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www.sbs-bvs.be

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# TABLE OF CONTENTS

12 <sup>th</sup> Annual Meeting in Vielsalm	2
News from the Biostatistics Section	5
Member News	8
Announcements	9
Continuing Education – Courses in Statistics	11
Recent PhD Theses	13

# 12TH ANNUAL MEETING OF THE BELGIAN STATISTICAL SOCIETY, VIELSALM, 8-9 OCTOBER 2004

# **Final program**

# Friday, 8 October 2004

9:00 - 10:15	Registration and coffee
10:15 - 10:30	Welcome address
10:30 - 11:00	Statistics in Belgium 1 Health Interview Survey – J.Tafforeau (IPH, Brussels)
11:00 - 11:30	Statistics in Belgium II Measuring migration flows with 'Registre National' data – Jean-Pierre Hermia (GéDAP, Brussels)
11:30 - 12:30	<u>Invited speaker I</u> Robust Linear Models - Stephan Morgenthaler (Lausanne Polytechnic School, Switzerland)

- 12:30 14:00 Lunch
- 14:00 15:40 Parallel sessions I and II

	Session I: Biostatistics	Session II: General methods
14:00-	J. Serroyen*, Z. Shkedy, L. Bijnens and T. Steckler, LUC,	M.C. Bramati <sup>*</sup> , M. Hallin and D. Paindaveine, ULB,
14:20	The lick suppression test: analysis of repeated time-to-	Nonparametric optimal tests for independence in the VAR
	event data in rats using frailty models and marginal survival models.	elliptical model
14:20-		Jan Annaert, G. Brys* and M.
14:40	Van Dun, LUC, A novel analysis of drug combination experiments using PROC	De Ceustet, UA, A new large sample test of univariate symmetry.
14:40-	<i>NLMIXED</i> . S. Goetgeluk* and S.	D. Cassart*, M. Hallin and D.
17.70-		Paindaveine, ULB, <i>Parametric</i>

15:00	and heritability in twin	and nonparametric tests for
	studies.	symmetry based on Edgeworth
		expansions.
15:00-	L. Bijnens*, R. Straetemans,	I. Van Keilegom and C.
	Z. Shkedy, G. Molenberghs,	Heuchenne*, UCL,
15:20	M. Desmidt, P. Vinken and B.	Nonparametric regression with
	Van Den Poel, Janssen	censored data based on
	Pharmaceutica, The	preliminary kernel smoothing.
	comparison of a nonlinear	
	mixed effects model to a two	
	stage procedure for the	
	analysis of toxicological data.	
15:20-	S. Fieuws* and G. Verbeke,	I. Gijbels, A. Lambert* and P.
	KUL, Random-effects models	Qiu, UCL, Edge preserving and
15:40	for multivariate longitudinal	denoising digital images and
	profiles: a pairwise modelling	regression surface estimation.
	approach.	

15:40 – 16:10 *Coffee* 

16:10 - 17:00	Oral poster session
17:00 - 18:00	<u>Invited speaker II</u> Luc Devroye (Mc Gill University, Canada)
20:00	Conference barbecue dinner at the swimming pool (*)

# Saturday, 9 October 2004

9:30 - 10:00	<i>Statistics in Belgium III</i> Granger causality analysis for business and consumer surveys - Christophe Croux (KULeuven)
10:00-10:30	Coffee
10:30 - 12:10	Parallel sessions III and IV:

