Interuniversity Attraction Pole (IAP)

Overview document

P5/24 – Statistical techniques and modeling for complex substantive questions with complex data

http://www.stat.ucl.ac.be/IAP

July 1, 2005

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1 Introduction

1.1 General information

Title of the network

Statistical techniques and modeling for complex substantive questions with complex data.

Partners

Network coordinator:

1. Léopold Simar (UCL: administrative co-ordinator) and Ingrid Van Keilegom (UCL: scientific co-ordinator)
   Institution: Université catholique de Louvain, Institut de statistique
   Type: Principal partner

Associate partners:

2. Paul De Boeck (KUL-1)
   Institution: Katholieke Universiteit Leuven
   Type: Associate partner

3. Emmanuel Lesaffre (KUL-2)
   Institution: Katholieke Universiteit Leuven
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4. Noël Veraverbeke (LUC)
   Institution: Limburgs Universitair Centrum
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5. Marc Hallin (ULB)
   Institution: Université Libre de Bruxelles
   Type: Associate partner

European partners:

6. Hans-Hermann Bock (RWTH - Aachen)
   Institution: Aachen Technical University, Aachen, Germany
   Type: European partner

7. Anestis Antoniadis (UJF - LMC - IMAG)
   Institution: Université Joseph Fourier, Grenoble, France
   Type: European partner

Budget

The following table shows the available budget (in euros) per partner and per item for the total period of 2002-2006.

	Personnel	Operating costs	Equipment	Overheads	Sub-contracting	Total
UCL	600,590	190,452	69,405	39,553	0	900,000
KUL-1	472,908	69,350	55,630	27,112	0	625,000
LUC	263,188	85,000	9,402	17,410	0	375,000
ULB	224,992	97,910	35,936	16,162	0	375,000
RWTH-Aachen	50,000		Not allowed	Not allowed	Not allowed	50,000
UJF-LMC-IMAG	50,000		Not allowed	Not allowed	Not allowed	50,000
Total						2,375,000

1.2 History

Not relevant.

1.3 Summary of the objectives of the research project

A key task for statistics is to provide researchers with tools to frame their substantive questions within formal models so as to make them amenable to empirical research. Regarding the latter, an important related task in statistical analysis is to take into account the very nature of the data. In this respect, nowadays one may note an increasing demand in many fields to capture more adequately the complexity of the data that are collected to investigate substantive research questions. Moreover, the substantive research questions themselves also display an ever increasing complexity, especially since the last decade.

We illustrate both types of complexity.

(1) Regarding complexity of data: incomplete data (missing data, censoring,...); latent data; high-dimensional data.

(2) Regarding complexity of substantive questions: move to more realistic accounts of phenomena (nonparametric estimation of frontiers,...); allowing for heterogeneity of experimental units (heterogeneity of individuals in the study of emotions in psychology and heterogeneity of medical centers taking part in a clinical trial,...); questions regarding complex structures in time and/or space (nonstationarity and multiple breakpoints,...).

Both types of complexity constitute a major challenge for contemporary statistics. Novel models and techniques are clearly needed to handle questions and data with a complicated underlying structure, using up-to-date methods in statistical modeling and inference and often involving adaptations/modifications of techniques available for simpler structures.

The point of departure of the proposed network activities is that of a broad range of complex substantive data sets and questions arising in various disciplines (including psychology, biomedical sciences, economics, and climatology). The overall aim of our project then is to develop appropriate statistical models and techniques to deal with these data and questions.

As such, the network activities are organized into 6 work packages which have been further grouped in two major sections. Section I includes 4 work packages (WP1-WP4) that focus on 4 well-delineated classes of models. Section II includes 2 work packages (WP5-WP6) that can be considered to deal with statistical meta-modeling aspects; the latter can be studied in their own right but, in addition, can also be included within different classes of models as distinguished within Section I.

The key aims of the six work packages (WPs) can be summarized as follows:

- WP1 (Functional estimation): to expand classical functional estimation of one- and multi-dimensional curves in line with more realistic (but more complex) substantive theories (for instance, economic theories involved in frontier estimation) and to capture in appropriate ways change or break points;
- WP2 (Time series): to deal with two major sources of complexity in the analysis of time series: nonstationarity and high-dimensional data;
- WP3 (Survival analysis): the study of nonparametric regression models with a complex censoring mechanism or involving discontinuities, and of frailty models to capture heterogeneity;
- WP4 (Mixed models): to look for adequate random effects distributions;
- WP5 (Classification and mixture models): how to capture the heterogeneity in a population and what its exact nature is;
- WP6 (Incompleteness and latent variables): the development of (semi)parametric missingness models for incomplete and latent data, and the study of sensitivity to various assumptions implied by this modeling.

Integration of the network activities can be achieved on four different levels:

(1) substantive: data sets are shared by different work packages and as such will be analyzed in terms of different, complementary models;

(2) cross-links are established between pairs of work packages: e.g., survival models are studied in WPs 3 and 4; latent variables are addressed in WPs 5 and 6;

(3) interaction between Section I and Section II: e.g., classification techniques and mixture models as studied in WP5 to capture heterogeneity are applied within various WPs of Section I;

(4) common methodological ground: (a) the vast majority of the work packages makes use of smoothing and bootstrap/Bayesian data analysis techniques as common methodological tools; (b) a number of methodological research topics are addressed by assembling methodological findings from different work packages, which finally leads to the drawing of generic conclusions.

The proposed research results into novel types of statistical methods, models and model expansions that fit better to complex substantive theories as well as to complex data. As such they provide researchers with more effective and useful analysis tools for answering important contemporary questions.

1.4 Summary of the objectives of the partnership

First, the research network really acts as a network, meaning that we organize and manage collaborations between the various groups of the network. Second, we encourage and train young researchers. Third, the network does not act as a closed network but as an open network, with connections to other statistical groups within Belgium as well as internationally.

The proposed network results in:

(1) more intensive and effective exchanges within a considerable part of the Belgian statistical community

(2) more and richer training opportunities for young statistical researchers

(3) strengthening of possibilities to recruit suitable PhD students/researchers through joint advertising/operating on the international job market

(4) strengthening of international position of the partners (benefit from complementarities in international contacts; increased visibility of their work).

These goals could be achieved through the following types of research and research-related activities: research by doctoral students and by post-docs, workshops, seminars, staff meetings, intensive courses, a website and newsletter and open network activities.

Workshops are planned to play a key role in the organization and planning of the project: it was planned to organize them as follows.

- Workshop 1: beginning of year 1
  The aim of the workshop is to communicate to all partners the types of applications and substantive problems that will be focused on in the distinct work packages, so that one becomes maximally familiarized with the kind of applications and data of other partners/work packages.

- Workshop 2: beginning of year 2
  Meeting on two categories of statistical tools that will be used in all or almost all work packages: (1) smoothing techniques, and (2) resampling/Monte Carlo techniques.

- Workshop 3 (extended two-day meeting): half way of year 3
  The workshop is planned in order to exchange results obtained from the work packages regarding their primary objectives and cross-links and from research on methodological issues, and to prepare intensive interactions between sections.

- Workshop 4: half way of year 4
  This will be a follow-up workshop on transfers started in workshop 3.

- Workshop 5: beginning of year 5
  The aim of the workshop is to report on further work package results and cross-link research, and to assemble methodological findings from the different work packages in all previous stages, and, most importantly, to prepare research on generic methodological conclusions.

More details about these workshops can be found in Section 3.1.1.

2 Research results

In this section the scientific achievements of each of the six work packages are outlined. For each work package we describe below briefly which results have been obtained and we refer to publications and/or discussion papers for more details about the obtained results. The first goal of the research activities of the network was to achieve the objectives that were described in the project. Apart from these objectives, network members also made important contributions in other areas, closely related to the main objectives of the project. We describe below both the main and the additional achievements. All the work packages have made important contributions in their field, and have benefited from discussions with researchers working in other work packages.

2.1 Work package 1: Functional estimation

Summary of the scientific results

1. **Frontier estimation**

   This field of research is concerned with the estimation of the boundary of the support of a multivariate random variable. One of the main applications is in productivity and efficiency analysis where firms produce a set $Y \in \mathbb{R}_+^q$ of outputs (quantity of goods or services produced by the firm) by using an amount $X \in \mathbb{R}_+^p$ of inputs (factors of production, like capital, labor, energy, ...). Technically, the attainable set $\Psi = \{(x, y)|x \text{ can produce } y\}$ is the support of the random variable (X, Y). In productivity analysis we seek for optimal plans of production (for instance the maximal amount of output y that can be produced when using a fixed amount of input x) that defines the efficient frontier of Ψ. Then, the efficiency of each firm is measured by its distance to the efficient frontier and so, for instance, firms can be ranked according to their efficiency score. The main results in this field of research have been obtained in three directions: Deterministic nonparametric frontier models, Stochastic frontier models (semi and nonparametric) and Applications in various directions. Simar and Wilson (2005) have been invited to write a chapter in a book on efficiency measurement presenting most of the results obtained in this field.

   (a) Deterministic models. Here, we state that $\text{Prob}((X, Y) \in \Psi) = 1$ and so, no noise is allowed. The most popular estimators are the envelopment estimators: Data envelopment analysis (DEA) and Free disposal hull (FDH). Kneip, Simar and Wilson (2003) have determined the asymptotic distribution of the DEA in the full multivariate setup (p and $q \geq 1$) and proved the consistency of the bootstrap, by doing appropriate smoothing or by subsampling. Jeong and Simar (2005) have proven the consistency of the bootstrap for the FDH estimator and define a new estimator with better properties (the LFDH: linearized FDH). Badin and Simar (2004) propose a simple way (with an analytical expression) for correcting the bias of the FDH estimator. At UJF, Girard, Iouditski and Nazin (2005) propose some new optimal estimators for the Lipschitz frontier of a set of points. They are defined as sufficiently regular kernel estimators, covering all the points and whose associated support is of smallest surface.

   These envelopment estimators are known to be very sensitive to extreme data points or outliers. Cazals, Florens and Simar (2002) propose a new concept of frontier (the order-m frontier, where m is interpreted as a "trimming" parameter), with a nonparametric estimator which appears to provide, under an appropriate choice of m, a robust estimator of the full frontier. In the same spirit, Daouia and Simar (2004) have developed, for the full multivariate case, a concept of order-α efficiency score and an α-quantile frontier, which is based on a nonstandard conditional quantile. Here again a nonparametric estimator is proposed which does not envelop, as for the order-m case, all the data points and so is more robust to extremes. Daouia and Simar (2003) indicate how to modify these robust estimators to produce estimators of the frontier that are monotone.

The econometric literature in productivity analysis was mainly interested in parametric estimates of the frontier. The existing methods are regression-based methods (using OLS or MLE) adapted to the particular case of one-sided error term. They rely on restrictive assumptions (homoscedasticity, parametric specification of the distribution of the error, ...) and since they are regression-based methods, they capture the shape of the cloud of points near its center, not near its boundary. Florens and Simar (2005) propose a new way to estimate parametric frontier models by using a nonparametric (robust) estimator of the frontier as a first step and then fit the selected parametric model to the obtained frontier. These parametric estimators present much better properties and overcome most of the drawbacks of the previously existing methods.

Explaining efficiency is an important concern for practitioners: this is usually done by introducing external or environmental factors $Z \in \mathbb{R}^r$ in the model. Simar and Wilson (2003) define a model for the data generating process which allows to estimate the effect of Z on the efficiency scores. It is based on a two-stage procedure using the bootstrap for correct inference. Daraio and Simar (2003) propose an alternative method based on conditional efficiency scores, that is not based on a separability condition as in the two-stage methods. Daouia and Simar (2004) follow the same idea with the order-α conditional quantile frontiers. Daraio and Simar (2005) generalize the approach to convex attainable sets.

(b) Stochastic frontier models. Here, noise is allowed and some data points might be outside the attainable set Ψ. The random distance from the frontier is now the convolution of the inefficiency term plus the noise. In a full nonparametric setup, the model is not identified but Hall and Simar (2002) have shown that if the noise is of moderate size (in terms of noise to signal ratio), we can improve the performance of envelopment estimators to estimate the boundary points by correcting the bias. This involves the estimation of the derivative of the convoluted density near the boundary. The idea has been extended in Simar (2003) in a full multivariate setup. Kumbhakar, Park, Simar and Tsionas (2004) have used a local maximum likelihood approach to estimate a nonparametric stochastic frontier model. The idea is to obtain the nonparametric flexibility by localizing a parametric anchorage model. In a situation where a panel of data is available, Park, Sickles and Simar (2003a, 2003b) determine the efficient semiparametric estimator of the frontier model under various dynamic specifications of the model. This work has direct links to **WP4**, where the same type of longitudinal data are studied in another context.

(c) Applications. Extending some of their previous works, Simar and Wilson (2002) show how the bootstrap can be used with the DEA estimator for testing return to scale hypothesis on the production process. In Simar and Wilson (2004), a double bootstrap method is proposed to improve the performance of the simple bootstrap with DEA. Comparing groups of firms is also an important issue in practice. Simar and Zelenyuk (2003) base the comparison on weighted group averages and Simar and Zelenyuk (2004) use a nonparametric test based on estimates of the density of the efficiency scores within each group to test the equality of the two distributions. Beguin and Simar (2004) uses the technique proposed by Simar (2003) to detect outliers in data on expenses linked to hospital stays. Bonacorsi, Daraio and Simar (2004) use the robust estimators of the frontier to investigate and compare the performance in universities. Daraio and Simar (2004) analyze the performance of mutual funds using the same tools.

2. **Non- and semiparametric regression**

   (a) Change point analysis and landmark detection. A survey of nonparametric kernel-based methods for the estimation of change points can be found in Gijbels (2003). Antoniadis and Gijbels (2002) consider wavelet-based methods for detecting irregularities in a regression function. This procedure also allows to estimate the number of discontinuities. Gijbels and Goderniaux (2004a, 2004c) propose a fully data-driven procedure for detecting jump points in a regression curve or its derivative, while Gijbels and Goderniaux (2004b) deal with testing the null hypothesis that a regression function is continuous versus the alternative hypothesis that it is a discontinuous function, relying on a two-steps data-driven procedure. Gijbels, Lambert and Qiu (2004) deal with the nonparametric estimation of a regression curve where the estimation should preserve possible jumps in the curve. At each point x at which one wants to estimate the regression function, the method chooses in an adaptive way among three different local linear kernel estimates.

   Jeremie Bigot has defended his PhD thesis at UJF in 2003 and was a post-doctoral researcher of the IAP network at UCL in 2003-2004. Bigot (2003a) proposes a nonparametric approach to estimate the landmarks of a signal observed with noise, which yields a new technique to automatically align two sets of landmarks. The paper by Bigot (2003b) is concerned with the problem of the alignment of multiple sets of curves and their comparison with FANOVA techniques.

   Bigot (2005) deals with the problem of determining the singularities of a curve when it is observed with noise. A nonparametric approach, based on appropriate thresholding of the empirical continuous wavelet coefficients, is proposed to estimate the wavelet maxima of a noisy signal. A new tool, "the structural intensity", is also introduced to represent the locations of the singularities of an unknown signal via a density function.

   The KUL-1 team started working on a change-point model for test performance. The change-point itself is considered a random effect, the density of which can be estimated with a non-parametric kernel method (De Boeck, Wollack and Cohen, 2005). In this way, the overall perspective of heterogeneity as formulated in the IAP proposal, can be applied to a change-point model using a functional density estimation.

(b) Model selection and goodness-of-fit tests. Hjort and Claeskens (2003a, 2003b) and Hjort and Claeskens (2003a, 2003b) deal with model selection and model averaging. Hjort and Claeskens (2003a,b) develop methodology and theory to deal with estimators averaged across different models. As a special case this includes estimators found via a model selection procedure. In Claeskens and Hjort (2003) it is explained that the model selector should focus on the parameter singled out for interest; in particular, a model which gives good precision for one estimand may be worse when used for inference for another estimand. This yields a new, focussed informative criterion, the FIC. While the above papers concentrate on estimators after model selection, the work by Claeskens and Hjort (2004) focuses on testing hypotheses where the test statistic involves a model selection procedure.

Penalized regression spline models afford a simple mixed model representation where variance components control the degree of non-linearity in the smooth function estimates. This is the motivation for Claeskens (2004) to study lack of fit tests based on the restricted maximum likelihood ratio statistic. Aerts, Claeskens and Hart (2004) propose and analyze nonparametric tests of the null hypothesis that a regression function belongs to a specified parametric family. The tests are based on BIC approximations to the posterior probability of the null model, and may be carried out in either Bayesian or frequentist fashion.

Van Keilegom, González-Manteiga and Sánchez-Sellero (2004) also construct a test statistic for the hypothesis that a regression function belongs to some parametric family, but their approach is based on a different idea. Their test statistic is based on the distance between the empirical distribution function of the parametric and of the nonparametric residuals. Wang, Akritas and Van Keilegom (2002) propose a new test statistic for the hypothesis of a constant regression function. The test statistic is inspired by the classical test for this hypothesis in the context of repeated measurements. All of the above papers are restricted to the case of independent observations. When the errors form a stationary time-series, Wang and Van Keilegom (2004) propose a new nonparametric method for testing the parametric form of a regression function. The paper forms a bridge between WP1 and **WP2**. A problem related to the ones above is the problem of testing whether two populations have the same regression curve. In Pardo-Fernández, Van Keilegom and González-Manteiga (2004), this hypothesis is tested by using an approach similar in spirit to the one developed by Van Keilegom *et al.* (2004) described above. Pardo-Fernández and Van Keilegom (2005) have obtained an extension of this test to the case of censored data; this paper forms a bridge with **WP3**.

(c) Inference for curves under shape restrictions. An overview of nonparametric methods for estimating a monotone regression function has been provided in Gijbels (2004). J. Zhang and Gijbels (2003) rely on sieve empirical likelihood methods to deal with estimation in constrained parametric or nonparametric regression models with unspecified error distribution.

Antoniadis, Bigot and Gijbels (2005) (J. Bigot was a IAP postdoc at UCL in 2004 and got his PhD at UJF) focus on nonparametric estimation of a constrained regression function using penalized wavelet regression techniques. This results into a convex optimization problem under linear constraints. The estimator is easily obtained via the dual formulation of the optimization problem.

In collaboration with Paul Eilers (Leiden University Medical Centre), the KUL-1 team has been working on simple and multiple P-splines regression for problems in which the relationship between predictor and criterion variables is constrained to be of a particular nonparametric functional form (such as monotone, single-peaked , or U-shaped)
(Bollaerts, Van Mechelen and Eilers, 2003)

(d) Estimation of the regression curve in complex models. Amato, Antoniadis and Pensky (2004) consider regression problems with univariate design points and estimate the regression function by a wavelet based reproducing kernel Hilbert space (RKHS) technique with the penalty equal to the sum of blockwise RKHS norms. Antoniadis, Gijbels and Nikolova (2005) study a general methodology for nonparametric regression via regularization. The approach chosen consists of penalized likelihood regression for generalized linear models with nonquadratic penalties.

Hall and Van Keilegom (2003) suppose a nonparametric regression model with autoregressive errors, and propose a new method to estimate the regression function, the autoregressive parameters and the error covariances. This work relates to **WP2**. Claeskens and Van Keilegom (2003) study confidence bands for a regression function and its derivatives, using local polynomial estimation. A smoothed bootstrap approach is used. Einmahl and Van Keilegom (2003) consider the nonparametric regression model $Y = m(X) + \varepsilon$, where ε is independent of X and m is unknown, and construct omnibus tests for the independence between ε and X.

In Heuchenne and Van Keilegom (2003, 2005b, 2005a) the problem of estimating the regression function when the response is subject to right censoring, is considered. The proposed estimators (constructed respectively under a polynomial, non-linear and nonparametric model) use so-called ‘synthetic’ data points to replace the unknown censored observations. See **WP3** for more details. In addition, many research results have been obtained in the context of nonparametric regression with censored responses, including e.g. estimation of the conditional density and hazard function, construction of confidence bands for the conditional survival function, regression models in which the response is subject to partially informative censoring,... We refer to **WP3** for a detailed description of these results.

The related problems of estimating regression functions in the spatial context of random fields have been considered in Hallin, Lu and Tran (2004b, 2004a); see **WP2** for details.

(e) Dimension reduction techniques. Amato, Antoniadis and De Feis (2004) develop some new two-dimensional reduction regression methods to predict a scalar response from a discretized sample path of a continuous time covariate process. The methods take into account the functional nature of the predictor and are both based on appropriate wavelet decompositions.

Single-index models offer a flexible semiparametric regression framework for high-dimensional predictors. Bayesian methods have never been proposed for such models. Antoniadis, Grégoire and McKeague (2004) develop a Bayesian approach incorporating some frequentist methods. Fort, Lambert-Lacroix and Peyre (2004) propose nonparametric single-index models in generalized linear models as potential reduction method for supervised classification of microarray data. G. Geenens in his PhD (advisor: L. Simar) analyzes, in collaboration with M. Delecroix (ENSAI, Rennes) the possibility of modelling the probabilities in a multinomial process by single index models. The idea is to let these probabilities be related to some explanatory variables in a semiparametric way. Geenens and Delecroix (2005) develop a survey on single index models, while Geenens, Simar and Delecroix are currently investigating the properties of a new estimator based on a maximum rank correlation criterion.

An extension of partial least squares and dimension reduction in logit models is proposed in Fort and Lambert-Lacroix (2004a). The extension works also when the number of covariates is far larger than the number of observations.

Climov, Hart and Simar (2002) and Climov, Delecroix and Simar (2002) consider semiparametric estimation of Poisson regressions. More precisely, they analyze the properties of the proposed estimators and discuss the bandwidth selection issue. Brouhns, Denuit and Van Keilegom (2004) describe the Poisson log-bilinear model for mortality projection. They derive confidence intervals for expected remaining lifetimes with the help of the bootstrap.

(f) Discriminant analysis. A related topic is the work on classification trees and discriminant analysis, considered in De Macq and Simar (2005). In De Macq and Simar (2005) an exact algorithm based on hyper-rectangular partitioning trees has been implemented. It has optimal properties but the computing complexity limits its applicability. An approximated (faster) algorithm, based on the quantiles for building the splitting rules has been implemented. The work has close connections with **WP5**, where classification problems are studied under the angle of clustering.

