wakounig.

We would like to thank Sabine Glöckl, Karin Brauneis, Natalie Vachuda and many other colleagues at CeMSIIS for their help in organizing the symposium.