	Session III: Robustness, misclassification and related methods	Session II: General methods
10:30-	M. Hubert and S. Engelen*, KUL, <i>Fast cross-validation of</i>	G. Massonnet*, T. Burzykowski and P. Janssen,
10:50	high-breakdown resampling methods for PCA.	LUC, Resampling plans for frailty models.
10:50-	E. Roelant*, S. Van Aelst and	S. Litière <sup>*</sup> , A. Alonso, G.
11:10	G. Willems, UG The multivariate least weighted squared distances Estimator.	Molenberghs and H. Geys, LUC, Impact of misspecified random-effects distribution on maximum likelihood estimation in generalized linear mixed
11.10		models.
11:10-	Hubert, KUL, An improved	C. Vanderhoeft and P. Slock*, Statistics Belgium, <i>Survey</i>
11:30	boxplot for skewed distributions.	sampling and contacting in waves using homogeneous primary sampling units.
11:30-	D. Magis, ULg, Goodness of	Ch. Ritter, UCL, Problem
11:50	fit testing and data set stability with respect to misclassification.	oriented undergraduate and graduate teaching in statistics.
11:50-	S. M. Mwalili*, E. Lesaffre	M. Mauer, A.F. Donneau*, F.
12:10	and D. Declerck, KUL, <i>Regression models for counts</i>	Sartor and A. Albert, ULg, A <i>flexible two-step randomised</i>
12.10	with misclassification applied	response model for estimating
	to a oral health study.	the proportions of individuals
12:10 - 14:	00 Lunch	with sensitive attributes
12.10 - 14.	00 Lunch	
14:00 – 15:00 <u>Invited speaker IV</u> Skewness a la mode?		
- Frank Critchley (Open University, UK)		
15:00 – 16:00 <u>Invited speaker IV</u> How flexible in practice can clinical trials be ?		
- Andy Grieve (Pfizer R&D, UK)		
16:00	Closing and coffee	

(\*) Due to the tropical atmosphere at the Aquafun (swimming pool of the SunParks resort), casual clothes are recommended. The swimming pool will remain open the whole evening.

# BIOSTATISTICS SECTION OF SBS/BVS Minutes of GENERAL ASSEMBLY



- **Date**: Thursday, May 27, 2004, 16:30 18:00
- Place: Lilly Development Centre, Louvain-la-Neuve
- **Present:** J. Bogaert , B. Boulanger, L. Danielson, P. Lambert, D. Rosillon
- **Excused:** L. Bijnens, C. Dubois
- 1. 2003-2004 report from the president (L. Danielson)
- The Biostatistics section of SBS/BVS organised :
  - Biostatistics session of the SBS/VBS Annual Meeting, La Roche, October 2003. The quality of the presentations was excellent.
  - Joint Meeting with PSDM (NL) "Challenges for the next 10 years", Janssen Pharmaceutica, Beerse, December 2003
  - DIA non-clinical statistical meeting organised by B. Boulanger, Dublin, April 22-23, 2004.
  - Practical course for micro-array data, Paul Eilers, Lilly, Louvain-la-Neuve, May 26-27,2004
- Two members (L. Danielson and B. Boulanger) of our section represented Belgium at the EFSPI :
  - Participation to 2 meetings (Paris and Maidenhead).
  - Instalment of Committees and working parties:
    - Regulatory Affairs (K. Smidt, DK)
    - PR materials (P. Koopman, NL)

- Non-clinical statistics (B. Boulanger, B)
- Scientific Meetings (A. Ebbut, UK)
- Qualifications and trainings (K. Roes, NL)
- Regulatory / Industry issues:
  - No new points to Consider were sent in 2003 for comments;
  - Comments were sent on the finalised PtC on baseline covariates, especially regarding minimisation. A meeting is planned in 2004.
- The EFSPI website has been updated (www.efspi.org)
- Scientific meetings committee:
  - Scientific meetings and courses are now posted on the EFSPI website
  - PSI (UK) would be interested in organising joint PSI/EFSPI meetings
- 2. <u>Presentation of the financial report</u> by the treasurer (B. Boulanger)
  - The current balance is + 2,852 Euros
  - The financial report has been approved by the GA
- 3. <u>Election</u> of the new members of the board
  - Two members of the board have reached the end of their term and elections are organised: One candidate from the pharmaceutical industry and for one candidate from a CRO or a research institution (other than academia)
  - There were two candidates : and Jan Bogaert (CRO/research institution) and Cécile Dubois (Pharmaceutical industry)
  - There were 51 valid votes, results are:
    - \* Jan Bogaert 32 votes
    - \* Cécile Dubois 45 votes
- According to the by-laws of the section, Cécile Dubois who has the highest number of votes will be the next president in two years.

The new Board is:

- President : Philippe Lambert,
- Treasurer and Secretary: Bruno Boulanger,
- Members: Cécile Dubois and Jan Bogaert.

# 4. Further Activities

Two events are planned:

- Joint meeting of the 3CC, Biostatistics Section, and Quetelet Society, Janssen Pharmaceutica, Beerse, June 22, 2004.
- Annual meeting of the SBS/BVS, Vielsam, October 8-9, 2004. Organisation of the Biostatistics session with an invited speaker, Andy Grieve and contributed presentations.