3. **Nonparametric density and hazard estimation**

(a) Estimation of the density function in complex models. In his Ph.D., T. Bouezmarni (currently IAP-postdoc at KUL-1, but he obtained his Ph.D. at UCL) focuses on estimation of a density function that has a bounded support and/or is unbounded. Bouezmarni and Rolin (2004) consider the estimation of densities by a Beta kernel. They found the exact asymptotic behavior of the mean integrated absolute error and its upper bound. Bouezmarni and Scaillet (2003) consider asymmetric kernel estimators and smoothed histograms for the class of densities defined on the positive real line. Weak uniform convergence on each compact for these estimators as well as weak convergence in L_1 are established. Bouezmarni and Rolin (2003) show the weak and strong consistency of Bernstein estimators of a density function defined on $[0,1]$, if the underlying density presents an infinite pole at $x = 0$ and/or $x = 1$. Bouezmarni, Mesfioui and Rolin (2003) establish the asymptotic expression and upper and lower bounds of the mean integrated absolute error of the asymmetric kernel estimators and the smoothed histograms.

Functional estimation is an important topic of interest for the estimation of random effect densities as they appear in generalized linear and nonlinear mixed models. Often the normal distribution is assumed, but nonparametric and semiparametric methods are available as well. An overview of methods is given in Tuerlinckx *et al.* (2004). More recently, Bouezmarni has developed a nonparametric kernel method to estimate the densities of random effects in a logistic mixed model, using the expertise from the UCL team. Manuscripts on this topic are in preparation.

(b) Deconvolution problems. Delaigle and Gijbels (2002) deal with the problem of how to estimate nonparametrically the density of a random variable when the measurements on this variable contain errors. They propose practical bandwidth selection procedures. A finite sample comparison between the discussed procedures, a bootstrap procedure, a plug-in procedure and a cross-validation procedure, has been carried out. Theoretical properties (including consistency) of the bootstrap and plug-in procedures have been established. Delaigle and Gijbels (2003) propose a consistent estimator for the unknown support of a density in case of measurement errors. They establish the bias and variance properties of the estimator, as well as its rate of convergence.

(c) Inference for curves under shape restrictions. Gijbels and Heckman (2004) deal with the problem of testing whether an unknown hazard function can be assumed to be increasing (or decreasing). They also illustrate how to apply their methodology to type II censored data. The paper is therefore also linked to **WP3**. Their technique is based on local versions of an existing global test using normalized spacings. The same testing problem is studied in Hall and Van Keilegom (2004). Unlike previous approaches, their test is not based on the assumption that the null distribution is exponential.

A related topic is shape-preserving estimation of probability densities (pdf) and cumulative functions (cdf) with wavelets in higher dimensions. Cosma, Scaillet and von Sachs (2005) develop wavelet estimators which do not necessitate any pre- or postprocessing to respect positivity or monotonicity. As an application they consider wavelet estimation of conditional quantiles of financial time series. The project is at the intersection between WP1 and **WP2**.

4. **Inference by means of empirical likelihood techniques**

   Empirical likelihood methods offer an alternative to the classical approaches based on asymptotic normality or bootstrap approximation. Li and Van Keilegom (2002) construct confidence bands for the conditional distribution and quantile function of a response subject to censoring, given a completely observed covariate. The bands are based on a local empirical likelihood approach. See also **WP 3** for more details. In Hjort, McKeague and Van Keilegom (2004) the scope of the empirical likelihood methodology is extended in three important directions. A range of examples from survival analysis (see **WP3**) and nonparametric statistics are provided to illustrate the main results. Although not considered in the paper, the results can be applied to a much wider class of applications, including time series models (see **WP2**), and settings with incomplete data (see **WP6**). Cao and Van Keilegom (2004) study the problem of testing whether two populations have the same law, by comparing kernel estimators of the two density functions. The proposed test statistic is based on a local empirical likelihood approach. Wang and Veraverbeke (2004b) used an empirical likelihood based approach to deal with missing data. See **WP3** for more details. Finally, a paper on U-quantile estimation in the presence of auxiliary information by means of empirical likelihood techniques is in preparation by Van Keilegom and Veraverbeke (2005).

5. **Functional data analysis**

   In Bugli and Lambert (2004) (UCL) it is shown how one can use P-splines in a functional ANOVA framework to decompose event related potentials extracted from electroencephalograms into physiologically meaningful components from which the effect of a drug on the brain can be interpreted and quantified. At UJF, Abramovich, Antoniadis, Sapatinas and Vidakovic (2004) consider the testing problem in a fixed-effects functional analysis of variance model. They test the null hypotheses that the functional main effects and the functional interactions are zeros. In Govaerts and Noel (2005), a review is given of the available methodology for analyzing the results of a designed experiment when the response is a curve and the methods are applied on a case study from the metal injection moulding industry.

   An important issue in functional data analysis consists in deciding whether there is any significant difference between 2 sets of curves. This problem is studied under two different angles by Hall and Van Keilegom (2005) and by Bugli, Lambert and Bigot (2005). In the former paper a new test is proposed to test whether two populations of curves have the same distribution, while in the latter paper the goal is to synchronize individual curves by means of a registration technique based on fractional polynomials.

6. **Functional estimation for microarray data**

   One of the important issues here is to classify complex microarray data (see also **WP5**). One feature of microarray studies is the fact that the number of samples collected is relatively small compared to the number of genes per sample. An efficient way to solve this problem is by using dimension reduction techniques in conjunction with nonparametric discriminant procedures. Antoniadis, Lambert-Lacroix and Leblanc (2003) view the classification problem as a regression problem with many predictor variables. They use an adaptive dimension reduction method that allows them to solve the 'curse of dimensionality problem'. The paper has been selected to be reproduced in the 2004 'Year Book of Medical Informatics'. Fort and Lambert-Lacroix (2004b) continue this line of research and propose a new method combining partial least squares and ridge penalized logistic regression. The proposed procedures are compared with some currently used classifiers.

   A. Antoniadis (UJF) and a team of biologists of the Institute Marie Curie in Paris (see Ercier *et al.* (2004)), study the determination of the biological effects of low doses of pollutants by means of a nonparametric ANOVA like DNA microarray analysis designed for the investigation of small intracellular changes induced by irradiation at varying low doses.

7. **Nonparametric functional estimation by means of wavelets**

   Wavelet-based denoising techniques are well suited to estimate spatially inhomogeneous signals. Waveshrink (Donoho and Johnstone) assumes independent Gaussian errors and equispaced sampling of the signal. In Sardy, Sardy, Antoniadis and Tseng (2004) a unifying L1-penalized likelihood approach to regularize the maximum likelihood estimation by adding an L1 penalty of the wavelet coefficients is developed. Antoniadis and Fryzlewicz (2004) investigate a parametric thresholding procedure which takes advantage of the increasing sparsity of the wavelet coefficients across scales. Antoniadis and Bigot (2004) focus on non-parametric estimators in inverse problems for Poisson processes involving the use of wavelet decompositions.

Delouille, Simoens and von Sachs (2004) have presented a new methodology to construct smooth wavelets, which adapt automatically to the stochastic design of a non-parametric curve estimation problem, and which circumvent the usual restrictions of classical wavelets (dyadic sample size, boundary treatment, non-equispaced design). Delouille and von Sachs (2004) furnish some theoretical results on the optimality of this new estimator which parallel classical wavelet thresholding for equispaced data. Moreover they develop these in the more difficult time series context of a non-linear autoregressive design and show how their original algorithm can be adapted to various time series situations (including ARCH-type models). This research is linked with research under **WP2**. In the two-dimensional situation, first Delouille and von Sachs (2003) transfer their univariate results to the special case of a sufficiently regular bivariate design with possibly different smoothness in different directions by a tensor product approach. Delouille, Jansen and von Sachs (2004), finally present an approach to treat fully irregularly spaced data in two dimensions.

8. **Other topics in functional estimation**

(a) M-estimation. M-estimators in non-standard contexts are considered by Chen, Linton and Van Keilegom (2003). They suppose that the criterion function is not necessarily continuous and that it depends on a preliminary nonparametric estimator. They obtain general conditions that guarantee the consistency and asymptotic normality of this type of estimators. Following this line of research, Van Keilegom and Carroll (2005) study the backfitting and profile methods for this type of criterion functions. They show that under certain conditions the two estimation procedures produce asymptotically the same estimator of the parameter of interest.

(b) Copula modeling. In Vandenhende and Lambert (2004) a new family of Archimedean copulas is defined using a continuous piecewise log-linear combination of existing Archimedean generators. We provide an efficient least-squares method to estimate the involved coefficients. We show that these coefficients can be interpreted as local dependence measures. A smooth estimate is obtained with a penalized approach.

Denuit, Purcaru and Van Keilegom (2004) consider an application of bivariate Archimedean copula modeling in non-life insurance. The data in their application are subject to censoring (an observation is censored when the amount of the claim exceeds the policy limit). The paper has a natural connection with **WP3**.

In his PhD thesis, V. Schmitz (RWTH) studied an application of copulas in the context of finance mathematics. The properties of copulas when modeling dependence structures, as well as the impact on the theory of discrete-time Markovian and Brownian processes are investigated.

Main achievements

The research objectives of this work package as mentioned in the project description, are threefold : (a) Nonparametric estimation of a frontier function in case of stochastic frontiers, (b) Automatic detection of change-points in regression, hazard and density functions, and (c) Modeling of heterogeneous regularities in time series and analysis of such time series. In addition to the results obtained in these three areas (which we outline below), a lot of progress has been made in other research areas in the domain of functional estimation, including model selection, inference for curves under shape restrictions, dimension reduction techniques, empirical likelihood and semiparametric M-estimation, as shown above.

(a) Nonparametric estimation of a frontier function in case of stochastic frontiers. The main achievements can be summarized as follows: (i) we have the asymptotic distribution of DEA estimator in a full multivariate setup, with a way for performing the bootstrap consistently, (ii) we can perform the bootstrap with the FDH estimator and improve the FDH by LFDH, (iii) we developed new methods for estimating frontiers in a robust way, in particular by using nonstandard conditional quantile in a full multivariate setup, (iv) we propose a new way for estimating parametric frontier models which outperform existing methods, (v) we develop new procedures for explaining inefficiency of firms, (vi) we improve the envelopment estimators (DEA-FDH) in the presence of noise, (vii) we introduce local polynomial estimators of stochastic frontier models (using local ML), (viii) we introduce dynamics in stochastic semiparametric panel models and (ix) these procedures have been applied in different setups.

When looking to the initial objectives of the project, we have obtained much more in the field of deterministic frontier models than expected (see (i), (ii), (iii), (iv), (v)). For stochastic frontier models, we propose new ways for approaching this difficult problem (see (vi) and (vii) for nonparametric models and (viii) for semiparametric dynamic panel models); the partial frontiers (α-quantile and order-m frontiers in (iii)) provide an alternative perspective for approaching stochastic nonparametric frontier models. The various applications (ix) indicate how useful the methods can be for solving real complex problems.

(b) Automatic detection of change-points in regression, hazard and density functions. Intensive collaboration between the different partners has taken place in this area: (i) A. Antoniadis (from UJF) and I. Gijbels (from UCL/KUL) have used a wavelet approach to detect changepoints in regression, (ii) I. Gijbels has worked with two PhD students on change point detection by means of kernel methods in one and two dimensional regression problems and they have written a series of papers on this subject, (iii) I. Gijbels has written a survey of nonparametric kernel based methods for the estimation of change points, (iv) J. Bigot (PhD from UJF, IAP-postdoc at UCL) worked out two new techniques to align two or more sets of curves, (v) he also determined singularities of a curve when it is observed with noise by means of a wavelet approach, and (vi) the KUL-1 team worked on a change point model for test performance, where the change point is considered as a random effect.

(c) Modeling of heterogeneous regularities in time series and analysis of such time series. The main achievements in this area are : (i) a new methodology has been developed to construct smooth wavelets, that adapt automatically to the stochastic design of a nonparametric curve estimation problem, (ii) theoretical results on the optimality of this type of estimators are obtained, (iii) the univariate results are transferred to the two-dimensional situation for the special case of a sufficiently regular bivariate design and (iv) for the more general fully irregularly spaced case in two dimensions.

Scientific input of each partner

This work package is coordinated by UCL. The following partners participated actively in obtaining research results in the following areas :

- UCL : frontier estimation, change point detection, model selection, inference for curves under shape restrictions, estimation of the regression and density curve in complex models, dimension reduction techniques, functional ANOVA, deconvolution problems, empirical likelihood techniques, functional estimation by means of wavelets, M-estimation, copula modeling
- KUL-1 : change point detection, inference for curves under shape restrictions, estimation of the density curve in complex models
- LUC : model selection, empirical likelihood techniques, estimation of the regression and density curve in complex models
- ULB : estimation of the regression curve in complex models and spatial context (spatially correlated observations)
- RWTH : copula modeling
- UJF : change point detection, inference for curves under shape restrictions, estimation of the regression and density curve in complex models, dimension reduction techniques, functional ANOVA, microarray data, functional estimation by means of wavelets

2.2 Work package 2: Time series

Time-series analysis, in which the observations depend on time and exhibit serial dependencies, is one of the main domains of expertise in two of the teams of the network, UCL and ULB. Beyond time dependencies, three main sources of complexity have been tackled: nonstationarity (Section 2.2.1), dimensionality (high dimensional time series, Section 2.2.2), and unspecified densities (semiparametric inference based on ranks and signs, Section 2.2.3). These complexities unfortunately are the rule rather than the exception in a number of applications, including stock exchange data, EEG-curves, macroeconomic data, environmental data, or data from clinical monitoring. Finally, spatial data and images also constitute a more complex form of time series, inasmuch as space can be considered as a multivariate time index (lacking some of the specific features of time, though), and have been considered by the ULB team: see Section 2.2.4.

Summary of the scientific results

1. **Approaches to nonstationarity**

   This part is concerned with the development of appropriate methods to analyze covariance nonstationary time series. This delicate problem is of crucial importance in many substantive real life questions. Indeed, many time series in the applied science are not covariance stationary and show a time-varying second-order structure. Both ULB and UCL teams have made this observation for instance on stock prices (Azrak and Mélard, 2004; Van Bellegem and von Sachs, 2004b); . Other examples have been studied in the analysis of multivariate biomedical time series, such as EEG (Ombao, von Sachs and Guo, 2005). Ignoring nonstationarity often affects the quality of the fitted models and prediction (as studied in detail in Van Bellegem and von Sachs (2004a) on financial data) and then may lead to erroneous decisions. During the past few years both teams worked on various statistical strategies to analyze nonstationary data. These strategies may be summarized in the three following points. The two first points concern univariate time series, and the third point presents multivariate approaches and the related question of dimension reduction.

   (a) Time-varying coefficient models. The first idea to model nonstationary time series is to start from parametric stationary models and to let their coefficients vary with time. A typical example is given by autoregressive-moving average (ARMA) models with time-dependent coefficients and heteroscedastic innovation process. This situation has been considered by Azrak and Mélard (2004) and by Van Bellegem and Dahlhaus (2005).

   The first paper considers the situation where the time-varying coefficients and the innovation variance are deterministic functions of time depending on a finite number of parameters. These parameters are estimated by maximizing a quasi likelihood function. Deriving conditions for consistency and asymptotic normality and obtaining the asymptotic covariance matrix are done using some assumptions on the functions of time in order to attenuate non-stationarity, mild assumptions on the distribution of the innovations, and some mixing conditions. Two other related papers in this direction are in progress: a generalization of the theory to multidimensional processes and a paper focussing on pure AR models and an alternative ϕ-mixing condition.

   The paper by Van Bellegem and Dahlhaus (2005) aims at estimating the time-varying coefficients nonparametrically. They use the model of local stationarity introduced in Dahlhaus (1997) and propose a maximum Whittle likelihood estimator on sieves. The properties of the estimator are given without assuming that the observed process belongs to a specific class of time-varying parametric models. In the correctly specified case, the best rates of convergence of the estimators are found (in the minimax sense). The fitting of tvAR(p) processes is discussed in detail, including the problem of the selection of the order p, and an iterative algorithm for the computation of the estimator is proposed.

   A particular case of time-varying models are the periodic ones, providing an attractive alternative to the traditional differencing approach to seasonality. The problem of optimal (in the Le Cam sense) detection of periodicities in a variety of models is the subject of S.

Lotfi's thesis "Efficient tests for the periodic structure of some time series models", which was defended at ULB (supervisor: M. Hallin) in 2004. Together with M. Hallin, she also published a paper (Hallin and Lotfi, 2004) on the optimal detection of periodicities in the coefficients of m-variate d-periodic VAR(p) models. Periodic ARCH models also have been considered in her dissertation.

(b) Nonparametric wavelet-based model. A fully nonparametric model based on wavelets has been studied in Van Bellegem and von Sachs (2003, 2004b), Fryzlewicz, Van Bellegem and von Sachs (2003). This model is again written in the Dahlhaus' framework of local stationarity and, in contrast to previous work, allow the evolutionary autocovariance to change very suddenly in time. We are now able to model time series with intermittent phenomena, such as transients followed by regions of smooth behavior. A notion of time-varying "wavelet spectrum" is uniquely defined as a wavelet-type transform of the autocovariance function with respect to so-called "autocorrelation wavelets". This leads to a natural representation of the autocovariance which is localized on scales.

Similarly to the classical theory of stationary time series, a wavelet periodogram can be defined as a preliminary estimator of the wavelet spectrum. One particularly interesting question is to test the significance of the coefficients of the wavelet periodogram. In the above papers this problem is addressed, and some theoretical properties of the test of significance, including a discussion on its consistency, its power, and its local alternative are derived. The test rule is based on a non-asymptotic result on the deviations of a functional of the periodogram. This key result also allows to derive a new pointwise adaptive estimator of the wavelet spectrum.

The delicate problem of how to forecast the wavelet mode is also studied. A new predictor is defined in Fryzlewicz *et al.* (2003) who derive the prediction equations as a generalization of the Yule-Walker equations. The usefulness of wavelet methods for nonstationary data is established through several case studies, including the prediction of the wind speed anomaly index or the analysis of change-point in the autocovariance structure of the heart rate.

(c) Multivariate approach. Ombao *et al.* (2005) is the latest in a series of publications on the SLEX ("Smooth Localised complex EXponentials") methodology (see, e.g. Ombao, Raz, Guo and von Sachs (2002)), and addresses the problem of complexity reduction for high dimensional second-order non-stationary data such as EEG with transient phenomena. An automatic, fast and fully nonparametric algorithm, based on principal component analysis in the frequency (SLEX) domain, is proposed to adapt a piecewise stationary frequency domain model to the data and to estimate the spectral density matrix, phase and coherency in this model. Here, the paradigm is to find the best-adapted time segmentation (in a truly multivariate sense) of a high dimensional, long time series by a fast algorithm. Donoho, Mallat, von Sachs and Samuelides (2003) present an alternative, though univariate, to finding the best-adapted segmentation of a possibly covariance non-stationary time series by means of local cosine functions. Optimal rates of convergence are derived for spectra which vary with a Sobolev regularity over time by using the concept of "macro-tiles". Guo, Dai, Ombao and

von Sachs (2003), finally, apply the smoothing spline methodology to estimation of a time-varying spectrum of a locally stationary time series. For the price of needing to impose more regularity in order to show the theoretical results, the advantage of this method compared to the previous ones is that no explicit segmentation in time is needed for constructing the estimator.

Main achievements

(i) In the time-varying coefficient models, the estimation techniques have desirable theoretic and empirical properties. From the theoretical side, the main challenges were to propose estimators for models with non-Gaussian innovations, or estimators in the misspecified situations (i.e. the true underlying process may not be in the studied class of models). From the empirical side, our methods give very good results even for small sample sizes ($T = 50$). Considering the complexity of the problem, this fact is remarkable.

(ii) The properties of our estimator for the wavelet-based model are evaluated in a non-asymptotic setting, which is new in the context of nonstationary time series modelling. This result is very important in order to measure the quality of the procedure on real data sets (i.e. on finite sample sizes). Moreover the model is now able to catch intermittent phenomena and the pointwise adaptive estimator we proposed showed in theory and in practice a very good sensitivity to the change points.

(iii) (Cross) spectral analysis of high-dimensional time series with a time-varying covariance structure is a difficult problem only recently being addressed. For this situation we developed new fast and efficient algorithms and derived their theoretical properties by a combination of two key ingredients: introducing a new localized Fourier basis into a statistical set-up which allows for multivariate spectral estimation, including theory, and development of a new model for non-stationary multivariate time series. In particular we generalized classical EEG analysis wildly used by medical engineers and physicians to the situation of data with transient phenomena (such as epileptic seizures) and furnished a remarkably improved diagnostic tool.

2. **Analysis of high-dimensional time series data**

A second major objective in this workshop was the analysis of time series data in (very) high dimension. Practioners nowadays typically have access to information scattered through a huge number of observed time series. This situation is typical of such important fields of application as macroeconometrics or finance, where the number of series available is often of the order of one thousand, which precludes applying any of the traditional, parametric or nonparametric, multivariate time series methods. In order to handle such (very) high dimensional data, a generalized dynamic factor model has been proposed by Forni, Hallin, Lippi and Reichlin (2000).

(a) Methodological progress. The initial paper by Forni *et al.* (2000) proposed the method to be used in subsequent developments, and established its “plain” consistency under very weak assumptions. In Forni, Hallin, Lippi and Reichlin (2004), the corresponding rates are

investigated as both the cross-sectional dimension n and the series lengths T are tending to infinity along some path $(n, T(n))$. The results show that, under suitable assumptions, consistency requires $T(n)$ to be at least of the same order as n, whereas an optimal rate of $\sqrt{n}$ is reached for $T(n)$ of the order of n^2. If convergence to the space of common components is considered, consistency holds irrespective of the path ($T(n)$ thus can be arbitrarily slow); the optimal rate then is still $\sqrt{n}$, but only requires $T(n)$ to be of the order of n.

As it stands, the method described in Forni *et al.* (2000) separates the common shock and idiosyncratic spaces via two-sided infinite-order estimated filters acting on the observations. Therefore, its performance at the end of the sample, hence in forecasting problems, is poor. A forecasting method is developed in Forni, Hallin, Lippi and Reichlin (2005), where a new forecasting method is proposed, which takes advantage, via the dynamic factor model, of the information on the dynamic covariance structure of the whole panel. They first obtain an estimation for the covariance matrices of common and idiosyncratic components. The generalized eigenvectors of this couple of matrices are then used to derive a consistent estimate of the optimal forecast. This two-step approach solves the end-of-sample problems caused by two-sided filtering, while retaining the advantages of an estimator based on dynamic information.