# 5. Other business

Number of members of the Biostatistics sections: 167

# **MEMBER NEWS**

# F. Thomas Bruss receives Deruyts Prize

Prof. F. T. Bruss (ULB) has been awarded the 14th Deruyts Prize in Mathematics (period 2000-2004) by the Royal Academy of Belgium (classe de sciences) for his contributions to Probability.



## ANNOUNCEMENTS

# STATISTICAL MODELLING SOCIETY

Recently (Leuven, Belgium, July 2003) a new society has been established called "The Statistical Modelling Society" (SMS) with the mission of promoting statistical modelling in its widest sense. The society supports the promotion of statistical modelling as the general framework for the application of statistical ideas; the promotion of important developments, extensions, and applications in statistical modelling; and the promotion of meetings/courses that bring together statisticians working on statistical modelling from various disciplines.

The society will support a wide range of activities, such as: the International Workshop on Statistical Modelling; scientific publications; research networks of statisticians interested in statistical modelling; short courses and focused workshops; and the exchange of ideas on statistical modelling via an electronic discussion forum.

People interested in joining the society can contact the secretary (Vicente Núñez-Antón) at <u>secretary@statmod.org</u> or should visit the webpage at <u>http://www.statmod.org/</u>.

## **IBC 2006**

## Call for invited sessions proposal

The Scientific Program Committee of the XXIII International Biometric Conference, to be held July 16-21, 2006 in Montreal (Quebec, Canada) is calling for invited session proposals.

An invited session typically brings together a set of speakers (and possibly discussants) to describe the latest research in an area of statistical theory or application, and make it accessible to a non-expert audience. We encourage topics addressing a wide variety of emerging issues in biological sciences and life sciences.

Please send proposals to the International Program Chair, Geert Verbeke (geert.verbeke@med.kuleuven.ac.be). Proposals should include

- Your name, affiliation, contact address, email address
- Suggested session title
- Description of the proposed session
- Suggested organizer (possibly yourself), speakers and discussant(s)

Proposals should be submitted before **October 1, 2004**. The Scientific Program Committee will then select a number of proposals to be worked out in more detail.



## **CONTINUING EDUCATION**

### **Course on Statistics**

To meet the needs of users of statistical methods, the Center for Statistics of Ghent University, in co-operation with the Institute for Continuing Education in Science (ICES), organizes a series of courses on statistics each year. Our goal is to provide insight in the basics of statistical research. Practical sessions on PC allow participants to obtain this through hands-on experience. Our courses are aimed at professionals and students with an academic training, who wish to refresh their knowledge, keep it up to date or discover new areas of research. The program is designed to offer very specific knowledge and skills through separate modules.

The 2004-2005 program consists of the following 7 modules:

M1: Introduction to SPSS M2: Statistical analysis with S-PLUS M3: Introductory Statistics. Basics of	(4 evenings, October 2004) (2 evenings, October 2004)
Statistical Inference	(7 evenings, NovDec. 2004)
M4: Short Course on Survival Analysis	(2 days, Dec. 2004)
M5: Analysis of Variance	(7 evenings, JanFeb. 2005)
M6: Linear Regression	(6 afternoons, FebMar. 2005)
M7: Categorical Data-analysis	(6 evenings, AprMay 2005)

Please watch our website <u>http://allserv.UGent.be/~shoste/ICES</u> for other short courses on specialised topics that will be announced during the course of the year.

Students and personnel in the government, the non-profit and social-profit sector can participate at a considerably reduced registration fee. The Flemish Community regards continuing training as an important aspect in its economic policy. Again this year professionals are granted financial support through the government's introduction of training cheques. More information about this stimulating initiative can be found on the ICESwebsite, and on the website of the Flemish Community, VDAB http://www.opleidingscheques.be, the and http://www.vdab.be/opleidingscheques.

In addition it is possible, for several of these modules, to obtain a certificate of Ghent University upon succeeding in the exam. These modules can therefore be incorporated as a course in a Ph.D. training.

Detailed information about this and other courses, is available at our website. If you would like to be kept informed personally about this or other courses please fill out the 'Information Request Form' at our website. Brochures can be sent to you on request.