(b) Econometric applications. Forni, Hallin, Lippi and Reichlin (2003) illustrate the applicability of the dynamic factor method and its efficiency on real-world data. The paper uses a large data set, consisting of 447 monthly macroeconomic time series concerning the main countries of the Euro area to simulate out-of-sample predictions of the Euro area industrial production and the harmonized inflation index and to evaluate the role of financial variables in forecasting. Two competing models are considered : Forni *et al.* (2000); Forni, Hallin *et al.* (2004) and Stock and Watson (1999). The performances of both models are compared to those of a simple univariate AR model. Results show that multivariate methods outperform univariate ones in the forecast of inflation at one, three, six, and twelve months, and in the forecast of industrial production at one and three months. It is found that financial variables do help forecasting inflation, but do not help forecasting industrial production.

Forni, Giannone, Lippi and Reichlin (2004) studies structural identification in these models, while Giannone, Reichlin and Sala (2003, 2004) develop empirical applications to monetary economics. Giannone, Reichlin and Sala (2005) aims at identifying shocks computed from the factor model forecast using restrictions based on economic theory and analyzes factor models as tools for estimating general equilibrium macroeconomic models.

Two doctoral theses connected to dynamic factor models were successfully defended within the ULB group: L. Sala (Essays in Monetary and Fiscal Policy) and D. Giannone (Essays on Dynamic Factor Models of Large CrossSections). L. Sala's thesis deals with applications of the model to monetary economics while D. Giannone's develops new econometric results. In particular, an important contribution of the thesis is the asymptotic analysis of dynamic principal components.

Main achievements

(i) In view of its importance in macroeconometrics and finance, the dynamic factor methodology is certainly a major achievement of this work package. Data sets in these fields indeed come under the form of very large panels of interrelated time series ($n = 1000$ is not unusual in that context), for which the theory of multivariate time series analysis is completely helpless. Under the dynamic factor paradigm, the observed series decompose into two unobserved components, a *common component*, and an *idiosyncratic* one. Common components have low dynamic dimension q, and can be handled by traditional multivariate time-series methods, whereas the idiosyncratic ones, being only mildly intercorrelated, can be treated one by one via univariate time series methods. The originality of our approach is that, contrary to the static models considered in the literature so far, we allow for a dynamic loading scheme of the unobserved factors: instead of matrices of "instantaneous" loadings, we thus have one-sided filters, also loading lagged values of the factors. Whether static or dynamic, factor models with large cross-section dimension are attracting increasing attention in finance and macroeconometric applications. In finance, they are at the heart of the extensions proposed by Chamberlain and Rothschild (*Econometrica* 1983), and Ingersol (*Journal of Finance* 1984) of the classical arbitrage pricing theory. In macroeconomics, they are used to identify economy-wide and global shocks, to construct coincident indexes, and to build up forecast by exploiting the information scattered in a huge number of interrelated series.

(ii) The dynamic factor method developed within this work package has attracted the interest of a number of economic and financial institutions, including several central banks and national statistical offices, who are using it in their current analysis of the business cycle, or intend to do so (the European Central Bank, the Federal Reserve, the National Bank of Switzerland, the Banca d'Italia, ...). A real time coincident indicator of the EURO area business cycle (EuroCOIN), based on our method, is published every month by the London-based Center for Economic Policy Research and the Banca d'Italia: see http://www.cepr.org/data/EuroCOIN/ Also based on our methods, a similar monthly index is established for the US economy by the Federal Reserve of Chicago.

(iii) The forecasting performances of the dynamic factor model have been intensively discussed and compared to those of alternative methods. Such comparisons have been carried out within the ULB team (see, e.g., D'Agostino and Giannone (2005)), but also by a number of independent experts. To quote only one of the most recent, den Reijer (Working Paper of De Nederlandsche Bank, February 2005) mentions that "*only the dynamic factor model systematically outperforms and encompasses the autoregressive benchmark model ... The forecasting gains in terms of mean squared errors range from 10% to 30% for forecast horizons up to six quarters ahead*".

3. **Semiparametric inference based on ranks and signs.**

High-dimensional observations are an important source of complexity, but the complexities resulting from high-dimensional parameter spaces are no less challenging. Treating the innovation densities of underlying classical parametric time series models as unspecified nuisance parameters leads to semiparametric models where the parameter spaces are infinite-dimensional.

(a) Elliptical time series models. A class of multivariate signed rank tests has been developed for the general linear model with VARMA error terms. This model includes, as particular cases, one- and m-sample location, multiresponse ANOVA and regression, and VARMA models with a linear trend, all with elliptical innovations. Two types of multivariate signs and ranks are considered: (i) hyperplane-based signs (Randles (1989)'s concept of interdirections), and ranks of lift-interdirections (a related concept of distance between pairs of points in $\mathbb{R}^k$), or (ii) spatial signs of sphericized residuals, and the ranks of pseudo-Mahalanobis distances (distances between the sphericized residuals and the origin in $\mathbb{R}^k$), where the sphericization is performed via a square-root of the multivariate M-estimator of scatter due to Tyler (1987). The resulting tests, which generalize univariate serial and nonserial signed-rank tests, are strictly affine-invariant, and asymptotically invariant under a group of monotone radial transformations acting on the residuals, hence asymptotically distribution-free. They are valid under the class of elliptically symmetric densities, without any moment assumption. Depending on the score function considered (van der Waerden, Laplace, ...), they allow for locally asymptotically optimal (a la Le Cam-Hájek) tests at selected densities (multivariate normal, multivariate double exponential, ...). Local powers and asymptotic relative efficiencies are derived with respect to the corresponding optimal parametric Gaussian tests, and with respect to some well-known competitors (Randles (1989)'s sign test and Peters and Randles (1990)'s Wilcoxon-type signed rank tests, Oja median tests, etc). Two famous (location) univariate results are extended to the multivariate case (both in the location and serial cases): (i) a multivariate version of the traditional Chernoff and Savage (1958) property, showing that the traditional Gaussian procedures (used in daily practice) are uniformly dominated, in the Pitman sense, by the van der Waerden version of our tests, and (ii) a generalization of the celebrated Hodges-Lehmann (1956)'s ".864 result", providing, for any fixed space dimension k, the lower bound for the asymptotic relative efficiency of Wilcoxon-type (or Spearman-type, in the serial case) tests with respect to the Gaussian tests.

Those results appear in Hallin and Paindaveine (2002b, 2003, 2004b, 2004a, 2005a, 2005c). The resulting test statistics are provided under closed form for several important particular cases, including generalized Durbin-Watson tests, VARMA order identification tests, etc. In Hallin and Paindaveine (2005b) these general results are put at work in two examples of practical relevance: (i) the multivariate Durbin-Watson problem (testing against autocorrelated noise in a linear model context), and (ii) the problem of testing VAR(p_0) against VAR(p_0+1) dependence. These two testing procedures are the building blocks of classical autoregressive order-identification methods.

A new concept of multivariate ranks, based on hyperplane counts, is also presented in Oja and Paindaveine (2005), which is an analogue, for distances between the observations, of the so-called Randles interdirections associated with the observed angles.

(b) Inference for shape. In a similar spirit, Hallin and Paindaveine (2005c) and Hallin, Oja and Paindaveine (2004) develop rank-based inference procedures for shape, with a distribution-free test of the hypothesis of sphericity that does not require any moment assumptions. Optimal rank-based inference methods (tests and estimation) for the shape matrix of an elliptically contoured multivariate density. Contrary to everyday practice Gaussian procedures, based on empirical covariances and requiring finite moments of order four, these methods remain valid without any moment assumption. Paindaveine (2005) moreover shows that the celebrated Chernoff-Savage result establishing the uniform Pitman-superiority of normal-score rank-based methods for location over their pseudo-Gaussian competitors also holds for shape matrices. The rank tests and R-estimators derived in the above papers thus uniformly dominate everyday practice, without requiring fourth order moments.

(c) Semiparametric efficiency. Hallin and Werker (2003) have established the fundamental role of invariants such as signs and ranks in producing semiparametrically efficient inference procedures. Rank-based inference (in a broad sense) thus constitutes a powerful alternative to more classical tangent-space approaches to semiparametric efficiency. These ideas are applied further in two papers Hallin, Vermandele and Werker (2004, 2005) on sign-and-rank-based methods for median- and quantile-restricted models (including a number of time-series models). These sign-and-rank methods allow for considerable efficiency improvements over the existing Least Absolute Deviation (LAD) and quantile regression methods that are generally considered. Both hypothesis testing and estimation problems are considered. Such techniques rely on a new class of statistics, involving the signs and the ranks (not the signed ranks), which are maximal invariant and distribution-free under median-centered noise.

(d) Autoregression rank scores. Another timely topic in rank-based inference is that of (auto)regression rank score methods. Regression rank scores were introduced by Gutenbrunner and Jurečková from a duality argument applied to Koenker and Bassett's celebrated regression quantiles. Regression rank scores are defined as the solutions of the parametrized linear program dual to the one defining regression quantiles. The "miracle" with regression rank scores is that, contrary to the more classical "aligned rank statistics" computed from estimated residuals, regression rank score statistics are insensitive to the presence of unspecified parameter values, and asymptotically reconstruct the actual corresponding rank-based statistics, even though exact residuals (hence exact ranks) cannot be computed from the observation. In Hallin and Jurecková (1999), locally asymptotically optimal tests based on such autoregression rank scores are derived for linear constraints on the coefficients of an autoregressive model. The related estimation procedures are provided in El Bantli and Hallin (2002a). These estimators are based on linear programming algorithms, combined with a discrete numerical optimization step. They are shown to be asymptotically equivalent to the R-estimators of autoregressive parameters proposed by Koul and Saleh (1993). In contrast with the latter, however, they are autoregression invariant, so that each component of the parameter can be estimated separately. This property allows for substituting p one-dimensional

discrete optimization steps for a unique p-dimensional one, which is computationally simpler. In El Bantli and Hallin (2002b), autoregression quantiles are used in order to compute an estimation of the quantile function or *sparsity function* $\alpha \mapsto f(F^{-1}(\alpha))$ associated with the innovation density f of an autoregressive model of order p. Estimating this sparsity is essential, as it has a direct impact on the variance of quantile estimators. Contrary to classical estimators based on estimated residuals, these estimates are autoregression-invariant and scale equivariant. Their asymptotic behavior is derived from a uniform Bahadur representation for autoregression quantiles. Kolmogorov-Smirnov tests based on autoregression rank scores are constructed in El Bantli and Hallin (2001). This investigation of inference methods for time series based on autoregression quantiles and rank scores is part of the doctoral dissertation of Faouzi El Bantli at ULB (supervisor M. Hallin).

Finally, Hallin, Jurecková and Koul (2005) propose a new class of serial statistics which, contrary to Koul and Saleh's, is entirely measurable with respect to the (auto)regression rank scores. They establish an asymptotic representation result, and the asymptotic normality of these new statistics, and show how they can be used as a tool for inference in (univariate) time series. Unlike their aligned rank counterparts, they are totally insensitive to any shift effect related with the estimation of underlying nuisance parameters.

Main achievements

(i) Only a few years ago, potential applications of the classical theory of rank-based inference were looking somewhat narrow; indeed, traditional rank-based methods

- were essentially limited to the context of general linear models with independent observations (location, scale, regression, ANOVA, etc.)
- only could handle univariate observations (except for methods based on componentwise rankings, which in most respects are quite unsatisfactory)
- were making little use of the power of the Le Cam theory (in general, only the so-called Le Cam third Lemma was used, mainly in order to compute local powers—a practice that goes back to Hájek and Šidák 1967).

The contribution of this work package allows for an extension of rank-based methods

- to a large variety of time series models, and, actually, to the very broad class of semiparametric models described below
- to more general concepts of ranks (related to appropriate group invariance arguments), such as signs and ranks for median- or quantile-restricted models (Hallin, Vermandele and Werker (2004, 2005)), ranks and some adequate indicators (in the context of Ornstein-Uhlenbeck processes, see Hallin, Koell and Werker (2000)), and, in a multivariate setting, pseudo-Mahalanobis ranks and signs, or hyperplane-based ranks and signs—see Hallin and Paindaveine (2002b, 2003, 2004b, 2004a, 2005a, 2005c, 2005b).

by fully exploiting the power of Le Cam's theory of locally asymptotically normal experiments, and the related theory of semiparametric efficiency (cfr Bickel, Klaassen, Ritov, and Wellner).

(ii) A far-reaching result in this respect has been obtained in Hallin and Werker (2003), where it is shown that conditioning central sequences with respect to the maximal invariants (ranks, for instance) of appropriate generating groups yields the same results as the more traditional tangent space projections, hence leads to semiparametrically efficient inference. This result provides a very strong justification for rank-based methods, by showing that ranks (or more general invariants) actually retain all the information related with the parameter under study, while everything else (typically, an order statistic) only carries information about the nuisance. Ranks are, in a sense, performing the tangent space projections, without requiring explicit computation of the tangents, and without any unpleasant ad hoc procedures such as sample splitting. This general result applies to a variety of models: location, scale, regression, ANOVA, of course, but also ARMA, bilinear models (in the vicinity of the linear ones), random coefficient autoregressive models (in the vicinity of the nonrandom ones), ARCH and GARCH models, ... as well, in the multivariate context, as to their elliptical counterparts. In all these models, this result allows for semiparametrically efficient (at some prespecified density f) distribution-free tests, or for uniformly (over classes of possible densities f) semiparametrically efficient permutation tests (see Hallin and Werker (2003) for details and examples).

(iii) In most of these contexts, generalizations of the classical Chernoff-Savage Theorem have been obtained: see Hallin and Paindaveine (2002b, 2002a) for nonserial and serial elliptical models, Paindaveine (2005, 2004) for other multivariate examples. This celebrated theorem, stating that rank tests based on Gaussian scores perform uniformly better than Student tests, thus holds in much more general cases. In time series, for instance, the asymptotic relative efficiencies, with respect to the corresponding daily practice correlogram methods, of the normal-score rank-based procedures developed in the above papers, are uniformly larger than one. Hallin and Paindaveine (2002b, 2002a) also obtained generalizations of the no less famous Hodges and Lehmann ".864" Theorem. In its original version, this theorem shows that the lower bound for the asymptotic relative efficiencies, still with respect to Student tests, of Wilcoxon-type methods for location, is .864. It is interesting to note that this Hodges-Lehmann bound is not a monotonic function of the dimension k (the Gaussian reference being Hotelling rather than Student), with maximum values of .916 (for location) and .913 (for serial dependence) at dimension $k = 2$. Such results should be a strong incentive for bringing ranks into practice in this context.

4. **Spatial data, image analysis, and inverse problems**

The analysis of spatial data and images can be considered as another more complex version of time series analysis. Here, instead of univariate time, the index is a multivariate spatial one that moreover does not possess all specific features of time.

(a) Spatial data. This part of the project is based on a collaboration of M. Hallin with Z. Lu (Academy of Sciences, Beijing, and London School of Economics) and L.T. Tran (Indiana

University, Bloomington). Hallin, Lu and Tran (2004a) discuss the L_1 approach to density estimation for random fields. Since the seminal work of Devroye, indeed, it is well recognized that this approach is the most relevant one in density estimation; sufficient conditions for L_1 convergence of kernel estimators are obtained under extremely general, verifiable conditions. Potential applications include testing for spatial interaction, the spatial analysis of causality structures, the definition of leading/lagging sites, the construction of clusters of comoving sites, etc. In the second paper (Hallin, Lu and Tran, 2004b), a local linear kernel estimator of the regression function of a stationary spatial process observed over a rectangular domain is proposed and investigated. Under mild regularity assumptions, asymptotic normality of the estimators of the regression function and its derivatives is established. The spatial process is assumed to satisfy some very general mixing conditions, generalizing classical time-series strong mixing concepts. The size of the rectangular domain is allowed to tend to infinity at different rates. Finally, a spatial regression quantile approach to the same problem is adopted in Hallin, Lu, and Yu (2005). Quantile regression yields a much richer information than traditional conditional mean regression. Consistency and asymptotic normality are obtained under unspecified (possibly extremely complex) spatial dependence structure. To the best of our knowledge, this is the first time regression quantiles are considered in a spatial context. This line of research is very closely connected to **WP1** (Section 2.1.2(d))

(b) Inverse problems and imaging. The main research theme of Christine De Mol has been the use of sparsity-enforcing penalties in regression and inverse problems. A typical penalty of this type is the L_1 norm of the sequence of coefficients of the expansion of the solution on a given arbitrary orthonormal basis (such as e.g. a wavelet basis) . In Daubechies, Defrise and De Mol (2004), it is shown that such penalty provides a proper regularization method for linear ill-posed inverse problems and that an iterative algorithm that amounts to a Landweber iteration with soft-thresholding applied at each iteration step converges in norm to a regularized solution. These results extend to the case of L_p-type penalties with p larger than 1 and apply straightforwardly to nonparametric regression with such sparsity-enforcing penalties ("lasso" or "bridge" regression), as well as to penalized maximum likelihood with a Gaussian noise model and a (generalized) Laplacian prior. The case $p = 2$ corresponds to a smoothness constraint and yields the usual quadratic regularization applied in ridge regression. De Mol and Defrise (2004) have generalized this framework to cover the case of mixed penalties, namely to recover solutions that are the sum of a smooth and of a sparse component. Using the technique of surrogate functionals, new iterative algorithms have been derived for solving linear inverse problems of this type which are encountered in several applications. As a special case, a Huber penalty or prior can be implemented, i.e. a quadratic L_2 penalty on the small coefficients and a L_1 penalty on the larger ones. On the other hand, in connection with the Ph. D. project of M. Banbura, C. De Mol has been working on the analysis and forecasting of nonstationary time-series, with emphasis on economic data. In the light of inverse problem theory, several methods proposed in the literature can be reformulated in a unified framework. They have been tested and compared numerically, with as a benchmark the inflation series in the univariate case and various macroeconomic

panels in the multivariate case. Wavelet-based analysis and forecasting methods have been devised and are under current investigation. Collaborative work with S. Van Bellegem (UCL) has also been started on the problem of density deconvolution. Besides, let us mention the paper by Bertero, Boccacci, Custo, De Mol and Robberto (2003) which deals with an image restoration problem of interest in infrared astronomy.

This research, which was essentially conducted by Chr. De Mol and her collaborators, is also closely connected to several points in **WP1**:

- deconvolution problems (Section 2.1.3 (b));
- the recent paper by Antoniadis, Gijbels, and Nikolova (Section 2.1.2.(d));
- microarray problems (Section 2.1.6);
- P-splines (Section 2.1.5).

5. **Related topics**

(a) Independence between multivariate time series. The problem of testing non-correlation and Granger-non-causality between two multivariate series is a problem of fundamental practical importance. Haugh (1976) developed an approach to the problem in the case of two univariate time series. His tests however have low power for two series which are related over a long distributed lag when individual lag coefficients are relatively small. As a remedy,Koch and Yang (1986) proposed an alternative method that performs better than Haugh's under such dependencies. A multivariate extension of Haugh's procedure was proposed by El Himdi and Roy (1997), but suffers the same weaknesses as the original univariate method. In Hallin and Saidi (2004), an asymptotic test generalizing Koch and Yang's to the multivariate case is developed. The method includes El Himdi and Roy's as a special case. Based on the same idea, a generalization of the El Himdi and Roy procedure for testing Granger-causality between two multivariate series is also proposed. Both procedures are applied to the relations between Canadian and U.S. economic indicators, and to a brief study of causality between money and income in Canada. A second paper (Hallin and Saidi, 2005) considers the same problem from the point of view of local asymptotic optimality. Assuming that the global process $\{(\mathbf{X}_t^{(1)}, \mathbf{X}_t^{(2)}), t \in \mathbf{Z}\}$ admits a joint VAR representation, they construct locally and asymptotically optimal pseudo-Gaussian tests for the null hypothesis of noncorrelation between $\{\mathbf{X}_t^{(1)}\}$ and $\{\mathbf{X}_t^{(2)}\}$, and compare their local asymptotic powers with those of the various tests (Haugh-El Himdi-Roy, and Koch-Yang-Hallin-Saidi) proposed in the literature.

(b) Computational issues in time series estimation. With A. Klein, J. Niemczyk, T. Zahaf and P. Spreij, G. Mélard has worked on several projects based on the information matrix of time series models. I. Klein and Mélard (2004) deals with the computation of the asymptotic Fisher information of univariate SISO (single input, single output) models where the polynomials appear as factors of regular and seasonal polynomials. A note by Klein, Mélard and Niemczyk on the computation of the exact information matrix of a multivariate Gaussian process has been submitted, building on a previous paper by Klein, Mélard and Zahaf. A. Klein, Mélard and Spreij (2005) establish a new algebraic characterization of VARMA models

by means of a tensor Sylvester matrix, and show how the Fisher information matrix evaluated numerically, contrary to the tensor Sylvester matrix, may fail to reveal common eigenvalues in the AR and MA matrix polynomials. Finally, Niemczyk (2004) considers the derivatives of the autocovariances of a VARMA process (with respect to the VARMA coefficients), and studies two applications.

H. Njimi under the supervision of G. Mélard is working on the improvement of the automatic ARMA modeling procedure of Mélard and Pasteels. Azrak, Mélard and Nijmi (2004) are applying this strategy to a problematic data set with many missing values and outliers. In order to apply the methodology to the shortest series of the M3-Competition, H. Njimi has used Ayadi and Mélard (2004). A paper by Mélard, Roy and Saidi (2005) on the computational estimation of the parameters of VARMA models either in structured form (scalar component model or echelon form) or with a unit root (the case of a partially non stationary model) is tentatively accepted, subject to minor revision. A. Ouakasse has defended a thesis at ULB (supervisor: G. Mélard) on a new method for recursive estimation of ARMA and SISO models. He proves asymptotic results, describes computational aspects and presents simulation results.

(c) Other topics in time series. Akharif and Hallin (2003) provide a locally asymptotically optimal method for detecting random coefficients in autoregressive time series of order p. Dufour, Farhat and Hallin (2004) establish exact bounds for the tail areas of distributions of autocorrelation coefficients under unspecified innovation density. This allows for controlling the level of tests of serial dependence without any assumptions on the actual densities. Ayadi and Mélard (2004) study the (very) small sample behavior of autocorrelations of a Gaussian white noise process, with simulation results in the case of some non-Gaussian white noise processes. Mouchart and Rombouts (2005) propose an efficient approach for the case of nowcasting, i.e. forecasting present values based on recent past data. A progressive specification strategy is elaborated and illustrated on R&D data for a panel of EU countries.

Scientific input of each partner

This work package is coordinated by ULB, and essentially involves the ULB and UCL teams:

- UCL : time-varying coefficient and local stationarity approaches to the analysis of nonstationary time series, nonparametric wavelet-based models, multivariate SLEX, nowcasting
- ULB : time-varying coefficient approach to nonstationarity, dynamic factor model methods in the analysis of high-dimensional time series and econometric applications, forecasting of very large panels of time series data, semiparametric inference based on signs and ranks, semiparametrically efficient inference in elliptical (time series) models, inference on shape, spatial analysis, testing independence between multivariate time series, computational aspects of time series analysis, inverse problems, and imaging.

2.3 Work package 3: Survival analysis

Summary of the scientific results

1. **Nonparametric estimation with censored data**

   Regression models in which the response variable is subject to censoring by two types of censoring variables, an informative and a non-informative one, have been studied by Braekers and Veraverbeke (2005a). For this model with partially informative censoring, they established the validity of a bootstrap approximation. They also used profile likelihood methods to study Cox's regression model with data subject to partially informative censoring. See Braekers and Veraverbeke (2005c).

   Braekers and Veraverbeke (2005b) studied nonparametric estimation of the conditional survival function under dependent censoring. The common (but untestable) assumption that lifetimes and censoring times are independent is indeed not always justifiable. Therefore, a model is considered in which the joint distribution of lifetime and censoring time is described by a known copula function. For the class of Archimedean copulas, an explicit form of the estimator can be obtained. Asymptotic properties have been established. Also regression quantiles under this dependent censoring model have been studied. See Veraverbeke (2005).

   Veraverbeke (2004) also obtained nonparametric estimators for two important functionals of the conditional residual lifetime beyond some fixed or random timepoint: the mean and any quantile. The observations are subject to random censoring and covariate information is taken into account.

   Members of the LUC team (Paul Janssen and Noël Veraverbeke) in collaboration with Ricardo Cao and Ignacio Lopez de Ullibarri (La Coruña, Spain) explored presmoothing in survival analysis. See Cao, Lopez de Ullibarri, Janssen and Veraverbeke (2005). Cao, Janssen and Veraverbeke (2003) also obtained new results on relative hazard function estimation with left truncated and right censored data. Paul Janssen and Noël Veraverbeke in collaboration with Jan Swanepoel (North-West University, Potchefstroom, South Africa) studied goodness-of-fit tests derived from a characterization of the uniform distribution. They derived normal and bootstrap approximations in P. Janssen, Swanepoel and Veraverbeke (2005). In P. Janssen, Swanepoel and Veraverbeke (2004) they also obtained a new variable bandwidth kernel estimator for distribution functions. Their new estimator reduces the bias considerably and keeps the variance unchanged with respect to the usual kernel distribution function estimator.

   Li Chun Wang proposed a criterion for choosing between two loss functions in a Bayesian analysis. See Wang (2004b). He also studied Bayes and empirical Bayes tests for the life parameter and studied asymptotically optimal rates of convergence. See Wang (2004a). Together with Veraverbeke he studied Bayes prediction in the exponential distribution under random censorship and where the prior distribution is of unknown form. See Wang and Veraverbeke (2004a). In Wang and Veraverbeke (2004b) they define an adjusted empirical log-likelihood for the mean response in the situation where responses are missing at random. Empirical likelihood methods for U-quantiles are presently explored by Van Keilegom and

Veraverbeke (2005).

Li and Van Keilegom (2002) and Van Keilegom and Veraverbeke (2002) consider a nonparametric regression model, where the response Y is subject to right censoring and the covariate X is always observed. In this context Van Keilegom and Veraverbeke (2002) study the estimation of the hazard function of Y conditionally on X and they suppose that the vector (X, Y) follows a heteroscedastic model. In Li and Van Keilegom (2002) the authors construct confidence intervals and bands for the conditional distribution function of Y given X. They use an empirical likelihood approach, which has several important advantages: it always produces intervals in $[0, 1]$, it does not require the estimation of the variance and it might produce asymmetric intervals.

Van Keilegom and Hettmansperger (2002) consider two random variables which are both subject to random right censoring, and they construct M-estimators for these two variables. A special case, which is studied in more detail, is the bivariate L_1 median.

Akritas and Van Keilegom (2003) study nonparametric estimation of the bivariate (and marginal) distribution of two random variables that are subject to censoring. Asymptotic properties of the proposed estimators are established, a bandwidth selection method is proposed and simulations are carried out. The work by Du, Akritas and Van Keilegom (2003) is situated in the domain of analysis of covariance with censored data. The authors develop a nonparametric method, which is useful in situations where the classical models (like additive risk model, proportional hazards model or proportional odds model) are not adequate. A test statistic for this model is proposed and its performance is studied for small and large sample sizes.

Van Keilegom (2004) proposes a new estimator of the bivariate and marginal distribution of two random variables subject to censoring. The estimator does not require the common assumption of independence between the vector of survival and censoring times, but allows for a certain type of dependent censoring. In Patilea and Rolin (2005) a new nonparametric estimator for the distribution of a life time is considered when the data may be left or right censored. The asymptotic properties of the proposed estimator are studied.

Heuchenne and Van Keilegom (2003) consider a polynomial regression model, in which the response is subject to random right censoring. A new estimation procedure for the parameters in this model is proposed, and the estimators are studied both via asymptotic properties and via finite sample simulations. An extension of this estimator to nonlinear regression is proposed and studied in Heuchenne and Van Keilegom (2005b), while in Heuchenne and Van Keilegom (2005a) a new method to estimate the regression function in a nonparametric way is studied. The interesting new feature of the proposed estimator is that it reduces the undesirable bias effects related to the presence of random censoring to a minimum.

For arbitrary functions φ, Sanchez Sellero and Gonzalez Manteiga (2004) consider the problem of estimating expectations of the form $E[\varphi(X, Y)]$ (where X is completely observed and Y is subject to random censoring), which appear in many statistical problems. Applications to goodness-of-fit testing in regression (see also **WP1**) and to inference for the regression depth, are considered in more detail.

In many applications it is reasonable to assume that the hazard function is an increasing (or decreasing) function. In this case nonparametric estimation of the hazard function should be done under this constraint. Gijbels and Heckman (2004) deal with the problem of testing whether the hazard function can indeed be assumed to be increasing (or decreasing). They also illustrate how to apply their metholodogy to type II censored data. This work is related to work in **WP1**. Gijbels and Gürler (2003) consider estimation of the hazard function, based on censored data, when the hazard function is assumed to be a step function with a (unknown) jump point. In real life applications, abrupt changes in the hazard function are observed due to overhauls, major operations or specific maintenance activities. The proposed estimation procedure is based on certain structural properties and on least squares ideas. A simulation study is carried out to compare the performance of the proposed estimator with two estimators available in the literature: an estimator based on a functional of the Nelson-Aalen estimator and a maximum likelihood estimator. This work is related to research on change-point detection in **WP1**.

Kocmanova and Lesaffre explored Bayesian approaches to model jointly repeated measurements and survival data.

A Generalized Estimating Equation-method for modeling multivariate interval-censored data has been developed, and has been applied to the emergence times of the permanent teeth as recorded in the Signal Tandmobiel Study (Bogaerts, Leroy, Lesaffre and Declerck, 2002). Furthermore an improvement to the current methodology to calculate the bivariate non-parametric estimate of a survival function for interval-censored data has been proposed by Bogaerts and Lesaffre (2004). Bogaerts and Lesaffre (2003) and Lesaffre and Bogaerts (2005) developed also a smooth bivariate estimate of the survival function, using a penalized likelihood approach. This methodology can be employed to have an improved estimate of association measures in bivariate survival models. In this respect, Lesaffre and Bogaerts developed an estimator for Kendall's tau using the bivariate smooth estimate of the survival distribution. The performance of this estimator in small sample sizes has been explored and good results were obtained. Also another association measure, the Spearman correlation coefficient, can be easily estimated using the same technique.

2. **Frailty models**

Frailty models provide a powerful tool to understand clustered time-to-event data. Clustered or multivariate survival data appear in a variety of applied domains such as: (i) animal breeding studies, e.g., the survival of lambs in the sub-humid tropics (Nguti, Janssen, Rowlands, Audho and Baker (2003)); (ii) veterinary sciences, e.g., the time to first insemination in dairy cows (Duchateau, Opsomer, Dewulf and Janssen (2004)); (iii) treatment outcome studies, e.g. the understanding the heterogeneity in survival data from patients that receive the same treatment Legrand *et al.* (2005) and Legrand, Duchateau, Sylvester, Janssen and Therasse (2004)); (iv) prognostic index analysis, e.g., is a prognostic index transportable to data sets different from the one used to construct the model (i.e., generalization of the use of a prognostic index). Frailty models are also useful to model recurrent event data. For such data the recurrent time points at which e.g. an asthma attack occurs are the event times, the data are now clustered within a patient/subject (Duchateau, Janssen, Kezic and Forpied, 2003).

For treatment outcome studies Legrand, Ducrocq, Janssen, Sylvester and Duchateau (2004) show the importance of the inclusion of a treatment-centre interaction, and they show the need for models with two random effects. To fit such models - using the Survival Kit software (freeware) - there was the need to expand the existing software (allowing only for one random effect) to models with two random effects. "A Bayesian approach to fit frailty models with one frailty term has been developped by Ducrocq and Casella. They showed that the Bayesian approach is very effective for this Bayesian methodology in Survival Kit (a freeware package to fit frailty models). To allow for an extra interaction frailty term Legrand, Ducrocq *et al.* (2004) extended the Bayesian methodology and expanded the software needed to fit these more complex frailty models.

To understand the impact of heterogeneity it is important to find appropriate ways to translate the presence of heterogeneity in multivariate survival data in terms of quantities that are relevant and understandable for the scientists, e.g., how does heterogeneity influence the median survival time or how does it influence the probability that the disease free survival is at least five years. Based on concrete examples, Duchateau and Janssen (2005) provide several examples demonstrating the impact of heterogeneity on the medical relevant quantities.

A further issue when dealing with frailty models is to obtain the standard error of the estimated heterogeneity. Massonnet, Burzykowski and Janssen (2003) show that model based resampling can be used to obtain good estimates of these standard errors; currently they explore a new method to estimate the heterogeneity parameters in frailty models via model transformations. The basic idea is that after the model has been transformed one can rely on the well established mixed model methodology to estimate the heterogeneity parameters.

A further result contributing to a better understanding of the statistical properties of frailty models is given in Nguti, Claeskens and Janssen (2004): they study the asymptotic distributional behavior of likelihood ratio and score tests for the presence of heterogeneity in the data (i.e., to test for the presence of a cluster effect).

In classical frailty models covariates have a linear impact on the logarithm of the hazard rate. In Duchateau and Janssen (2004a) it is shown that the use of smoothing splines to model this covariate impact provides a much more flexible way in explaining the effect of covariates on the hazard rate.

Accelerated failure time models with a shared random component are described in Lambert, Collett, Kimber and Johnson (2004); they are used to evaluate the effect of explanatory factors and different transplant centres on survival times following kidney transplantation. Different combinations of the distribution of the random effects and baseline hazard function are considered and the fit of such models is critically assessed. A mixture model that combines short-term and long-term components of a hazard function is developed. In Lambert and Eilers (2004) it is shown how one can use Poisson log-linear models in combination with Bayesian P-splines to set up flexible models for the hazard rate with time-varying regression coefficients. Bayesian inference tools based on the Metropolis-adjusted Langevin algorithm are proposed.

Within the larger context of modeling multivariate survival data, the joint modeling of survival times and covariate processes has received considerable attention in recent years. In Nguti, Burzykowski, Rowlands, Renard and Janssen (2005) joint modeling is used for animal breeding data.

The accelerated failure time (AFT) model of Komárek, Lesaffre and Hilton (2005) with a smooth error distribution being the mixture of Gaussian distributions further generalized by Lesaffre, Komárek and Declerck (2005) allowing the scale parameter of the AFT model to depend on covariates, was extended to allow for a bivariate random effects structure with doubly interval-censored data. For the smooth error distribution a frequentist approach and a Bayesian approach were developed which are extensions of the approach of Ghidey, Lesaffre and Eilers (2004). Alternatively, the Reversible Jump MCMC approach was developed for modeling the error structure (Komarek and Lesaffre, 2004). The final approach allows both the error as well as the random effects distribution be flexible. All approaches have been applied to solve the dental research questions originating from the Signal Tandmobiel study (Komárek and Lesaffre, 2005).

Komárek and Lesaffre have developed accelerated failure time models with or without a frailty component and with a flexible error distribution. Further, they collaborate in the comparison of several approaches for frailty models for the analysis of complex medical survival data with the LUC partner and EORTC.

Main achievements

The above results contribute to the two key objectives of WP3:

(1) The study of nonparametric regression models in which the censoring mechanism is complex or the regression function contains discontinuities.
In the papers of Braekers and Veraverbeke (2005a, 2005c, 2005b) and Veraverbeke (2005), new methodology has been developed to deal with complex censoring mechanisms such as informativeness and dependence between censoring time and lifetime.
Also the papers of Li and Van Keilegom (2002), Akritas and Van Keilegom (2003), Van Keilegom (2004), Heuchenne and Van Keilegom (2005b, 2005a) deal with new methods for complex regression problems with censored data.
As to the problem of discontinuities we mention the paper of Gijbels and Gürler (2003).

(2) The study of heterogeneity in terms of frailty models :
Applications: in the papers Nguti *et al.* (2003), Duchateau *et al.* (2004), Legrand *et al.* (2005), Legrand, Duchateau *et al.* (2004), Duchateau *et al.* (2003) we show that frailty models provide a versatile tool to describe heterogeneity in a wide range of scientific domains.
Methodology: in the papers Duchateau and Janssen (2004b), Nguti *et al.* (2004) and Legrand, Ducrocq *et al.* (2004) we provide further methodological insight in the understanding of frailty models.

Computing: in the papers Massonnet *et al.* (2003), Nguti *et al.* (2005), Legrand, Ducrocq *et al.* (2004) we contribute to computational aspects of fitting multivariate survival data.

Scientific input of each partner

- For the nonparametric regression with censored data part, there is cooperation between LUC (Veraverbeke) and UCL (Van Keilegom).
- For the frailty part, there is close cooperation between LUC (Janssen, Massonnet, Burzykowski, Cortiñas), KUL-2 (Lesaffre, Komárek) and UCL (Lambert, Claeskens (now KUL)). There exists a very active Frailty Working Group, coordinated by LUC. They have regular seminars and meetings. One of their activities is for example to study whether three different methods, developed at LUC, UCL and KUL-2, lead to the same conclusions when applied to the same data set of an EORTC clinical trial. The Frailty Working Group also cooperates with Universiteit Gent (Duchateau), EORTC, Brussels - European Organization for Research and Treatment of Cancer (Legrand, Sylvester), ILRI, Nairobi - International Livestock Research Institute (Nguti), and INRA - Jouy- en-Josas - Institut National de la Recherche Agronomique (Ducrocq).
- Duchateau and Janssen signed a contract with Springer Verlag to finish a book (in summer 2006) on Frailty Models.
- For nonparametric regression problems there are cross links between **WP3** and **WP1**.
- For frailty modeling, there are cross links with **WP4**.
- Organization of a meeting on frailty models by KUL-2 and LUC.
- Organisation of a course and a meeting on interval-censored data by the KUL-2, UCL and LUC partner on 15-17 November 2005.

2.4 Work package 4: Mixed models

Summary of the scientific results

For the linear mixed model an approach has been suggested and critically examined to replace the normal distribution of the random effects by a flexible distribution being a specific mixture of normal distributions. The approach has been contrasted to its competitors in an extensive simulation study and proved to be superior. Finally, the approach has been implemented in a variety of survival models and proved to be quite useful.

More generally, (generalized and nonlinear) mixed models can be generalized by allowing for a mixture of normals for the random effects distribution.

An approach has been suggested to analyze multivariate responses using a mixed model when the dimension of the response is high. Using a pseudo-likelihood approach the parameters are estimated. A simulation study shows the good properties of the method.

The random-effects approach to jointly analyze multivariate longitudinal profiles has been critically investigated.

Conditional linear mixed models have been introduced for the analysis of longitudinal continuous response profiles. These models do not assume any parametric form for the baseline differences between study participants.

Testing for variance components in mixed models does not follow standard testing theory because null hypotheses are on the boundary of the parameter space. Appropriate score tests have been constructed for this situation.

A pairwise modelling approach has been suggested to analyze multivariate responses using mixed models when the dimension of the response is high. The method is applicable for linear, nonlinear and generalized linear mixed models.

Dental data have most often a quite complex data structure. The Signal Tandmobiel Study is a longitudinal dental study on about 4500 children conducted in Flanders from 1996 to 2002 by the KUL-2 group. The caries data have an hierarchical structure (tooth surface on tooth within child within class of school) in time (6 years of follow-up). To tackle the dental research questions a variety of statistical approaches were necessary and have been employed and/or further developed. These include methods for analyzing repeated measurements analyses with a multivariate and hierarchical structure, survival methods taking into account left-, right- and interval censoring, methods to allow for missing data and methods to correct for measurement error and misclassification of the response and/or the covariates, to mention a few. The methods thus needed approaches which could be classified under WP4, **WP5** and **WP6**. Both Bayesian as well as frequentist approaches were developed.

Accelerated failure time models have been developed with a flexible error and random effects distribution for left-, right, interval and doubly-interval censored data.

Bounded outcomes (random variables on [0,1]) have been successfully modeled by assuming a latent (random) variable with a logistic-normal distribution.

A statistical framework for item response models was formulated from the perspective of generalized linear and nonlinear mixed models. Based on this framework, models with latent variables for items (in addition to latent variables for persons) have been formulated, and two approaches for residual dependence were developed: a conditional approach for ordered-category data, and a copula approach for binary data.

Main achievements

The aim of this work package is: *look for adequate random effects models.* Below we indicate the main achievements with respect to our objectives.

Ghidey *et al.* (2004) have developed a mixed model with a flexible random effects distribution that can be approximated by a smooth function of B-splines or of Gaussian densities. Penalized likelihood maximization delivers the estimated fixed effects and the smoothing coefficients of the random effects distribution. An extensive simulation study has been conducted to compare the performance of the approach to its competitors, i.e. the heterogeneity model of Verbeke and Lesaffre (1996), D. Zhang and Davidian (2001) and the Smoothening-by-Roughening approach of Shen and Louis (1999) in the case the other assumptions of the linear mixed model, namely on the error part and with regard to the process of missing data, are not fulfilled. The simulation results indicate superiority of our approach in the considered cases in terms of Mean Squared Error of estimating the random effects distribution.

Due to its flexibility, the random-effects approach for the joint modelling of multivariate longitudinal profiles received a lot of attention in recent publications. In this approach different mixed models are joined by specifying a common distribution for their random-effects. Parameter estimates of this common distribution can then be used to evaluate the relation between the different responses. Using bivariate longitudinal measurements on pure-tone hearing thresholds, Fieuws and Verbeke (2004) have shown that such a random-effects approach can yield misleading results for evaluating this relationship.

Studying longitudinal changes based on data from observational studies not only requires appropriate modelling of longitudinal effects, but also of cross-sectional effects, needed to correct for the high degree of heterogeneity among the study participants at baseline. In the context of linear mixed models, Verbeke, Spiessens and Lesaffre (2001) have shown that misspecification of the cross-sectional component of the model can seriously affect the estimation of the longitudinal component. They have therefore introduced conditional linear mixed models which allow to estimate all longitudinal effects in a linear regression model with subject-specific parameters, without having to rely on any parametric assumption about the baseline characteristics of subjects.

Whenever inference for variance components is required, the choice between one-sided and two-sided tests is crucial. This choice is usually driven by whether or not negative variance components are permitted. For two-sided tests, classical inferential procedures can be followed, based on likelihood ratios, score statistics, or Wald statistics. For one-sided tests, however, one-sided test statistics need to be developed, and their null distribution derived. While this has received considerable attention in the context of the likelihood ratio test, there appears to be much confusion about the related problem for the score test. Verbeke and Molenberghs (2003a) illustrate that classical (two-sided) score test statistics, frequently advocated in practice, cannot be used in this context, but that well-chosen one-sided counterparts could be used instead. The relation with likelihood ratio tests has been established, and all results are illustrated in an analysis of continuous longitudinal data using linear mixed models.

Classical mixed models are based on normally distributed random effects. This assumption has been relaxed by allowing for mixtures of normals, which has been implemented in a SAS-macro for linear as well as for generalized and nonlinear mixed models. The flexibility of these models has been illustrated by Fieuws, Spiessens and Draney (2004).

In the context of longitudinal data or repeated measurements, research questions are often formulated which require joint modeling of multivariate response vectors measured repeatedly within the participating subjects. We focus on a random-effects approach, where a mixed model is assumed for each outcome separately, and where the joint model arises from assuming a joint (multivariate) distribution for all random effects. A new model fitting approach is based on fitting all pairwise models and inferences follow from pseudo-likelihood theory (Fieuws and Verbeke, 2005a, 2005b, 2005c). Simulation studies (Fieuws and Verbeke, 2005a) show that this approach yields unbiased estimates and valid standard errors robust against model misspecification. Efficiency loss can arise when some parameters are shared by a set of outcomes.

The Signal Tandmobiel Study is a longitudinal dental study on about 4500 children conducted in

Flanders from 1996 to 2002. From the age of seven the children were examined annually by sixteen trained and calibrated dental researchers to collect dental data (plaque score, caries experience, gingivitis, etc.). Further, each year a questionnaire was given to the parents to learn about the oral health and dietary behavior of the child and the family of the child. To provide insight in the dental research questions a variety of techniques for the analysis of complex data have been explored and (further) developed with success, see Leroy, Bogaerts, Lesaffre and Declerck (2003a, 2003b, 2005a, 2005b). Therefore, the exploration of this dental data set is a typical example to illustrate the implications of analyzing complex data structures.

Komárek, Lesaffre, Härkänen, Declerck and Virtanen (2005) fitted a variety of Bayesian survival models with two random effects parameters (frailty parameter and birth of dentition parameter) to model the time from emergence to caries experience of the first permanent molars. That exercise was the basis for developing a new and different approach, i.e. based on an accelerated failure time (AFT) approach with a complex error structure not necessarily assuming classical assumptions like normality. Therefore, Komárek *et al.* (2005) developed an AFT model with a smooth error distribution being the mixture of Gaussian distributions. This approach was further extended by Lesaffre *et al.* (2005) allowing the scale parameter of the AFT model to depend on covariates. This model was further generalized by including a bivariate random effects structure to represent the hierarchical structure and allowing also doubly interval-censored data. For the smooth error distribution a frequentist approach and a Bayesian approach were developed which are extensions of the approach of Ghidey *et al.* (2004). Alternatively, the Reversible Jump MCMC approach was developed for modeling the error structure (Komarek and Lesaffre, 2004). The final approach allows both the error as well as the random effects distribution be flexible. All approaches have been applied to solve the dental research questions originating from the Signal Tandmobiel study (Komárek and Lesaffre, 2005).