Ghent University – ICES, Krijgslaan 281 S3, 9000 Ghent, Belgium Tel. +32 (0)9 264 44 26 Fax +32 (0)9 264 49 83 E-mail: <u>Heidi.DeDobbelaere@UGent.be</u>

http://allserv.UGent.be/~shoste/ICES.

## **RECENT PHD THESES**

### Faculté universitaire des sciences agronomiques de Gembloux

Hugues Prévot. *Comparison of statistical and neural networks based calibration methods in near infrared reflectance spectroscopy* (May 3, 2004 – Promotor: J.-J. Claustriaux).

The quantitative prediction abilities of various multivariate calibration methods are compared on real datasets arising from near infrared reflectance spectroscopy analyses of agricultural and food products.

The calibration methods compared include three traditional statistical methods (multiple linear regression with stepwise selection of variables, principal component regression and partial least-squares regression) and three neural networks methods based on the multilayer perceptron architecture. A theoretical and bibliographical study is given for each method taken into consideration.

Comparisons are done on 14 dependent variables bound to 5 spectral collections. The comparison criterium is the standard error of prediction.

A factorial experimental design is used to investigate the effects of three subsidiary factors: the calibration dataset size, three NIR spectra transformation methods and three levels of spectral simplification.

The results show that neural networks methods often compete with, or outperformed traditional calibration methods. Nevertheless, no method is uniformly the best one.

Practical recommendations based on the obtained results are given in order to help users in the calibration development process.

#### Limburgs Universitair Centrum

Roel Braekers. *Regression problems with partially informative or dependent censoring* (March 26, 2004 - Promotor: N. Veraverbeke)

At first sight some research areas in medicine, engineering, insurance, social sciences,... do not have anything in common. However, in each of these areas, researchers are interested in positive variables, which in most cases are expressed as a time until a certain event. For various reasons, the collected data in these situations may be incomplete. One of the sources of

incompleteness is censoring. This happens, for example, when a researcher does not have the time to wait until all the observations show the event of interest. We call this type of censoring, right censoring. In most trials or studies there will be only one mechanism which censors an observation independently of its time under study. However we can deviate from this situation in more than one way. When we do not restrict ourselves to one mechanism, we are in a competing risk setting. Although we observe now a number of reasons why an individual is leaving the study, we are only interested in one of these reasons and all the others will be considered as censoring. Another deviation from the independent censoring mechanism is to allow that the censoring mechanism depends on the time until the event of interest. In this case we are in a dependent censoring setting. A further feature which is often encountered in practical data analysis, is the availability of other measured variables (covariates), which influence the distribution of the time until the event of interest.

In this thesis we investigate two different censoring schemes and find in each scheme a non-parametric estimator for the distribution function of the time until the event of interest in the presence of covariates. In the first scheme we consider two different censoring variables. One of the censoring variables gives extra information about the distribution of the survival time of interest, the other does not. Both censoring variables are independent of the time until the event. We call this model the partially informative censoring model or partial Koziol-Green model. Based on the work of Van Keilegom and Veraverbeke (1996, 1997a and 1997b) for the Beran estimator, we find a non-parametric estimator which we call the partially informative censoring estimator. In various chapters of this thesis we look at different aspects of this estimator. For example, in Chapter 2 we prove the weak convergence, in Chapter 3 we establish goodness-of-fit statistics with their asymptotic distributions and in Chapter 4 we develop a bootstrap procedure as alternative for the asymptotic normal approximation. This procedure also allows us to construct confidence bands for the partially informative censoring estimator.

In the second censoring scheme we consider only one censoring variable but we assume that it depends on the time until the event of interest. The dependence will be modelled via a copula and we refer to this model as the copula-graphic model. Using the ideas given by Zheng and Klein (1995, 1996), we find a non-parametric estimator for the distribution function. We assume that the underlying association between the survival time and the censoring time is given by a know Archimedean copula. This estimator is another extension of the Beran estimator and we call it a copula-graphic estimator. In Chapter 5 we establish the weak convergence and investigate the misspecification bias that is introduced when the underlying association is not correctly given.

In the last chapter, Chapter 6, we return to the partially informative censoring scheme and introduce an extension of the semi-parametric Cox's

classical regression model (Cox (1972, 1975)). The main results in this chapter are the consistency and asymptotic normality of the maximum likelihood estimators. Furthermore we perform a simulation study to explore the effect of a misspecification in the relation between the informatively censoring time and the survival time.