Lesaffre, Rizopoulos and Tsonaka (2004) developed models to analyze U- and J-shaped cross-sectional data bounded to [0,1]. Bounded outcome scores occur frequently in compliance studies as the percentage of days that a patient takes his/her drug correctly. The models assume that underlying the observed score there is a latent score (random effect) which has on a transformed scale (logit-scale) a normal distribution. This allows to employ classical (random effects) models to analyze these data. Further, the power and sample size for this model has been worked out (Rizopoulos, Tsonaka and Lesaffre, 2005).

An important part of the work done by the KUL-1 group concerns item response models. These models can be seen as generalized linear and nonlinear mixed models with a logit link, a topic that is also of relevance to **WP6** (latent variables). Our work has been concentrated on five issues. Statistical framework for item response models (IRT). Well-known item response models such as the LLTM and DIF models were generalized into random weight variants (Rijmen and De Boeck, 2002); (Van den Noortgate and De Boeck, 2004). In the same vein, generalized linear and nonlinear mixed models have been described as a general framework for IRT (Rijmen, Tuerlinckx, De Boeck and Kuppens, 2003). This framework is then used in a volume published by Springer in the series on Statistics for Social Science and Public Policy (De Boeck and Wilson, 2004) in order to redefine and discuss item response models as explanatory models and not just measurement models. It is an edited book, but written as a monograph, in a collaboration between researchers involved in WP4 (Geert Verbeke, Steffen Fieuws), **WP5** (Paul De Boeck, and many others), and **WP6** (Geert Molenberghs) on the one hand, and the educational measurement research group from UC Berkeley (Mark Wilson) on the other hand.

We have developed a conditional approach for modeling residual dependency for mixed logistic models, in the line of earlier work (e.g., Tuerlinckx and De Boeck (2004a); Smits, De Boeck and Hoskens (2003)), but now for ordered-category data, including partially-ordered-category data, and this model was compared with a partly marginal approach (Ip, Wang, De Boeck and Meulders, 2004). The model is further adapted to investigate latent trajectories through a two-dimensional space of manifest categories (Meulders, Ip and De Boeck, 2005), making use of the rating scale model. As an alternative to the conditional approach, Braeken, Tuerlinckx and De Boeck (2005) have developed a dependency model for binary data based on Frank's copula, so that the simple logistic form is retained in the marginal models. This line of modeling is a break through in handling residual dependencies, because it allows for rather simple estimation and preserves a simple marginal form.

We have investigated models for covariate effects that are a function of other covariate effects. These are the so-called MIRIDs (models with internal restrictions on item difficulty), which were developed by the KUL-1 team (as explained in the proposal). The model was applied to emotion data (Smits and De Boeck, 2003), software has been developed (Smits, De Boeck and Verhelst, 2003), and a random weights version was developed (Smits and Moore, 2004). The MIRID model has led to the formulation of a double-structure structural equation model (De Boeck and Smits (2004)), a model with latent variables for two of the three modes of a three-mode data set.

We have shown that a well-known latent trait model (the 2PLM) can be derived as the marginal choice probability model from a diffusion model (a Wiener process with constant drift and variance and two absorbing boundaries) (Tuerlinckx and De Boeck, 2004b). On the other hand, we have formulated a random-effect (or latent trait) version of the bivariate diffusion model (Ratcliff and Tuerlinckx, 2002), and we have worked on the computation of the distribution function (Tuerlinckx, 2004a). Tuerlinckx (2004b) has proposed a multivariate counting process with positive dependencies for reaction times that can be approached as a random-effects model with independent non-homogeneous Poisson processes (conditional on the random effect).

Mixed models are used in actuarial science to account for some (residual) heterogeneity among the risks passed to the insurance company. This heterogeneity is taken into account a priori, with the help of risk classification techniques. Denuit and Lang (2004) proposed a fully Bayesian approach to the problem.

A posteriori ratemaking techniques are used to correct the premium amount for this heterogeneity. In that respect, bonus-malus systems and credibility theory are very efficient techniques to refine the a priori risk classification. The papers by Pitrebois, Denuit and Walhin (2004) and Purcaru, Guillen and Denuit (2004) propose new methods to reevaluate the future premiums taking into account the past claims history. Pitrebois, Denuit and Walhin (2005a, 2005b) implemented some refinements of bonus-malus scales, integrating different types of events (as claims with or without bodily injuries in motor third party liability insurance) or combining the scale with deductibles.

Scientific input of each partner

1. Work on the score test and conditional linear mixed models is the result of a collaboration between KUL-2 and LUC.

2. The application of the mixture modelling approach in the context of generalized linear mixed models was made possible by collaboration between KUL-1 and KUL-2.

3. KUL-2 had initial discussions with Irene Gijbels for the development of flexible random effects models (acknowledged in Ghidey, Lesaffre and Eilers, 2004).

4. KUL-2 has regular meetings with Paul Janssen (**WP3**), Luc Duchateau (RUGhent) and EORTC concerning the comparison of different random effects survival models.

5. Antoniadis and Sapatinas (2004) consider a general functional mixed-effects model that inherits the flexibility of linear mixed-effects models in handling complex designs and correlation structures.

2.5 Work package 5: Classification and mixture models

With respect to mixture models, we have concentrated on three types. The first type of mixture models concerns the random effects in logistic models. We have developed a model for the transition between heterogeneous components, we have developed a global approach for the differentiation between types of mixture components, and mixture and kernel methods have been developed for the smoothing of random effect distributions. The second type concerns models with binary latent variables for two of the three modes. These models have been extended and Bayesian estimation methods have been investigated. The third type concerns errant processes. For various contexts, we have developed mixture models to capture errant processes.
With respect to classification models other than mixtures, on the level of one-mode clustering methods, significant contributions include the development of Kohonen maps for analyzing interval-type data and of a one-mode addititive clustering model for two-way two-mode data. On the level of two- and three-mode clustering methods, a comprehensive structured review of such methods has been established. Other contributions include the development of two-way clustering methods for contingency tables (which includes the development of a k-tangent clustering algorithm as a general tool for analyzing heterogeneity), and extensive work within the hierarchical classes family, a comprehensive family of simultaneous overlapping clustering methods for multimode data.

Main achievements

1. **Specific types of mixture models**

   In the proposal, three types of mixture models are given explicit attention. The first concerns extensions of the generalized linear and nonlinear mixed model of the logistic type with a mixture distribution for the random effects. The data are binary or ordered-category data of the person x item type. The mixture distribution is a distribution for the random person effects, such as in the mixture Rasch model. These models are called heterogeneous mixture models in the following (1a).

The second specific type concerns mixture models with mixture distribution for persons as well as for items, so that crossed random effects are obtained. However, we have first continued our research on regular crossed random effects, without mixture distributions (R. Janssen, Schepers and Peres (2004); Van den Noortgate, De Boeck and Meulders (2003)), also in collaboration with **WP4** and **WP6** ((Tibaldi, Verbeke *et al.*, 2004)), and in the current research we rather concentrate on multidimensional crossed random effects (De Boeck and Smits, 2004). Because of this orientation away from mixture models for this particular aspect of the proposal, we will not further report on this second specific type.

The third type concerns models for binary three-mode data, with binary latent variables for two of the three modes, to be combined with a disjunctive/conjunctive rule to explain the data. They are stochastic versions of the hierarchical classes models to be discussed in Section 3 of the main achievements. These models are the so-called probability matrix decomposition models (1b).

In addition, we have started a line of research on mixture models with an errant process (1c).

(a) Heterogeneous mixture models. Heterogeneous mixture models are finite normal mixtures for random effects in mixed models of the logistic kind. We call the mixtures heterogeneous when the variance of each mixture component is larger than zero. Depending on the fixed effects, we call them quantitative mixture models (equivalence of fixed effects) or qualitative (no equivalence of fixed effects). A well-known psychometric example of a qualitative heterogeneous mixture model is the mixture Rasch model (Rost, 1997). This model can be used for test data, so that the fixed effects are the difficulties of the test items (e.g., Rijmen and De Boeck (2003)). In such a model, a random intercept explains the heterogeneity of the respondents, and each mixture component represents a different set of difficulties, for example because a different strategy is implied depending on the mixture component.

The achievements are of three kinds. First, the KUL-2 team has developed a SAS-macro to estimate (quantitative and qualitative) mixture models with nonequivalent fixed effects using the NLMIXED procedure (Fieuws *et al.* (2004)). Second, the (quantitative and qualitative) mixture models were extended into models for change, by adding a transition matrix to the model (Rijmen, De Boeck and van der Maas (2004)). Another approach to change is to model random change parameters with a mixture distribution, so that latent trajectories are obtained. This method is used in applications on childrens' aggressive and delinquent problem behavior (De Fraine, Van Damme and Onghena, 2004) and on self-concept (Prinzie, Onghena and Hellinckx (2004)). Work in progress concerns the use of variational approaches and graphical techniques, so that the more complex change models can be estimated. Third, we investigated the possibilities to differentiate between quantitative and qualitative mixture models. This has resulted in a manuscript (Rijmen and De Boeck, 2004) showing how in special cases a qualitative mixture model with more than one mixture component can be mapped into a quantitative model with one component (collapsing the mixture structure). Further work includes a global approach to differentiate in a statistical way between types of manifest categories (quantitative heterogeneous, quantitative homogeneous, qualitative heterogeneous, and qualitative homogeneous) (De Boeck, Wilson and Acton, 2005). The approach can easily be extended to latent categories (mixture components).

(b) Probability matrix decomposition models (PMD models). PMD models are models for binary three-way three-mode data. As a typical example, take person x situation x behavior data. The model explains the data from binary latent variables for two of the three modes (e.g., for situations and persons), and a disjunctive/conjunctive combination rule for the realizations of the binary latent variables from the two modes. The model was developed in a Bayesian context (Meulders, De Boeck, Van Mechelen, Gelman and Maris, 2001) and linked to the family of generalized linear models by Meulders, De Boeck and Van Mechelen (2001) for the case of a single pair of latent variables.

The original model has been extended in three different ways, two of which are related to the study of heterogeneity, one of the meta-modeling aims of the proposal.

- We have extended the model with a mixture model for the third mode (persons in case situations and behaviors are the first two modes), so that each component has a probability for each of the latent variable pairs to apply (Meulders, De Boeck and Van Mechelen (2002); Meulders, De Boeck, Kuppens and Van Mechelen (2002)).
- We have extended the model so that for a given person the situation (or behavior) keeps its realized value of the latent variable over all behaviors (or over all situations), so that individual differences in situational interpretations (or in behavioral functions) can be explained (Meulders, De Boeck and Van Mechelen (2003)).
- In line with a methodological aim of the proposal, relating to the Bayesian approach, a hierarchical extension of the model has been developed, with hyperparameters referring to the distribution of the probability parameters associated with elements of the first two modes (Meulders, De Boeck, Van Mechelen and Gelman (2004)). The hyperparameters can inform us about the categorization tendency in processes underlying the interpretation of situations. The particular application described by Meulders *et al.* (2004) concerns the perception of emotions (first mode) in faces (second mode).

(c) Mixture models with an errant process. It often occurs in psychological studies that not all data are generated through the assumed process, but instead through a minority process that is considered as an errant process. Guessing is an example. This process can be captured in a mixture component that is differentiated from the dominant normal process.

We have extended an extant diffusion process model with such an errant component (Ratcliff and Tuerlinckx (2002)), we have extended a Rasch model with random effects for the component probabilities of the errant process component (San Martin, Del Pino and De Boeck, 2003), and we have extended a Rasch model with a drop-out process (Tuerlinckx, De Boeck and Lens (2002)). In all three, the mixture components are components of repeated observations within persons and not components of persons. For a totally different kind of data (large claims data), Beirlant, Joossens and Segers (2003) have proposed an extension of the generalized Pareto distribution to model excesses of claim amounts.

2. **Methods to decide on the number and type of components and smoothing**

   A comprehensive approach for model checking in models with missing or latent data has been developed in collaboration between KUL-1 and KUL-2 (Gelman, Van Mechelen, Verbeke, Heitjan and Meulders (2005)). This approach, proposed within a Bayesian framework, extends the multiple imputation principle from the domain of model estimation to that of model checking, and especially relies on graphical tools. It includes the case of mixture models (which involve latent data) and checking problems with regard to the number and type of mixture components as a special case (Berkhof, Van Mechelen and Gelman, 2003). The number of clusters issue has further been given special attention within the study of classification techniques other than mixtures (see below).

   This second topic is kernel estimation as a smoothing technique, which can be used also to determine the number of mixture components of the random effects. Now that Taoufik Bouezmarni from the UCL team has joined the KUL-1 team, this collaboration with **WP1** has resulted in a kernel estimation method for the random effects in logistic random intercept models, such as the Rasch model (Bouezmarni, Rijmen and De Boeck, 2005), and we plan to extend this method into a one-step estimation method, so that also the number of mixture components of the random effect distribution can be estimated.

   On the other hand, mixture based smoothing approaches are developed and investigated by the KUL-2 team for their use in the context of linear models. Ghidey *et al.* (2004) have developed, in collaboration with Paul Eilers (University of Leiden) a mixed model with a smooth random effects distribution. For instance, the model allows a long-tailed distribution for the random effects, as well as a mixture of normal distributions. The smoothing approach will reveal the underlying mixture structure, though without explicitly detecting the components of the mixture. Penalized likelihood maximization delivers the estimated fixed effects and the smoothing coefficients of the random effects distribution. A similar approach was developed for survival models with left-, right and interval censoring: Komárek *et al.* (2005) developed an accelerated failure time (AFT) model with a smooth error distribution. Results show that this model nicely reveals the mixture structure of the error distribution, if present. This approach is now being extended to the random effects AFT model (frailty AFT model). Bogaerts and Lesaffre (2004) have developed the approach for fitting a bivariate survival model. A Bayesian model with normal random effects and an error structure being a classical (unpenalized) normal mixture with unknown number of mixture components was developed (Komarek and Lesaffre, 2004). An alternative to the classical mixture with unknown number of components is a penalized mixture with higher number of fixed components used already in the approach of Komárek *et al.* (2005).

3. **Classification techniques other than mixtures**

   Work in this section has focused on the one hand on one-mode clustering methods (i.e., methods that yield a clustering of a single set of elements only) and on the other hand on two- and three-mode clustering methods (i.e., methods that yield *simultaneous* clusterings of several sets of elements as implied by the data).
   With regard to *one-mode clustering methods*:

(a) RWTH-Aachen has investigated and proposed several methods for the classification of 'symbolic data' where classical data points are replaced by data rectangles in $I\!R^p$. In particular, they have developed and implemented three methods for constructing Kohonen maps for such data. See Bock (2003b) and De Carvalho, Brito and Bock (2004) for some extension of classical k-means-type clustering strategies to the case of symbolic data, including rescaling and standardization problems. The problem of defining, and estimating, a suitable mean value for random sets or rectangles in $I\!R^p$ has been investigated by Nordhoff (2003, 2005).

(b) The work of Hans Bock on proximity measures to start from in clustering is recognized with an article in the Encyclopedia Statistics in Behavioral Science (Bock (2004)).

(c) The KUL1 group studied a one-mode additive clustering model for two-way two-mode data. The mathematical characteristics of this model (including the special case of a model with nested clusters) have been investigated and a novel algorithm to estimate it has been developed (Depril and Van Mechelen (2005)).

(d) The KUL1 group developed a conjunctive model for picky any/n data that represents choice behavior in terms of clusters of choice objects in a low dimensional space (defined by a set of ordinal variables with a prespecified number of categories) (Leenen and Van Mechelen (2004)).

With regard to *two- and three-mode clustering methods*:

(a) First of all, a comprehensive taxonomy of simultaneous two-mode clustering methods has been developed by the Leuven and Aachen teams, implying a set of novel structuring principles for this fairly heterogeneous set of methods that are scattered around in the literature (Van Mechelen, Bock and De Boeck (2004, 2005)).

(b) The KUL-1 group investigated simultaneous partitioning approaches for multi-mode data with the aim of data reconstruction. In particular, for the three-mode case, a novel algorithm has been developed, and its performance has been evaluated and compared with that of two alternative algorithms in a comprehensive simulation study (Schepers, Van Mechelen and Ceulemans (2004)).

(c) The design and mathematical investigation of a convexity-based clustering criterion for analyzing heterogeneity in data sets is an important topic of research in the Aachen group. This kind of clustering is directly suited to the simultaneous partitioning of the rows and columns of a contingency table such that the resulting row and column partitions are maximally related to each other. The results of a theoretical study, a description of algorithms, and applications can be found in Bock (2003a). Clustering algorithms were derived which use the concept of 'maximum-support-plane partitions' as analogues to 'minimum-distance partitions' in the classical theory.

(d) The KUL-1 group has extensively investigated novel extensions of the hierarchical classes (HICLAS) family, which is a comprehensive family of simultaneous overlapping clustering models for multimode data. The research in this area has proceeded along six different lines:

- First, a family of three-way hierarchical classes models has been developed that parallels the family of three-way PCA models (Ceulemans, Van Mechelen and Leenen, 2003); uniqueness properties of these models (as well as of a generalization to N-way N-mode models) have been investigated by Ceulemans and Van Mechelen (2003b). In addition, various constrained versions of these models have been developed, the constraints reflecting various kinds of substantive considerations. See Ceulemans, Van Mechelen and Kuppens (2004). Most recent contributions include the development of novel three-mode HICLAS models that do not reduce all three modes of the data (Ceulemans and Van Mechelen (2004b)), and three-way models that represent heterogeneity in sequential, chain-type processes.
- Second, the two-way hierarchical classes model for binary data (as well as the associated algorithm) have been extended to rating data by Ceulemans and Van Mechelen (2003a) and Van Mechelen, Lombardi and Ceulemans (2003). This novel extension of the family implies a considerable enlargement of its scope.
- Third, hierarchical classes analogues of other models than PCA have been developed, for example, of the discriminant analysis model in Lombardi, Ceulemans and Van Mechelen (2003) and Lombardi and Van Mechelen (2005).
- Fourth, new algorithmic variants (based on new types of starting configurations and simulated annealing-type algorithms) have been developed to deal with enduring local minima problems; those algorithms have been evaluated in extensive simulation studies (Ceulemans and Van Mechelen (2004a)).
- Fifth, we have been working on the addition of confidence information to point estimates of parameter vectors through nonparametric bootstrap methods and through MCMC estimation procedures of minimal stochastic extensions of deterministic HICLAS models (Leenen, Van Mechelen, Gelman and De Knop (2004)); one may note that the latter approach also paves the way for novel types of model checking.
- Sixth, new tools for model selection (including the number of clusters issue) have been developed, especially with regard to the modeling of three-mode data; more in particular, a novel convex hull based automated model selection procedure has been developed for three-mode HICLAS models, which appeared to perform excellently in simulation studies (Ceulemans and Van Mechelen (2004c)); the latter finding has further be proven to generalize to the additive real-valued setting of multiway component models (Ceulemans and Kiers (2005)).

4. **Methodological problems**

The methodological problems mentioned in the proposal concern four issues:

- Methods for detecting heterogeneity were investigated and compared for logistic regression models (Balazs, Hidegkuti and De Boeck (2004)).
- The identifiability of finite mixture models has been investigated in the context of several of the studies we mentioned earlier in this report (Berkhof *et al.*, 2003; Rijmen and De Boeck, 2004; Rijmen *et al.*, 2004).

- Inference on the number of mixture components was studied in Berkhof *et al.* (2003), and Bouezmarni *et al.* (2005).
- The choice of priors is an aspect in several publications on the Bayesian approach (Gelman *et al.* (2005); Meulders *et al.* (2004)).

Scientific input from each partner

- **UCL**: Input from the UCL was used to formulate a kernel estimation method for random effect distributions in item response models. The method will also allow us to estimate the number of mixture components of such a distribution.
- **KUL-1**: Item response models have been framed as generalized linear and nonlinear mixed models, an elaboration of the framework and its extension to new models, including models with mixture distributions. This framework was an important basis for substantive contributions to psychology. Another important input was the development of a broad range of novel simultaneous clustering methods for multiway data, and a comprehensive structured overview of simultaneous clustering methods which functions as a basis for further developments in clustering (three-way and higher).
- **KUL-2**: The input for the KUL-2 relates to mixture modeling (a SAS macro for the estimation of mixture item response models, model checking in models with missing or latent data; mixture components for smoothing), Bayesian approaches, and generalized linear mixed models in general.
- **LUC**: The input from the LUC concerns crossed random effects and missing data strategies (sensitivity analysis, local influence).
- **RWTH**: This partner focused on the analysis of symbolic (interval) data, on clustering algorithms for convexity-based clustering criteria, and on partitioning methods for two-way data tables.

2.6 Work package 6: Incompleteness and latent variables

Main achievements

The research team has focused, to a large extent, on fundamental methods for incomplete data, modelling incomplete data in practice, and incomplete data in clinical trials. There has been a large activity in the area of sensitivity analysis for incomplete data. On these topics, a number of papers have appeared

(1) from the LUC research group (Jansen, Molenberghs, Aerts, Thijs and Van Steen, 2003),

(2) in collaboration with partners from KUL-2 (Thijs, Molenberghs, Michiels, Verbeke and Curran (2002); Molenberghs, Renard and Verbeke (2002); Curran, Molenberghs, Thijs and Verbeke (2003), Molenberghs, Thijs, Kenward and Verbeke (2003); Molenberghs, Burzykowski, Alonso and Buyse (2004)),

(3) in collaboration with international partners. This includes the Harvard School of Public Health (Molenberghs, Williams and Lipsitz, 2002; Lipsitz, Molenberghs, Fitzmaurice and Ibrahim, 2004), the London School of Hygiene and Epidemiology (Kenward, Molenberghs and Thijs, 2002; Molenberghs, Thijs, Michiels, Verbeke and Kenward, 2004; Molenberghs, Thijs, Jansen *et al.*, 2004), Texas A&M University (Aerts, Claeskens, Hens and Molenberghs, 2002; Mallinckrodt, Carroll *et al.*, 2003; Mallinckrodt, Kaiser, Watkin, Molenberghs and Carroll, 2004; Mallinckrodt, Scott Clark, Carroll and Molenberghs, 2003; Mallinckrodt, Watkin, Molenberghs and Carroll, 2004; Molenberghs, Thijs, Jansen *et al.*, 2004), Janssen Pharmaceutical Research and Development (Michiels, Molenberghs, Bijnens, Vangeneugden and Thijs, 2002), and Eli Lilly & Company (Molenberghs, Renard and Verbeke, 2002; Mallinckrodt, Carroll *et al.*, 2003; Mallinckrodt, Kaiser *et al.*, 2004; Mallinckrodt, Scott Clark *et al.*, 2003; Mallinckrodt, Watkin *et al.*, 2004; Molenberghs, Thijs, Jansen *et al.*, 2004; Dmitrienko, Molenberghs, Christy Chuang-Stein and Offen, 2005).