References:

- D.R. Cox, (1972) Regression models and life tables, Journal of the Royal Statistical Society. Series B. Methodological, 34, 187-220.
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- M. Zheng and J.P. Klein, (1996) Identifiability and estimation of marginal survival functions for dependent competing risks assuming the copula is known, Lifetime Data: models in reliability and survival analysis (eds. N.P. Jewell, A.C. Kimber, M.-L.T. Lee and G.A. Whitmore.), Kluwer, Dordrecht, 401-408.

#### **University of Antwerp**

Sabine Verboven. *Robust calibration methods* (June 4, 2004 – Promotor: M. Hubert).

Classical calibration methods use multivariate statistical methods such as least squares linear regression (LS), principal component analysis (PCA), principal component regression (PCR) and partial least squares regression (PLSR). However, these techniques are vulnerable towards possible outlying observations. In this thesis several robust calibration methods that are less sensitive towards outliers are presented.

Chapter 1 investigates the behavior of several well-known robust estimators of location and scale at small sample sizes. We considered both explicit estimators, like the median, and the MAD, but we also focused on M-estimators that are implicitly defined. At the end some recommendations are given as to which estimators to use.

From then on we focus on high-dimensional calibration data. In this case the explanatory variables typically consist of spectra, whereas the response variable(s) contain concentrations of certain constituents. Hence, the number of regressors p is usually much larger than the number of observations n. Moreover, the variables are correlated, which is known as multicollinearity. Consequently the ordinary least squares regression estimator cannot be computed anymore, or it has a very high variance in large sample sizes. Principal component regression and partial least squares regression provide a solution to this problem. To robustify PCR and PLSR, a robust method for principal components analysis is required. This is the topic of Chapter 2.

Subsequently, a robust PCR method (RPCR) is constructed by combining robust PCA with robust regression. This is outlined in Chapter 3. In case of a univariate response variable, the LTS regression estimator is used, whereas we apply the MCD-regression if several responses are to be modeled at once. A robust RMSECV value and a robust R<sup>2</sup>-value are proposed as exploratory tools to select the number of principal components. Also the prediction error is estimated in a robust way. Moreover we introduce several diagnostic plots that are helpful to visualize and classify the outliers. The robustness of RPCR is demonstrated through simulations and the analysis of a real data set.

Chapter 4 illustrates the RPCR method on a data set obtained by Fourier Transform Infra Red spectroscopy (FTIR). The goal was to build a calibration model for the determination of the concentration of glycerol monostearate (GMS) in a sample of polypropylene beads.

In Chapter 5 we compare our robust PCR method with a robust PLSR approach (RSIMPLS). The comparison includes the classical PCR and the SIMPLS algorithm as well.

All the methods developed in this thesis have been implemented in MATLAB. The functions are collected into a library, called the `MATLAB Library for Robust Analysis', shortly noted as LIBRA. With the help of a graphical interface, the users are guided through the relevant plots for their data analysis. Chapter 6 highlights some of the main functions of the toolbox and shows its use through several examples. This toolbox is freely available at the websites

http://www.wis.kuleuven.ac.be/stat/robust.html http://www.agoras.ua.ac.be/

### Université catholique de Louvain

Isabelle De Macq. *Hyperrectangular space partitioning trees* (May 7, 2004 – Promotor: L. Simar).

Decision trees are one of the most widely used tools for "supervised classification" problems: provided a sample of correctly classified data is available, they allow to establish rules for explaining and/or predicting a categorical response (membership to classes) on the basis of observed values of predictive variables. Besides efficiency, this hierarchical method is endowed with many additional advantages. In particular decision trees are very flexible and can handle heterogeneous data types, they are invariant under monotone transformations of the data, they perform internal feature selection as an integral part of the procedure, and they generate solutions allowing qualitative understanding of the generated prediction rules. All these properties, often essential in data mining applications, explain the major place occupied by tree methods in this field.

A plethora of tree algorithms have been developed, most of them being but variants of the original CART and C4.5 algorithms. A large part of academic research has focused on incremental modifications to current machine learning methods, and on the speed up of existing algorithms. The main contribution of this work has been to consider a theoretically sound decision tree classifier, initiated by Devroye, Györfi and Lugosi, and to evaluate its expected performance and efficacy as compared to traditional tree methods by evolving it into a practical tool. It is presented in a larger framework including an overview of related approaches issued from different fields, and potential developments.

Enhanced problems related to the splitting method of ordinary trees include the instability of the solutions, the unnecessarily complex expression of the identified structure or the failure of the classifier when complex interrelations between predictors and class cannot be detected. Hyperrectangular Space Partitioning trees on the other hand are based on a different cutting method, and despite their greedy construction, they have been proven to be consistent without any additional tricks. However their practical implementation is a challenge due the computational burden involved. We explore its specific features, strong and weak points, by means of a massive search working tool, while a two-stage approach has been developed for approximating HSP tree solutions, allowing to tackle moderate dimensional problems from commonly used data bases.

## Université libre de Bruxelles

Rachid Massaad. *Echangeabilité et approximation de Poisson dans des modèles d'urne* (March 4, 2004 – Promotor: C. Lefèvre).

Depuis la publication des livres « *Urn Models and their Application* » par Johnson et Kotz (1977) et « *Random Allocations* » par Kolchin, Sevast' yanov et Chistyakov (1978), les modèles d'urne ont fait l'objet d'un intérêt croissant chez les probabilistes et statisticiens. Ces modèles permettent d'aborder un grand nombre de problèmes dans des domaines aussi variés que les méthodes d'échantillonnage et de capture-recapture, les processus de recherche et d'apprentissage, l'algorithmique et l'informatique, l'épidémiologie et la génétique, les designs pour les essais cliniques...

En général, la théorie sur les modèles d'urne se concentre surtout sur leur comportement asymptotique. C'est, bien sûr, l'approximation normale qui a d'abord pu être étudiée, en recourant à des méthodes bien établies. Un grand nombre de résultats sur ce thème sont donnés dans les deux ouvrages cités. Plus récemment, l'attention s'est portée plutôt sur des approximations de Poisson, et notamment en utilisant la méthode puissante de Stein-Chen. C'est cette voie que nous avons exploré dans notre travail, séduit notamment par le joli article de Barbour et Holst (1989).

Parmi les différents modèles d'urne envisagés, nous examinons principalement le modèle dit d'occupation et celui dit avec renforcement et diminution dans leur version initiale ou randomisée. Le modèle d'occupation est un modèle d'urne classique, sans doute le plus connu, dans la littérature (voir, par exemple, Feller (1968). Le modèle avec renforcement et diminution a été introduit par Bernard (1977) dans un contexte biologique, puis étudié et généralisé dans plusieurs travaux (par exemple Donnelly et Whitt (1989)). Nous analysons également une version bivariée du modèle.

Comme annoncé, notre motivation mathématique initiale est de montrer sous quelles conditions une approximation de Poisson ou de Poisson composée peut être établie pour les modèles d'urne envisagés. Grâce aux méthodologies suivies, cependant, d'autres résultats de convergence en loi sont également obtenus. Par ailleurs, nous verrons que la structure fondamentale sous-jacente dans les modèles est celle d'échangeabilité ou d'échangeabilité partielle au sens de de Finetti (1937). C'est sur base de ces deux éléments que nous avons choisi le titre de notre travail.

La thèse se subdivise en cinq chapitres : les deux premiers concernent des modèles d'urne univariés, les trois suivants des modèles multivariés. Elle s'inscrit dans la suite de la thèse soutenue par Kissami (1993).

### Next issue

We would like to publish in this Newsletter any statistical matter such as :

- information about universities, institutes (1 to 3 pages);
- lists of recent publications and technical reports;
- abstracts of recent PhD theses;
- news of members;
- forthcoming statistical events and announcements;
- short papers about teaching methods in statistics, statistics in the industry, official statistics, etc.

Suggestions are welcome: please, contact us.

Suitable information for the next issue, prepared as (LA)TEX or WORD FILES, should reach the editors of the Newsletter BEFORE December 31, 2004, preferable by e-mail to:

Mia.Hubert@wis.kuleuven.ac.be lambert@stat.ucl.ac.be

#### Any change of job, address, phone number, ... ?

Please notify the Secretary of the Society:

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