Several of the aforementioned papers are devoted to estimation methods for incomplete data where missingness is missing not at random. For example, Lipsitz *et al.* (2004) and Ibrahim (2004) use a so-called protective estimator, where the missingness mechanism need not be addressed explicitly, yet valid estimators can be obtained. The work done jointly with the London School (Michael G. Kenward), Eli Lilly & Company (Craig Mallinckrodt and colleagues), and Texas A&M University (Raymond J. Carroll), is dedicated to a large extent to properly deal with incomplete longitudinal clinical trial data. This includes Molenberghs, Thijs, Michiels *et al.* (2004); Molenberghs, Thijs, Jansen *et al.* (2004); Molenberghs *et al.* (2003); Mallinckrodt, Carroll *et al.* (2003); Mallinckrodt, Kaiser *et al.* (2004); Mallinckrodt, Scott Clark *et al.* (2003); Mallinckrodt, Watkin *et al.* (2004); Jansen *et al.* (2003); Dmitrienko *et al.* (2005).

Paul De Boeck (**WP5**), Geert Verbeke (**WP4**), Geert Molenberghs (WP6) (Molenberghs and Verbeke, 2004; Tuerlinckx *et al.*, 2004), and colleagues within their teams, have contributed to an edited Springer-Verlag volume on the use of generalized linear mixed models in psychometric applications and testing theory. Editors Paul De Boeck (**WP5**) and Mark Wilson (University of California at Berkeley) (De Boeck and Wilson (2004)) have been very successful with this initiative, since the book was the best selling Springer text at the International Meeting of the Psychometric Society. The project has led to intense research collaborations between the teams of KUL-1, KUL-2, and LUC in the interconnected areas covered by **WP4**, **WP5**, and WP6. We refer to the report on packages **WP4** and **WP5** for additional references. We further refer to the two-day postgraduate course that took place in Leuven, 2003, on statistical optimization theory. The course was taught by KUL-1, KUL-2, and LUC members and was taken by a number of network members. Moreover, it helped disseminate the strengths and standing of the network, since a large number of international colleagues participated in the course.

Geert Molenberghs (WP6) and Geert Verbeke (**WP4**) wrote a Springer monograph on discrete longitudinal data (Molenberghs and Verbeke (2005)). It appears in Summer 2005 and brings together research in the areas of incomplete data, latent variables, longitudinal data, and mixed models. As such, it combines expertise and work from **WP4**, **WP5**, and WP6. The text, totalling approximately 700 pages, complements the Springer book by Verbeke and Molenberghs (2000). While the earlier text deals with continuous data, the second one is devoted to non-Gaussian data.

Based on the work laid out in the text, both authors have undertaken a number of scientific and dissemination activities. This includes invited talks and tutorials at conferences, as well as short courses taught around the world. For more details see 4.2.2 in this report. We also refer, apart from the joint articles in refereed journals mentioned above, to a number of contributions to proceedings volumes.

At LUC, an active research group on surrogate marker evaluation (Burzykowski and Molenberghs) is based, with participation of colleagues from various other groups. The research team published several papers (Molenberghs, Buyse *et al.* (2002)). Pharmaceutical companies and contract research organizations with which methodological papers have been jointly published include Virco-Tibotec (Alonso, Geys, Molenberghs and Vangeneugden, 2002; Vangeneugden, Laenen, Geys, Renard and Molenberghs, 2004), Eli Lilly (Renard, Geys, Molenberghs, Burzykowski and Buyse, 2002; Renard, Molenberghs and Geys, 2004; Claeskens, Aerts and Molenberghs, 2003; Vangeneugden *et al.*, 2004; Tibaldi, Torres Barbosa and Molenberghs, 2004; Alonso, Geys, Molenberghs and Kenward, 2004),(Tibaldi *et al.*, 2003), (Tibaldi, Molenberghs, Burzykowski and Geys, 2004), Janssen Pharmaceutical Research and Development (Renard *et al.*, 2004; Alonso, Geys, Molenberghs and Kenward, 2003; Alonso, Geys *et al.*, 2004; Alonso, Molenberghs *et al.*, 2004), (Tibaldi, Molenberghs *et al.*, 2004), and the International Drug Development Institute (Tibaldi *et al.*, 2003),Molenberghs, Buyse and Burzykowski (2004), Burzykowski, Molenberghs, and Buyse (2004)). Note that the paper by Tibaldi *et al.* (2003) included colleagues from the SAS Insitute (North Carolina) and the Erasmus Universiteit Rotterdam among its authorship. Alonso, Molenberghs *et al.* (2004) is co-authored by Michael G. Kenward from the London School of Hygiene and Tropical Medicine.

(Burzykowski, Molenberghs and Buyse, 2005) published a Springer book on the topic in March 2005. The book was the best-selling Springer text at the 2005 Spring Meeting of the Eastern North American Region of the International Biometric Society (Austin, Texas, March 2005). It is worth mentioning that a number of renowned statisticians contributed to the book. This includes Mitch Gail (US National Cancer Institute), Michael Hughes (Harvard School of Public Health), Aloka Chakravarty (Food and Drug Administration), Ross Prentice (University of Washington, Seattle), and Laurence Freedman (Bar Ilan University, Israel). Through the work laid out in this text, the research group has had a major impact on the research activities in this field, which was started around 1989 by Ross Prentice (University of Washington, Seattle). The work has been disseminated by invited talks, research visits, and short courses. The team collaborates with researchers from most major pharmaceutical companies, and has contacts with colleagues specializing in this and related topics at the National Institutes of Health (including the National Cancer Institute), and the Food and Drug Administration. The team has published a variety of papers, that can be found in the list of references.

LUC and KUL-2 collaborated on several PhD projects. We will briefly review them. Ellen Andries (LUC, Institute for Material Physics) and grantee of the IWT, defended a thesis on the use of mixed and mixture models in the context of material-physical reliability studies. Geert Molenberghs was thesis advisor. Geert Verbeke (**WP4**) and Geert Molenberghs (WP6) collaborate with Arnost Komárek (KUL-2) on implementation of mixed and mixture models in standard statistical software, such as SAS. Ivy Jansen (LUC, supervisor Geert Molenberghs) and Niel Hens

(LUC, supervisor Marc Aerts) defend their thesis in June 2005 on incomplete data and sensitivity analysis. There has been a strong collaboration with KUL-2.

Verbeke and Molenberghs (2003b) and Molenberghs and Verbeke (2004) indicate how complex models, including but not restricted to mixed models, should be examined for their meaningfulness. Especially generalized linear and non-linear mixed models are prone to a number of subtle complexities that may easily be overlooked by the practitioner, and a fundamental reflection is therefore at hand.

In the context of hierarchical binary data, pseudo-likelihood ideas based on a probit model formulation are used by Renard *et al.* (2004), a collaboration between LUC, Eli Lilly & Company, and Johnson & Johnson Pharmaceutical Research and Development.

Reliability estimation is typically done in the context of psychometric or sociological studies. However, it is also of relevance in clinical and epidemiological studies, e.g., in the context of psychiatric clinical trials, quality of life assessment, etc. To allow using clinical trial data for this purpose and when interested in extension to generalizability theory, Vangeneugden, Laenen, Geys, Renard, and Molenberghs have collaborated on several papers and proceedings contributions, including Alonso *et al.* (2002) and Vangeneugden *et al.* (2004). Related to this, Garcia-Zattera, Jara, and Lesaffre (KUL-2) explore the notion of conditional independence in a modelling context by comparing the association structure of a multivariate binary response vector on the latent and observed scale.

Tsonaka, Verbeke, and Lesaffre (KUL-2) investigate a recently published approach based on a latent class model (discrete mixture model) for modelling repeated measurements data with intermittent missing data. Rizopoulos, Verbeke, and Lesaffre (KUL-2) examine models for the analysis of repeated measures data for which the timing that the measurements are taken is informative to the disease status of the subject.

A number of developments take place in the fields of censoring (see **WP3**) and misclassification, that are intimately linked with incomplete data. The approaches that Komárek and Lesaffre have developed for accelerated failure time models allow interval censored data. Cecere and Lesaffre explore Bayesian methods for modelling the covariance matrix of multivariate interval-censored data. Mwalili and Lesaffre explore frequentist and Bayesian methods for the analysis of misclassified responses and/or covariates in regression models.

3 The networking

3.1 Major joint activities

The scientific collaborations between various groups of the network were organized at six different levels:

- **Workshops.** Three workshops (out of a total of five) took place until now. They play a key role in the organization of the project and join together all members of the IAP network.
- **Meetings.** A set of meetings was organized related to the topics of the network. These meetings were attended by researchers of the IAP network but were also open to other researchers.
- **Research seminars.** In the institutional seminar series of each group of the network, we organized seminars on topics of direct interest for the research network. In addition, a number of seminars have been organized by the network itself.
- **Working groups.** Their goal is to facilitate the interaction between a limited number of members from the network on a specific topic. They often lead to specific collaborations between members of the network.
- **Training.** Intensive courses on various topics of the network were organized by the seven partners. These courses were taught by members of the network or external experts. Special attention was paid to encourage doctoral and post-doctoral students to attend these courses. However the audience was not limited to the members of the network and very often external students attended these intensive courses too.
- **Mobility of researchers.** Some exchanges of researchers were organized within the network.

These six levels of joint scientific activities are now described in detail. Overall, from 2002 on, the number of scientific collaborations within the network growed continuously, as can be seen from the list of joint activities below.

3.1.1 Workshops

The five main workshops are organized by different partners of the network and play an essential role in the organization of the network. The scheduling over time links up with the advancement of the whole project.

A **starting scientific meeting** took place on February 22, 2002, at the Institute of Statistics at the UCL. This one-day meeting consisted of presentations, one for each WP. Each presentation aimed at explaining to all members of the network the main issues that will be studied in each package, as well as the links with items in other WP. About 65 people participated at this meeting.

The **first workshop** took place on May 21-24, 2002 at UCL. The first part (May 21-23, 2002) consisted of an international workshop on **"Statistical Modelling and Inference for Complex Data Structures"**, organized by UCL in collaboration with LUC (Noël Veraverbeke) and UJF

(A. Antoniadis). [1] The aim of the second part of the workshop (May 24, 2002) was to communicate to all partners the scientific goals, main applications and substantive problems that are focused on in the distinct work packages. We organized six consecutive panel discussions. About 55 people participated in a lifely and fruitful discussion.

With the beginning of Phase 1 was organized the **second workshop** on "Statistical Modelling for Complex Data". It took place at the Limburgs Universitair Centrum, Diepenbeek, from March 31 till April 2, 2003, and was organized by the LUC, in collaboration with colleagues from the KUL and the UCL. There were tutorial lectures, invited presentations and contributed papers (oral/poster) on functional estimation, mixed models, classification and mixture models, incompleteness and latent variables. The tutorial lectures were meant to give a good introduction and review to a topic, whereas the invited lectures were focused on more specific research topics. The workshop was attended by many members of the network, among others.

The third and fourth workshops were scheduled during Phase 2. The **third workshop** was organized at ULB as a set of two successive events. A workshop took place on May, 12-13, 2005[2]. The general theme was "asymptotic statistics" and the keynote speaker was Steve Portnoy (University of Illinois). This workshop was initially scheduled in 2004 but had to be delayed due to the constraints of the keynote speaker, who received the international Francqui Chair in 2005. This workshop was followed on May 13-14 by the third edition of the Brussels-Prague Seminar in Mathematical Statistics [3], where distinguished statisticians from Charles University in Prague and young Belgian members of the IAP gave talks on various aspects of their research. Many people attended both events.

The **fourth workshop** will be organized by KUL-1 in Leuven on September, 30, 2005. The theme is "how to deal with heterogeneity", which appears to be one of the meta-modeling aspects of the scientific project. In this regard, we want to use a broad concept of heterogeneity that covers questions from several work packages, for instance, nonstationarity in time series analysis (WP2), random effects as included in mixed and survival (frailty) models (WP3/4), as well as the presence of different subpopulations as assumed in mixture models (WP5). During this workshop several contributions resulting from collaboration between different universities of the network will be presented in relation to this central question of the IAP.

In 2006 the coordinator at UCL will be the host for a **fifth workshop**, during which the achievements of the past years will be summarized.

A specific report for each workshop may be found on the web page (see "Archives").

3.1.2 Meetings

Apart from the above workshops, several meetings were organized in relation to the IAP network.

From the year 2003 on, an annual meeting, the **Young Researchers Day** (YRD), is organized by the PhD students of the Institute of Statistics, UCL, who invite (among others) young speakers from all partner universities. The YRD's are attended by researchers of the whole network. The 1st YRD was organized on 19th May 2003 on the two topics "Nonparametric Approaches in Survival

[1] Program and details: `http://www.stat.ucl.ac.be/IAP/archive.html`
[2] Program and details: `http://www.stat.ucl.ac.be/IAP/download/Francquiws.pdf`
[3] Program and details: `http://www.stat.ucl.ac.be/IAP/download/3praguebrussels2.pdf`

Analysis" and "Synchronisation and Shape Analysis in Biostatistics". 46 participants took part in this meeting (including 23 doctoral or post-doctoral students). The 2nd YRD took place on 30th April 2004 on the topic "Many explanatory variables? A challenge for regression modelling" and was followed by 86 attendees (including 55 doctoral or post-doctoral students).[4] The 3rd YRD is foreseen for 2nd December 2005 on the topic "Bayesian statistics and applications".

Another half-day meeting took place on 30th November 2004 in Leuven and focussed on **"Frailty models"**. It was organized by the KUL-2 and LUC. Four researchers (two from inside and two from outside the network) have given invited presentations at this meeting.

On November 15-17, 2005, members of the KUL-2, UCL and LUC teams organize a three-day meeting around the topic of **interval censored data**. This meeting will consist of two parts: a short course of two days followed by a day of research presentations.

Many Belgian members of the network also participate to the **meetings of the Belgian Statistical Society** (BSS), since most of the members of the network are also member of this Society. The BSS organizes an annual meeting where the research results of the IAP-network are presented by our researchers.[5]

3.1.3 Research seminars

Each of the participating partners organizes on a regular basis statistics seminars at their universities. Announcements of these seminars are sent out to most Belgian statisticians, including these participating in the network.

We took the opportunity of these seminars to facilitate the transmission of our research results within the network. In particular, each group invited on a regular basis members of the partner teams to present their research. A list of these seminars is presented below.

Moreover, apart from the regular statistics seminars, several other seminars have been organized under the IAP-statistics network. These are included in the list below and indicated with the sign (*).

- March 2002 at ULB: M. Denuit (UCL), "Positive dependence in actuarial models".
- March 2002 at UCL: T. Burzykowski (LUC), "Validation of surrogate endpoints from multiple randomized clinical trials".
- April 2002 at UCL: M. Hallin (ULB), "Semiparametric efficiency, distribution-freeness and invariance".
- April 2002 at KUL-1: B. Spiessens (KUL-2), "Estimation in nonlinear and generalized linear mixed models".
- May 7, 2002 at KUL-1: T. Harkanen (KUL-2), "Bayesian survival analysis".
- October 8, 2002 at KUL-1: C. Fairon (UCL), "Automatic item text generation in educational measurement".
- (*) October 23, 2002 at LUC: D. Belomestny (University of Bonn, Germany), "Statistical inferences based on transformed data: identifiability aspects".

[4] Program and list of participants: `http://www.stat.ucl.ac.be/YRD`

[5] More informations about the BSS and the annual meeting may be found at `http://www.sbs-bvs.be`

- October 29, 2002 at KUL-1: A. Komarek (KUL-2), “Bayesian modelling in dentistry involving doubly interval censored data”.
- November 12, 2002 at KUL-1: S. Mwalili (KUL-2), “Correcting for inter-observer effects in a geographical oral health study”.
- (*) November 27, 2002 at UCL: F. Enikeeva (Moscow State University), “Asymptotically Minimax Estimation in the Wicksell Problem”.
- November 2002 at UCL: L. Bruckers (LUC), “Persistent disturbing behaviour”.
- March 17, 2003 at KUL : R. Braekers (LUC), “Non-parametric regression in fixed-design, under dependent censoring”.
- (*) May 7, 2003 at LUC: Arnošt Komárek, (Katholieke Universiteit Leuven), “Accelerated failure times model for arbitrarily censored data with smoothed error distribution”.
- (*) May 9, 2003 at UCL: special afternoon on “Modelling and Inference for frailties”. Speakers were Prof Paul Janssen (LUC Diepenbeek), “The shared frailty model”; and Prof Yi Li (Harvard University, USA), “Inference on clustered survival data using imputed frailties”.
- (*) May 14, 2003 at LUC: G. Molenberghs (LUC Diepenbeek), on “The use of score tests for inference on variance components”.
- (*) June 18, 2003 at LUC: K. Bogaerts (KUL), “A smooth estimate of the bivariate survival density in the presence of left, right and interval censored data”.
- October 29, 2003 at ULB: I. Van Keilegom (UCL), “Estimation of semiparametric models when the criterion function is not smooth”.
- November 14, 2003 at ULB: I. Van Keilegom (UCL), “Empirical likelihood in some non-standard settings”.
- December 5, 2003 at UCL: D. Paindaveine (ULB), “Non parametric procedures for testing elliptical randomness”.
- February 13, 2004 at UCL: T. Bruss (ULB), “The odds-theorem of optimal stopping and its descendants”.
- March 2004 at ULB: S. Van Bellegem (UCL), “Adaptive estimation in locally stationary wavelet processes”.
- March 26, 2004 at UCL: F. Tibaldi (LUC), “Pseudo-likelihood estimation and inferences for a marginal multivariate survival model”.
- April 2004 at ULB: A. Antoniadis (UJF), “Wavelet kernel penalized estimation for random design regression”.
- October 1, 2004 at UCL: M. Aerts (LUC), “Model selection based on incomplete and nonrandom samples”.
- (*) October 29, 2004 at UCL: S.-O. Jeong (UCL), “Linearly interpolated FDH estimator for non-convex frontiers”.
- December 2004 at ULB: G. Claeskens (UCL), “Focussed model selection for the Cox regression model”.
- (*) December 17, 2004, UCL: S. Van Bellegem (UCL), “Semiparametric estimation by model selection for locally stationary processes”.

- (*) December 17, 2004 at UCL: T. Snijders (University of Groningen, The Netherlands), "Frequentist MCMC estimation methods for multilevel logistic regression".
- February 2005 at ULB: L. Simar (UCL), "Nonparametric efficiency analysis: a multivariate conditional quantile approach".
- February 15, 2005 at KUL-1: S. Fieuws (KUL-2), "Random-effects models with multivariate repeated responses"
- February 18, 2005 at LUC: I. Van Keilegom (UCL), "Empirical likelihood tests for two-sample problems via nonparametric density estimation".
- February 25, 2005 at ULB: N. Veraverbeke (LUC), "Some recent generalizations of the Kaplan-Meier estimator"
- March 1, 2005 at KUL-1: S. Mwalili (KUL-2), "Zero-inflated negative binomial regression model with correction for misclassification"
- May 2005 at ULB: L. Simar (UCL), "Nonparametric stochastic frontiers: a local maximum likelihook approach".
- July 5, 2005 at RWTH: I. Van Keilegom (UCL), "Estimation for semiparametric statistical models: backfitting versus profiling in general criterion functions".

3.1.4 Working groups

The interaction between researchers of the network is facilitated through the working groups. They allow an intensive discussion on specific topics between a limited number of researchers. Below we mention the most significant working groups.

- *Frailty Models and Inference.* A very intensive collaboration started in 2002 between several members of the network on modelling heterogeneity via frailty. The working group concentrates on research issues under Work Package 3. The coordinating team is here the LUC-team (headed by P. Janssen) and participating teams are KUL-2 (E. Lesaffre, ...) and UCL (P. Lambert). Since 2002, the group met in a regular way to discuss research progress and for a series of seminars mainly to introduce relevant methodology to new PhD students.

  Participants in 2003 were: T. Burzykowski (LUC), J. Cortiñas (LUC), L. Duchateau (UGent), P. Janssen (LUC), C. Legrand (EORTC), G. Massonnet (LUC), R. Nguti (LUC-UON), R. Sylvester (EORTC), and (from time to time) V. Ducrocq (INRA). Participants in 2004 were Burzykowski (LUC), Cortiñas (LUC), Duchateau (RUGhent), Janssen (LUC), Legrand (EORTC), Massonnet (LUC), Sylvester (EORTC) and for some of the meetings Ampe (RUGhent), Goethals (RUGhent), Ducrocq (INRA), Lesaffre (KUL-2), Komárek (KUL-2) and Lambert (UCL).

- *Regularization methods.* Regularization methods are studied by different partners of the group, in particular in the context of ill-posed inverse problems. The problems appear in several aspects of WP 1 and WP 2. The involved researchers include A. Antoniadis (UJF), J. Bigot (UJF/UCL/Toulouse), C. De Mol (ULB), I. Gijbels (UCL/KUL), M. Nikolova (ENST Paris), S. Van Bellegem (UCL).

- *Simultaneous two-mode clustering methods.* The KUL-1 team (P. De Boeck, I. Van Mechelen) and the RWTH-team (H.-H. Bock) worked intensively on "two-way clustering". This collaboration lead to a set of joint articles in journals and encyclopedia. The working group started in 2002, meets between about two and five times a year, and is still active. A current topic of joint research is the modeling of individual differences heterogeneity in terms of person by situation interactions through clustering with a convexity-based clustering criterion.

- *Estimating mixtures of random effects, item-response modelling and SAS-macro.* The teams of KUL-1 and KUL-2 have been collaborating on estimating mixtures of random effects. The KUL-2 team developed a SAS-macro which has been applied to item-response models encountered mainly by the KUL-1 team.

- *Generalized linear mixed models in psychometric applications and testing theory.* An intensive collaboration between the LUC-team and the teams from the KUL-1 and KUL-2 on the use of generalized linear mixed models in psychometric applications and testing theory is going on. An edited Springer book with authors/editors from the various teams was published in 2004.

- *Discrete repeated measures.* Members from the LUC-team (Geert Molenberghs) and the KUL-2 team (Geert Verbeke) are continuing their collaboration on linear mixed models for longitudinal data. A Springer book on discrete repeated measures was published in 2005.

- *Use of mixed and mixture models in reliability studies.* Geert Verbeke from KUL-2 and Geert Molenberghs from LUC collaborated on a doctoral research project of Ellen Andries (LUC, Institute for Material Physics) on the use of mixed and mixture models in the context of material-physical reliability studies. This working group stopped one year ago due to the PhD defense of E. Andries.

- *Implementation of mixed and mixture models in standard statistical software, such as SAS.* Members from the KUL-2 team (Geert Verbeke and Armost Komarek) and from the LUC-team (Geert Molenberghs) are jointly working on implementation of mixed and mixture models in standard statistical software, such as SAS.

- *Goodness-of-fit problems.* A growing number of researchers from several teams are working on goodness-of-fit problems for the shape of a regression function (Aerts (LUC), G. Claeskens (former member of UCL, now at KUL) and I. Van Keilegom (UCL)).

- *Interval censored data.* Researchers from KUL-2 (E. Lesaffre and some of his students) and from UCL (I. Van Keilegom) started collaboration on interval censored data problems. Expertise on theoretical issues (UCL) and on applied issues (KUL-2) are here nicely combined and lead to better insight from both sights. A three-day meeting on this topic will be organized jointly by both research groups and by LUC on November 15-17, 2005.

- *Surrogate marker evaluation.* At LUC, an active research group on surrogate marker evaluation (T. Burzykowski and G. Molenberghs) is based, with participation of colleagues from various other groups, including pharmaceutical companies (Vangeneugden, Virco-Tibotec;

Tibaldi and Renard, Eli Lilly) and contract organizations (Buyse International Drug Development Institute). The team published a Springer book on the topic in 2005. The group started 10 years ago and intensified considerably (more contacts, many of which more international) thanks to the network.

- *Longitudinal and incomplete data.* There is an active research group on incomplete data and sensitivity analysis at LUC (Molenberghs and Aerts) with collaboration from KUL-2 (Verbeke), and participation from pharmaceutical companies (Mallinckrodt, Eli Lilly US), Texas A&M University (Carroll), and the London School of Hygiene and Tropical Medicine (Kenward). The working group has had an impact on both theory and practice in the field of incomplete data. It started in 1998 and has considerably intensified thanks to the network.

- *Multivariate time series analysis.* Several informal and mutually beneficial discussion meetings have been organized beween the ULB and UCL teams around methodological questions (static versus dynamic factor models, SLEX) and practical problems in different fields (EEG, macroeconomic panels).

- *Database sharing in clinical trials.* A database in clinical trials is shared by LUC, KUL-2 and UCL. Researchers from these three universities are analysing common data. In collaboration with the European Organisation for Research and Treatment of Cancer (EORTC, Brussels) frailty models have been used to study the validity of prognostic indices and to understand heterogeneity in outcome between participating centres in multicentre studies. To model the presence of heterogeneity in multivariate survival data different approaches have been proposed in the statistical literature. Frailty models are an approach that adds a random effect to the Cox regression model. Other approaches include accelerated failure time models for correlated survival models (Lesaffre and Komarek (KUL-2)) and the penalized Poisson regression approach (Lambert (UCL)). An important question is to study whether these three different methodological tools lead to the same conclusions when applied to the same data set. To answer this question they are analyzing the data of an EORTC multicentre trial; this will lead to a comparison of the different models that are used to do statistical inference on heterogeneity.

- *Nonparametric estimation of random effects in mixed models by means of kernel methods.* Joint work by Taoufik Bouezmarni (UCL, KUL-1) and Frank Rijmen (KUL-1) that started early 2005; group that is still active (informal meetings once every two weeks)

- *Nonstationary time series of longitudinal multilevel emotion data.* Collaboration between UCL, ULB and KUL-1, coordinated by Sébastien Van Bellegem (UCL) and Kristof Vansteelandt (KUL-1); started 2005, meets about once a month, and is still active.

- *Time pressure item response models (involving nonrandom missingness, sensitivity with regard to misspecifications of the missingness mechanism, and heterogeneity with regard to the start and speed of response degrading).* Working group that started in 2005, meets once every two weeks and is still active; partners include Paul De Boeck and Yuri Goegebeur (KUL-1), Geert Molenberghs (LUC) and Geert Verbeke (KUL-2).

3.1.5 Training

Several short (intensive) courses have been organized within the framework of the IAP-statistics network. These courses were intended for all members of the network, and in particular (but not exclusively) for the PhD-students. The announcements were each time sent out to all members and posted on the web site. No (or reduced) registration fees were required for IAP-members.

- A short course on "Goodness-of-fit tests and survival analysis", given by Professor Ricardo Cao (La Coruña, Spain) has been offered to IAP-members. This course took place in October 2002.
- Professor Alois Kneip, University of Mainz, Germany, gave a short course on "Functional data analysis with applications in biometrics and econometrics"; course of 7.5 hours, in March-April 2003, at the Institute of Statistics, UCL;
- Professor Joel Horowitz, Northwestern University, Illinois, USA, presented a short course on "Bootstrap methods for cross-sectional and time series data"; course of 7.5 hours in May 2003, at the Institute of Statistics, UCL;
- Professor Petros Dellaportas, Athens University of Economics and Business, Greece and Imperial College, London, UK, gave an intensive course of two days on "Advanced Use of MCMC methods", on September 25 and 26, 2003, at the Katholieke Universiteit Leuven, Center for Biostatistics.
- Two lectures by Professor Ray Carroll, Deparment of Statistics, Texas A&M University, USA. A first lecture on "Nonparametric and semiparametric regression for longitudinal and clustered data", on September 24, 2003, at the Institute of Statistics, UCL.
  A second lecture on "Functional data analysis for colon carcinogenesis experiments", on October 1, 2003, at the Institute of Statistics, UCL.
- Three lectures on time series topics by Professor Jiti Gao, University of Western Australia, Perth, Australia. All lectures took place at the Institute of Statistics, UCL.
  A first lecture "Recent Developments in Semiparametric Time Series Regression: A Personal Overview", on October 2, 2003.
  A second lecture on "Simultaneous Model Specification Testing in Nonparametric and Semiparametric Time Series Econometrics", on October 8, 2003.
  A third lecture on "Nonparametric Estimation and Comparisons in Stochastic Short-Term Interest Rate Models", on October 9, 2003.
- A short course by Professors Geert Molenberghs (LUC) , Francis Tuerlinckx (KUL-1) and Geert Verbeke (KUL-2) (2003) on "Numerical Techniques for Statisticians". This intensive course was organized jointly by the "Interuniversity Graduate School of Psychometrics and Sociometrics" (organizers: KUL-1 and LUC). The course took place on November 13 and 14, 2003, at the Katholieke Universiteit Leuven.
- A short course by Professor Helmut Kuechenhoff, University of Munich, Germany on "Measurement error in epidemiologic studies", on November 17 and 18, 2003, at the Katholieke Universiteit Leuven, Center for Biostatistics.
- An intensive course of 7.5 hours on "The power of penalties" given by Professor Paul Eilers (Leiden university) in December 2003 and February 2004 at UCL.
- An intensive course of 7.5 hours on 'Frontier estimation and the use of bootstrap methods' given by Professor Paul Wilson (Texas University, Austin, USA) in February-March 2004 at UCL.
- An intensive course of 7.5 hours on 'Design of experiments' by Professor Holger Dette (University of Bochum, Germany) in February-March 2004 at UCL.

- An intensive course of 15 hours on 'Smoothing techniques and nonparametric testing' given by Professor Gerda Claeskens (UCL, 'terugkeermandaat'/'mandat de retour' from the DWTC/ SSTC) in Spring 2004 at UCL.
- An intensive course of 7.5 hours on 'Advanced bootstrap methods' by Professor Peter Hall (Australian National University) in November-December 2004 at UCL.
- Series of lectures (11 lectures of 2 hours) given by Steve Portnoy (University of Illinois, USA), receiver of the 'Chaire Francqui interuniversitaire au titre étranger' (shared between ULB and KUL) in Spring 2005 at ULB and KUL.
- An intensive course of 7.5 hours on 'Statistical denoising of images, with applications in astronomy' by Véronique Delouille (Royal Observatory of Belgium) in Spring 2005 at UCL.
- An intensive course of 2 days on 'Mixed Models and Incomplete Data' by Geert Verbeke (KUL-2) and Geert Molenberghs (LUC) on 31 March and 1 April 2005 at UCB Pharma (Braine l'Alleud).
- An intensive course of 2 days on 'Introduction to cluster analysis' by Hans-Hermann Bock (RWTH) and Iven Van Mechelen (KUL-1) on 2-3 May 2005 at KUL-1.
- An intensive course of 2 days on 'Introduction to bayesian inference in biomedical applications' by Nicky Best (Imperial College, London) on 3-4 May 2005 at UCL.
- An intensive course of 7.5 hours on 'Nonparametric regression techniques' by Byeong Park (Seoul National University, South Korea) in Spring 2005 at UCL.
- A one-week Summer School on 'Quantile Regression and Applications', by Roger Koenker (University of Illinois at Urbana Champaign), Ivan Mizera (University of Alberta), Bas Werker (University of Tilburg), and Siegfried Heiler (University of Konstanz) on 12-16 September 2005 at La Roche-en-Ardenne. Organizers: the ULB team, in the context of the "European Courses in Advanced Statistics" series.
- An intensive course of 2 days and 1 day of lectures on 'Interval censoring with medical applications' by Guadalupe Gómez, Klaus Langohr (Technical University of Catalonia, Barcelona), M. Luz Calle and Ramon Oller (Universitat de Vic, Barcelona) on 15-17 November 2005 at KUL-2 (organized by KUL-2, LUC and UCL).

The short courses organized by the UCL were also part of the doctoral programme of the Graduate School in Statistics of the UCL.

3.1.6 Mobility of researchers.

The exchange of researchers within the network helped to disseminate the gained expertise between different partners of the network.

In Section 2, a large number of researchers are mentioned with whom network members have written joint papers. In many cases visits have been paid in both directions, thanks to the network.

Moreover, we organized the exchange of two young researchers within the network:

1. J. Bigot, who got his PhD in Statistics at UJF-LMC-IMAG (Grenoble) in 2003 under the supervision of A. Antoniadis. Then he was post-doctoral student at UCL for one year. At UCL, J. Bigot started scientific projects with I. Gijbels, R. von Sachs and Ph. Lambert joint with Grenoble's partner.

2. A second example is T. Bouezmarni, who got his PhD in Statistics at UCL in 2004 under the supervision of J.-M. Rolin on kernel smoothing. He is now post-doctoral researcher at KUL-1, where he works, among others, with P. De Boeck on kernel smoothing for generalized linear models.

Moreover, a number of members of the network used the framework of the IAP to exchange with the European partners. An example is given by Rainer von Sachs and Irène Gijbels (UCL) who visited Anestis Antoniadis (UJF) (and vice versa), while Hans Bock (RWTH), Paul De Boeck and Iven Van Mechelen (KUL-1) have visited each other on a regular basis. Ingrid Van Keilegom (UCL) has presented a seminar at RWTH. These exchanges must be more intensive in the future, in particular if we consider the inclusion of more EU partners in the network.

3.2 Added value gained through the network

The whole overview report and, in particular, the present Section 3 on networking reflects the high added value gained through the network. The researchers of the network are sometimes faced to similar problems but in different fields. An example is given by the analysis of heterogeneity, which will be the central theme of Workshop 4. In this respect, each partner clearly benefits from the expertise of the whole network.

The list of working groups (Section 3.1.4) illustrates other common scientific concerns between the members of the network. Overall, the network is in a unique position since it brings together researchers and hence methods from psychometrics, biostatistics, and mathematical statistics. This is testified, for example, by the frailty working group (biostatistics and mathematical statistics, KUL-2, LUC,...), and by the mixtures, mixed, and missing-data related interactions (WP4, WP5, WP6), where psychometrics and biostatistics have come together. A visible fact to support this point is given by the book by De Boeck and Wilson (2004), who was the best selling Springer book at the International Meeting of the Psychometric Society.

Moreover, the network has facilitated the application for significant additional research means within the research domain of the network and/or by several network partners. Examples include a bilateral grant proposal from KUL-1, KUL-2 and LUC (De Boeck, Lesaffre, & Molenberghs, 2005), a GOA grant obtained by KUL-1 (Van Mechelen, De Boeck, & Tuerlinckx, 2004: 1.5 million 2005-2009) (involving mixed models and models for classification and survival analysis).

The network also leads to a significant increase of our research activities in statistics in Belgium. To support this point, a large number of high level courses offered in Belgium were organized thanks to the network. Students from all univerities of Belgium (and sometimes from abroad) participated to these courses. We can say that the network pushed the Belgian statistical community to a more active and a more visible situation.

3.3 Circulation of information in the network

The above joint scientific activities constitute an important way to facilitate the circulation of information in the network. Apart from these activities, the network also developed a set of tools for this task. These are listed below.

- *Web site.* All activities of the IAP-statistics network can be followed very closely from our web site which was created in January 2002. The address of the web site is `http://www.stat.ucl.ac.be/IAP`. The web site contains e.g. the following information :
  - Our logo
  - Call for applications
  - Description of the project
  - List of scientific personnel working under the IAP project
  - Downloadable member list
  - Research activities (workshops, seminars, short courses,...)
  - Downloadable technical reports, list of publications and list of books written my members of the network
  - Annual reports and reports of scientific meetings
  - Contact details

- *Technical Reports and Publications Series.* Two series, available via the website, report on scientific results obtained within the IAP-statistics network: the Technical Report Series and the Publications Series. The IAP-statistics Technical Reports Series groups all papers written under the IAP-statistics network. Each paper in this series has been submitted for publication in an international journal. Once a paper has been accepted for publication in an international journal and has been printed, we list it in the IAP-statistics Publications Series.

  For the IAP-statistics Technical Reports Series we list (title and authors) all papers on our website and for each paper we post a document (ps file or pdf file of the paper) that can be downloaded from the site. For the IAP-statistics Publications Series we provide on the website a list containing titles and authors of published papers.

  The following table reports the number of written papers for each publication series :

	2002	2003	2004	2005*
Technical Reports	53	63	83	34
Publications	27	103	141	31

  (* until June, 30th)

- *B-Stat News.* This journal is the official journal of the Belgian Statistical Society. Most of the events organized within the IAP network are announced in this journal.

- *Mailing list.* An announcement of the events organized by the IAP are sent by e-mail to all members of the IAP network.

3.4 Functioning of the follow-up committee

The follow-up committee was originally composed of Prof. A. Albert (University of Liège), Prof. P. Groeneboom (University of Delft) and Prof. T.A.B. Snijders (University of Groningen). In November 2004, Prof. P. Groeneboom left the follow-up committee and was replaced by Prof. M. Delecroix (ENSAI, Rennes).

The follow-up committee stays informed of the activities of the network by means of the annual reports of the network. It also plays an important role during the administrative meetings. These meetings took place at UCL on April 18, 2001, September, 5, 2002, October, 16, 2002, October, 15, 2003 and December, 17, 2004. During these meetings we inform the committee about the last substantive questions addressed by the partners, and the administrative evolution of the IAP network. The committee made valuable comments and propositions on our work. For instance, they suggested to combine the administrative meetings with a scientific meeting of a half day. We followed this idea for our last administrative meeting, on December 17, 2004.

4 Position of the IAP Network

4.1 Cutting-edge research

4.1.1 Scientific highlights of the network

The network has been very active in making important scientific contributions in many areas of statistics : longitudinal data, mixed models, frontier models, censored data, classification models, nonparametric regression, time series, semiparametric models, etc. We list below a selection of important examples of these scientific highlights.

1. *Incomplete data.* Regarding incomplete data and, relatedly, longitudinal data, mixed models, and latent variables, there is a very large output coming from the network. Methodological work has been published in major journals, such as *Biometrika, Applied Statistics, Journal of the American Statistical Association, Biometrics, Journal of the Royal Statisticsl Society, Series B*, etc. These activities have not gone unnoticed and network members are invited to important scientific meetings, are asked to teach short courses, and are consulted both by industry and regulatory authorities regarding the treatment of longitudinal and incomplete data in, for example, clinical studies. The latter includes US based companies and authorities, such as the Centers for Disease Control and Prevention (CDC, Atlanta, Georgia) and the Food and Drug Administration (FDA, Rockville, Maryland). This is a major achievement since relatively few European teams are in this position.

2. *Frontier models.* The use of nonparametric frontier models is a hot research topic in efficiency and productivity analysis. Statistical inference is now available and the theory behind the bootstrap is now available. Extensions are also available allowing to handle noise, to condition on environmental variables and to be robust to extremes and outliers. Many papers were published in the best journals in the field (*Journal of Econometrics* (4), *Journal of the American Statistical Association*, *Journal of Productivity Analysis* (2), *Journal of Multivariate Analysis* and *European Journal of Operational Research*). The methods have known an increasing interest from practionners: publications in *Scientometrics* and *Health Care Management*, and two members from UCL-team were involved in a consulting project on the analysis of performance of air-controlers in Europe (for Eurocontrol). L. Simar was invited as expert to join an European network of excellence (PRIME) to implement these methods for the evaluation of the performance of European universities.

3. *Interval censoring.* Interval censoring has received recently great interest in survival analysis. The calculation of the non-parametric estimator of the survival function is considerably more difficult than for right-censored data, especially in the bivariate case. KUL-2 has developed an algorithm that speeded up the calculation considerably (up to 40). Further, in the class of accelerated failure time models, KUL-2 developed a methodology that allows for a flexible error and/or frailty distribution with interval, left- and right censored responses and/or covariates.

4. *Mixed models.* The search for alternative random effects distributions than the normal in a mixed model is an important applied research area. In linear mixed models such an

alternative distribution is important for the estimation of the random effects themselves, but in generalized linear and non-linear mixed models also the fixed effects estimates are affected by choosing a wrong random effects model. Especially alternative models which can do the calculations in an economical manner are of practical importance. KUL-2 has contributed to this topic by proposing a smooth estimate of the random effects distribution in a linear mixed model. It outperforms the current alternative approaches with respect to its computational stability and its estimation characteristics.

5. *Item response models.* The framing of item response models as generalized linear and non-linear mixed models is an important trend in the field of psychometrics. The KUL-1 team has contributed to this trend in several respects: by an elaboration of a framework and its extension to new models, including models with mixture distributions, and by using this framework for important substantive contributions to psychology (see publications in substantive journals, among others in the top journal in psychology *Psychological Review*).

6. *Classification.* With the advent of new highly complex data-analytic problems in domains such as bioinformatics, the classification domain has witnessed a surge of renewed interest in simultaneous classification methods and complex clustering methods such as clustering methods for multiway data. KUL-1 and RWTH have contributed to this trend with the construction of a comprehensive structured overview of simultaneous clustering methods (see publication in well-ranked journal *Statistical Methods in Medical Research*) and with the development of a broad range of novel simultaneous clustering methods for multiway data.

7. *Nonparametric regression with censored data.* Lots of research has been done by the UCL and LUC partner in the context of semi- and nonparametric regression with censored data. This is considered as an important research area, as in many practical situations the classical Cox and accelerated failure type models are too restrictive. This is e.g. the case for survival data that are clustured (multivariate survival data). Appropriate extensions using random effects are needed such as e.g. frailty models. Many methodological papers in this field were published in top journals such as *Journal of the American Statistical Association*, *Scandinavian Journal of Statistics* (2), *Bernoulli*, *Journal of the Royal Statistical Society-Series B*, *Biometrika*, etc. Also important applied papers have been published in top journals like *Biometrics*, *The American Statistician*, *Preventive Veterinary Medicine*, etc. Results on a regression model with partially informative censoring were published in *Nonparametric Statistics* and *Journal of Statistical Planning and Inference*. An important contribution towards dependent censoring appeared in the *Canadian Journal of Statistics*.

8. *Analysis and forecasting of high-dimensional time series data.* The dynamic factor method developed by the ULB team has attracted the interest of economic and financial institutions wordwide, including the European Central Bank, the Federal Reserve, the National Bank of Switzerland, the Banca d'Italia, ... A real time coincident indicator of the EURO area business cycle, based on the work of the team, is published every month by the London-based CEPR and, for the US economy, by the Federal Reserve of Chicago. Methodological papers on which these applications are based appeared in *Review of Economics and Statistics*, *Econo-*

metric Theory, the *Journal of Econometrics* (2), the *Journal of Monetary Econometrics*, and the *Journal of the American Statistical Association*.

9. *Semiparametric inference based on ranks and signs.* This line of research developed within the ULB team, aims at extending to a multivariate setting (including that of VARMA models) a variety of semiparametrically efficient rank-based methods that only were available in the univariate context. The papers resulting from this research have been published in some of the best statistical journals: the *Annals of Statistics* (5), *Bernoulli* (3), the *Journal of Multivariate Analysis* (2), *Statistical Science*.

10. Spatial data, image analysis, and inverse problems. A collaboration between the ULB team, the London School of Economics, Indiana University and Princeton has produced several excellent papers (*Communications on Pure and Applied Mathematics, Journal of Multivariate Analysis, Annals of Statistics*) in the areas of nonparametric estimation on random fields and ill-posed inverse problems.

4.1.2 Perspectives

Each of the results described above gives a (partial) answer to an important research question. In many cases, there are however still a lot of unsolved related questions, which definitely deserve and require further close attention in the near future. The following list of research topics is meant to give an idea of the research questions the network members plan to work on during the coming years.

1. *Dependent censoring models.* Theoretical results have been obtained for regression under dependence between censoring time and lifetime. This dependence is modelled by a known copula function. An important new practical question is : how to choose the right copula ? Another interesting issue is to study regression under both dependence and (partial) informativeness.

2. *Frailty models.* Relevant further topics that need further research to support the use of frailty models include: diagnostics (aptness of the model), comparison of the available methodologies to model clustered survival data (e.g. the use of accelerated failure time models versus the use of frailty models) and last but not least the further development of appropriate software to fit frailty models (the absence of software to fit frailty models with more than one random effect (random interaction and hierarchical models) is one of the main hurdles in advocating frailty models). Other themes for further study include the modeling of multivariate survival data that are subject to censoring schemes that are different from right censoring and the study of frailty models with random effects vectors that have correlated components.

3. *Mixed effects models.* An important problem is the choice of the random effects distribution in a generalized and a non-linear mixed effects model. Simulation studies indicate that wrongly assuming the normal distribution can have an important effect on the estimation of the fixed effects. The question is how a flexible choice can be made with elegant computational properties. A first step has been made by KUL-2 for a linear mixed effects model. The question remains whether and how this approach can be generalized.

4. *Interval censoring.* Interval censoring can also affect the covariates in a survival analysis. Statistical research is needed to develop models and suggest computational procedures to unbiasedly estimate the regression parameters. Research is also needed to derive the statistical properties of these models. KUL-2 has developed flexible procedures both in a Bayesian as well as in a frequentist way to analyze interval- and doubly-interval censored responses.

5. *Incomplete data.* In the area of incomplete data, more and more emphasis is put on sensitivity analysis to assess the impact of incomplete data as such and of modeling assumptions made to cope with it, on the conclusions reached. The team of WP6 has been very active in this respect and as earned a position at the forefront for many years. Consequently and in concertation with many international fellow researchers, the message has caught on among practitioners, including industry and regulatory authorities. This implies that a large number of additional questions are and will be raised, to deal with sensitivity issues in a multitude of data and model settings. WP6 is well positioned to deal with these issues in the near future.

6. *Item response models.* Further developments in several respects based on the framework we developed for item response models are planned. For example, an extension of structural equation models (SEMs) into double-structure SEMs for three-mode data (so that latent variables of persons and of situations can be used simultaneously), and a model for residual dependences among binary variables using copulas.

7. *Mixture models.* Graphical techniques for mixture models, as a basis for the estimation of models with transitions between mixture components, and of Bayesian network models in general, can be used for collaborative research in the field of bioinformatics.

8. *Clustering models for multiway data.* Further theoretical and algorithmic aspects of simultaneous clustering models for multiway data will be developed, as well as extensions of those models for the representation of multiple linked data sets, also to be used in bioinformatics applications.

9. *Semiparametric regression with censored data.* A lot of progress has been made over the last few years in obtaining theoretical results for semiparametric regression models, like additive regression models, partially linear models, single index models, transformation models, etc. However, very little is known so far about asymptotics for these models when the response is subject to censoring. Other aspects of these models, like consistency of the bootstrap, use of empirical likelihood techniques, choice of the bandwidth, etc. will also be explored.

10. *Frontier estimation.* In nonparametric frontier estimation the bootstrap needs complex smoothing methods to be correctly implemented. Hence, there is a need for a simpler method that could be more easily implemented by practionners. Introducing noise has been done in the nonparametric frontier models but the methods, even if flexible, are not completely free of appropriate assumptions. The next step would be to characterize the minimal set of assumptions that would allow the identification of a 'full' nonparametric model. Quantile and order-m frontiers are very appealing, their use should be extended in order to define more general directional distance functions (and not only radial distances). The asymptotics for

conditional efficiency scores is still to be provided, with appropriate bandwidth selection procedures.

11. *High dimensional time series.* The dynamic factor model so far has been considered from a frequency domain point of view. A time-domain approach would be highly desirable, as it automatically would resolve the problems related to two-sidedness of spectral concepts. This time-domain approach has been considered by L. Reichlin and her collaborators at ULB, but their investigation should be pursued much further.

12. *Elliptical models in multivariate analysis.* Classical multivariate analysis is entirely built on multivariate Gaussian assumptions and the extensive use of covariance matrices. M. Hallin and D. Paindaveine at ULB plan to reexamine classical procedures by extending them to elliptical models, with shape matrices playing the role of covariances, in the absence of any moment assumptions. Radial densities should remain completely unspecified in this approach, semiparametrically efficient distribution-free methods being the ultimate goal.

13. *Multivariate regression quantiles and related depth concepts.* A concept of multivariate regression quantile was introduced in B. Laine's Master thesis (advisor: M. Hallin). This concept and the related depth concept is described in detail in R. Koenker's recent monograph (*Quantile Regression*, Econometric Society Monograph Series, Cambridge University Press, 2005), and deserves further work.

4.1.3 Recognition/critical mass

The IAP network has built up over the last years an important recognition at national and international level. This recognition is the result of (1) the fact that the network is getting well known abroad because of the many announcements of workshops, meetings, short courses, job announcements, etc. that have been sent by the network; (2) successful collaborations between members of the network; and (3) important contributions/achievements of individual members of the network. The following list demonstrates this recognition by means of a number of examples.

1. *Actual position of former PhD students.* Many of the PhD students in the network have obtained after their PhD postdoctoral or academic positions. The following list gives an impression of their present positions.

    - Ariel Alonso (LUC): postdoc at LUC
    - Taoufik Bouezmarni (UCL): postdoc at KUL-1 (until 1 January 2006), postdoc at University of Montreal (from 1 January 2006 on)
    - Roel Braekers (LUC): assistant professor at LUC
    - Jose Cortiñas (LUC): postdoc at LUC
    - Aurore Delaigle (UCL): assistant professor at University of California at San Diego
    - Christel Faes (LUC): IWT postdoc
    - Niel Hens (LUC): FWO postdoc
    - Machteld Hoskens (KUL-1): postdoctoral position at the UC Berkeley

- Iwin Leenen (KUL-1): postdoctoral position at Complutense University, Madrid
- Eric Maris (KUL-1): associate professor at the Radboud University Nijmegen
- Abderrahim Oulhaj (UCL): postdoctoral position at Oxford University
- Davy Paindaveine (ULB): assistant professor at ULB
- Abdessamad Saidi (ULB): postdoctoral position at the Université de Montréal, and now assistant professor at ESSEC (Paris)
- Luca Sala (ULB): assistant professor at Bocconi University, Milan
- Ziv Shkedy (LUC): assistant professor at LUC
- Abdelouahid Tajar (UCL): research associate at the University of Manchester
- Francis Tuerlinckx (KUL-1): postdoctoral position at Columbia University NY, assistant professor at KUL-1
- Sébastien Van Bellegem (UCL): assistant professor at UCL
- Tom Verguts (KUL-1): assistant professor at the University of Ghent
- Catherine Vermandele (ULB): assistant professor at ULB

2. *Actual position of former postdocs.* The postdocs who have worked under the IAP-network, often found academic positions afterwards.

   - Jéremie Bigot (postdoc at UCL in 2003-2004) is now 'Maître de conférence' at the University of Toulouse I.
   - Gerda Claeskens (postdoc at UCL in 2003-2004, financed by 'terugkeermandaat/mandat de retour' du DWTC/ SSTC) is now associate professor at the KUL.
   - Seok-Oh Jeong (postdoc at UCL in 2003-2004) is assistant professor at the Department of statistics, Hankuk University of Foreign Studies, South Korea.
   - Li Chun Wang (postdoc at LUC in 2004-2005) is now assistant professor at the Department of mathematics, Beijing Jiaotong University, China.
   - Valentin Zelenyuk (postdoc at UCL at present) will be from 1 September 1 2005 on, director of UPEG (Ukrainian Productivity and Efficiency Group) at the new research center at the Stockholm School of Economics (Kiev) and a professor at EERC-Kiev.

3. *Important points of recognition of network members.* A number of members of the network have obtained important prizes, medals, elected fellowships, lectureships, etc. These points of recognition contributed in a large extent to the building of an important recognition of the network.

   - In 2002, Geert Molenberghs (LUC) received the *Guy Medal in Bronze* from the Royal Statistical Society. In 2003, Geert Molenberghs was elected Fellow of the American Statistical Association, an honour given to Geert Verbeke (KUL-2) in 2005. In 2003 and in 2005, Geert Verbeke and Geert Molenberghs jointly received the Excellence in Continuing Education Award of the American Statistical Association. This is particularly important since it is rarely awarded twice to the same lecturers. Since Verbeke and

Molenberghs are members of two different partners within the network, these recognitions are tangible benefits of the network's added value. In 2004, Geert Molenberghs was awarded the Myrto Lefkopoulou Distinguished Lectureship of the Harvard School of Biostatistics, Department of Public Health. He delivered a lecture on incomplete data in clinical trials, one of the main themes of WP6. In 2005, Geert Molenberghs received the Mitchell Lectureship of the University of Glasgow, Scotland, UK. Again, this is based on his work in incomplete data.

- Paul De Boeck (KUL-1) was awarded the Honorary Francqui Chair of Psychology at the Free University of Brussels (Belgium) 2001-2002 (after being awarded the same chair at the University of Ghent, 1992-1993).
- A paper by Léopold Simar (UCL) and Paul Wilson has been determined in 2002, by the ISI Essential Science Indicators, as a 'Fast Breaking Paper', being one of the most cited papers in the world in the field of 'Economics and Business', end of 2001, beginning of 2002.
- Frank Rijmen (KUL-1) was awarded the international prize of the Psychometric Society for the best PhD thesis in psychometrics (2003). He was the third member of the KUL-1 group to win the prize since it was first awarded 11 years earlier (the previous two were Eric Maris and Iwin Leenen).
- Two members of the network were awarded the "Marie-Jeanne Laurent-Duhamel Prize" delivered by the French Statistical Society (SFdS): D. Paindaveine (ULB) in 2003 and S. Van Bellegem (UCL) in 2005. This prize is delivered every two years to the best thesis in fundamental research in statistics.
- Lucrezia Reichlin (ULB) was appointed as the director of the scientific research group at the European Central Bank in Frankfurt.
- Gerda Claeskens (former postdoc at UCL, now at KUL) obtained in 2004 the Noether Young Scholar Award from the American Statistical Association.
- In 2002, Paul Janssen (LUC) and Noël Veraverbeke (LUC) together with Jan Swanepoel (South Africa) obtained the Herbert Sichel Award of the South African Statistical Association.
- In 2004, Noël Veraverbeke (LUC) obtained the medal of the Czech Mathematicians and Physicists-Mathematics research Section.
- In 2005, Noël Veraverbeke received the invitation to be one of the two Official Visitors of the South African Statistical Association (together with Peter Hall, Australia).
- Davy Paindaveine (ULB), Rainer von Sachs (UCL) and Ingrid Van Keilegom (UCL) became elected members of the International Statistical Institute.
- Marc Hallin in 2004 became 'Membre de la Classe des Sciences de l'Académie Royale de Belgique', of which he was Correspondant since 1999. Still in 2004, he was elected as Vice-President of the Société française de Statistique.

4. *Editorships/associate editorships of network members.* A number of members of the IAP network have contributed to the international recognition of the network, by accepting editorships/associate editorships of important journals in statistics.

    - Paul De Boeck is associate editor of *Psychometrika* (1995-2003), editor of the *Psychometrika* section 'Application Reviews and Case Studies' (since July 1, 2003), co-editor of *Measurement, Interdisciplinary Research and Perspectives*, consulting editor of *European Journal of Personality* (1996-2004), publication officer of the *International Federation of Classification Societies* (1998-2002), and consulting editor of the *European Journal of Psychological Assessment* (since 1999).
    - Iven Van Mechelen is consulting editor of the *European Journal of Personality* (2001-2004), member of the editorial board of *Methodology*, member of the council (2001-) and member of the executive committee (2005-) of the *International Federation of Classification Societies*.
    - Leopold Simar is associate editor of the *Journal of Productivity Analysis* (2003-) and member of the editorial board of the *International Journal of Statistics and System* (2004-).
    - Ingrid Van Keilegom is associate editor of the *Journal of the Royal Statistical Society - Series B* (2002-) and associate editor of the *Scandinavian Journal of Statistics* (2004-).
    - Rainer von Sachs is associate editor of the *Journal of the Royal Statistical Society - Series B* (2002-).
    - Geert Molenberghs served and serves as associate editor for *Biometrics* (1995-2000), *Biostatistics* (1999-), *Applied Statistics* (1997-2000), and *Archives of Public Health* (1996-2000), editor of *Biometric Bulletin* (1998-2001), *Newsletter of the International Biometric Society*, *Applied Statistics (Journal of the Royal Statistical Society, Series C)* (2001-2004), Wiley Series in Probability and Statistics Editor (2003-).
    - Anestis Antoniadis is a member of the editorial board of the *ISUP* journal since 1992, associate editor of the *Journal of the French Statistical Society* since 1998, co-editor in chief of the journal ESAIM: Probability & Statistics (2001-2005), associate editor of the same journal since 2005, associate editor for Wileys Encyclopedia of Statistical Sciences (2001-2005), associate editor of the *Journal Statistics and Computing* since 2002. He was elected Fellow of the Institute of Mathematical Statistics in 2003, and Fellow of the American Statistical Association since 2001.
    - Noël Veraverbeke was associate editor of *Statistica Neerlandica* (1998-2003).
    - Paul Janssen is associate editor of *Statistica Neerlandica* since 2003.
    - Michel Denuit is Proceedings editor for *Insurance: Mathematics and Economics*, editor of the *Belgian Actuarial Bulletin*, associate editor of the *Australian and New-Zeeland Journal of Statistics*, and member of the advisory board of the Wiley Encyclopedia of Actuarial Science.
    - Emmanuel Lesaffre is Co-Editor of *Statistical Modelling: An International Journal*.

- Hans Bock is managing editor of the publication series 'Studies in classification, data analysis, and knowledge organization' (Springer Verlag). He is member of the editorial board of *Statistical Methods and Applications*, *Journal of Classification*, *Revista de Matemáticas* and *Journal de la Société Française de Statistique*.
- Lucrezia Reichlin (ULB) is or has been editor of the *Journal of the European Economic Association*, the *Journal of Applied Econometrics*, *Les Annales d'Economie et Statistique*, *European Economic Review*, *Macroeconomic Dynamics*, *Research in Economics*, *Il Giornale degli Economisti*, the *European Economic Abstracts*, the *Journal of Macroeconomics*, *Economica*.
- Marc Hallin is associate editor of the *Journal of the American Statistical Association*, of the *Journal of Time Series Analysis*, of the *Journal de la Société Française de Statistique*, the *Annales de l'Institut de Statistique de l'Université de Paris*, and of *Statistical Inference for Stochastic Processes*; he is coordinating editor of the *Journal of Statistical Planning and Inference*, and member of the editorial boards of the Springer series 'Mathématiques et Applications' and 'Statistique et Probabilités Appliquées'.

4.2 International role

4.2.1 Collaboration with the European partners

The European partners of the network (H. Bock from RWTH, Aachen and A. Antoniadis from UJF, Grenoble) have been integrated into the network by means of a number of joint activities, visits and collaborations.
For RWTH :

- Co-organisation of a training course on cluster analysis for PhD students of the IAP-network at KUL-1 (May 2005).
- Mutual visits of senior researchers of RWTH and KUL-1.
- Intensive collaboration with KUL-1 with respect to biclustering (including construction of a structured comprehensive overview of the domain and ongoing joint work on maximizing interaction information in prediction problems with categorical predictors).
- Members of the RWTH groups attended many of the joint activities (workshops, meetings, etc.).
- Lectures by members of UCL and RWTH.

For UJF :

- Collaboration with UCL for the organization of the first workshop that took place on May 21-23, 2002 at UCL.
- Intensive collaboration between A. Antoniadis and I. Gijbels (on nonparametric regression via regularization), and between A. Antoniadis and R. von Sachs.

- J. Bigot obtained his PhD at UJF in 2003 and was a post-doctoral researcher of the IAP network at UCL in 2003-2004. During his stay he collaborated with R. von Sachs, I. Gijbels (on constrained regression estimation using penalized wavelet regression techniques) and Ph. Lambert (on synchronization of curves by means of a registration technique).
- Members of the UJF group attended many of the joint activities (workshops, meetings, etc.).

The budget of the European partners has been spent on (for the period 2002-2004) :

- For RWTH : personnel costs (29,590 Euro) and travel costs (410 Euro)
- For UJF : each year, 8500 Euro for invitations and travel costs + 1500 Euro (15% 'frais generaux' of the university)

The added value of having RWTH and UJF as European partners in the network is clear and important. H. Bock (RWTH) is a leading scholar in the field of classification (clustering, pattern recognition), one of the major topics of WP5, and an internationally prominent researcher. A. Antoniadis (UJF) has made important contributions in the field of nonparametric curve estimation, wavelets, survival analysis and point processes, which are closely connected with WP1 and WP3. Moreover, both have an excellent international reputation.

4.2.2 International activities

Many members of the network have been very active on international level, by participating in European and international research networks, giving important invited presentations at conferences, giving short courses, collaborating with researchers from all over the world, organizing international symposia, etc.

1. *Participation in European and international research networks.*

    - An international group of 17 universities submitted an application for a Marie Curie Research Training Network around the theme of non- and semiparametric curve estimation in November 2003 (reference: FP6-005420). The partners of the IAP network that work in this research area (i.e. UCL, LUC, KUL-2 and UJF) were included in this network. The main coordinator of this network was Ricardo Cao (University of La Coruña, Spain). Despite a quite positive and promising evaluation, the application was rejected. A new proposal will be submitted at the end of 2005.
    - Léopold Simar has been invited to join, as Associate Partner, the PRIME Network of Excellence (EC contract CITI-CT-2003-506596) within the FP6 of the EC. The idea is to develop methodology on frontier estimation initiated in the IAP project, in order to evaluate and compare the performance of European universities.
    - A bilateral project for scientific and technological collaboration between Flanders and Chile (BIL01/01) has been obtained, from December 2001, extended to April 2005, with the following partners: KUL-1 (Paul De Boeck), LUC (Geert Molenberghs), and the Department of the PUC in Santiago de Chile.

- A bilateral project for scientific and technological collaboration between UJF and CNR - Italy has been obtained, from December 2001, extended to December 2005, with the Department of Applied Mathematics of the CNR in Naples.
- A bilateral project for scientific and technological collaboration between UJF and the University of Cyprus (EGIDE - Zenon program) has been obtained, from June 2004 to December 2006, with the Department of Statistics of the University of Cyprus.

2. *Important invited presentations at conferences.* Below we mention some of the most important invited presentations that members of the network have given over the last years. The following list contains a number of examples of important invited presentations given by members of the network.

   - Paul De Boeck (KUL-1) gave a plenary lecture at the 'International Meeting of the Psychometric Society', Monterey CA, 2004, and he was keynote lecturer at the 'International Conference of Psychology', Beijing, August 2004 (this is the big worldwide conference of psychology which is held every four years).
   - Between 2002 and 2005, Léopold Simar (UCL) was invited keynote speaker and/or member of the scientific committee at several international workshops and conferences in US, Canada, Europe (North American Productivity Workshop, European Workshop on Efficiency and Production Analysis, Annual Texas Econometric Camp, International Symposium of DEA, Applied Stochastic Models and Data Analysis, etc.). Several seminars (15) and academic visits (10) at European and American universities.
   - Between 2002 and 2005, Ingrid Van Keilegom (UCL) was invited speaker at 8 conferences, including the Conference in Probability Theory and Mathematical Statistics dedicated to the Centenary of A. Kolmogorov, Tbilisi, Georgia (2003), the Joint Statistical Meetings, Toronto (2004) and the Workshop on 'Specification testing', Santander, Spain (2005).
   - Anestis Antoniadis (UJF) gave invited presentations at e.g. the GDR-MOMAS workshop, CIRM, Marseille (November 2003), at the Annual Meeting of the Statistical Society of Canada, SSC 2004, Montreal, Canada, at the workshop 'Wavelet And Multifractal Analysis 2004', Cargèse, Corse, France, (July 2004), and at the Journées Données Fonctionnelles, Rennes (24-25 September 2004).
   - Between 2002 and 2005, Noël Veraverbeke (LUC) was speaker at 10 international conferences and presented seminars at 14 universities.
   - During the period from 2002 till 2005, Hans Bock was invited (keynote) speaker at several international conferences in the US, Poland, France, Italy, Korea, Japan, Belgium and Australia.
   - Lucrezia Reichlin has given recent invited addresses at the NBER Macroeconomic Annual, Cambridge US (2004) and the Meeting of the Latin American Econometric Society, Sao Paulo (2002).

- Marc Hallin (ULB) was invited speaker at many international conferences, e.g. the European Meeting of Statisticians (Prague, 2002), ICORS 2003 (Antwerp) and ICORS 2005 (Jyväskylä).

3. *Short courses.*

- Paul De Boeck gave invited training courses at the NCME meeting, Montreal Canada, April 2005 and at the International Meeting of the Psychometric Society, Tilburg, July 2005.
- Numerous short courses on longitudinal data, mixed models, and incomplete data have been given by Verbeke, Molenberghs, and collaborators. Locations include: UCB (2), Johnson & Johnson Pharmaceutical Research and Development, Katholieke Universiteit Brussel, Queensland (Australia), Cairns (Australia), Barcelona (3), Navarra, Santiago de Compostela, Hannover, Tyrol, Freiburg (IBC), New York (ASA; Pfizer), San Francisco (ASA), Tampa (ENAR), Toronto (ASA), Minneapolis (ASA) Washington (Food and Drug Administration; ASA), Atlanta (CDC), Cuba (La Habana, Varadero), Turkey, Ireland, Finland, and Brazil. In particular, it is important to notice that they received several invitations to teach in North America, including four times at the Joint Statistical Meetings of the American Statistical Association, the Spring Meetings of the Eastern North American Region of the International Biometric Society, the CDC in Atlanta, and the Food and Drug Administration in Washington. They have contributed to changing practice of handling incomplete data in longitudinal clinical trials.
- Léopold Simar was invited speaker at the Summer School 2003 on 'Frontier Models', Institute of Economics and Business Administration, Technical University of Lisbon, Portugal.
- Anestis Antoniadis gave a short course on nonparametric function estimation at the '1st Probability and Statistics Seminar Series on Nonparametric Statistics and Time Series Analysis', University of Cyprus, November 2002, and on computational and statistical aspects of microarray analysis (jointly with R. Gentleman) at the University of Milan, Italy.
- Ingrid Van Keilegom and Anestis Antoniadis will be one of the speakers of the short course on 'Modélisation non-parametrique en régression' at the Journées Européens de Statistique (October 2006).

4. *Important international collaborations.* Many network members are very active on international level. The most important international collaborations are mentioned below.

- WP1 : Research projects on functional estimation have been carried out in collaboration with (among others) : R. Cao (University of La Coruña, Spain), R. Carroll (Texas A&M University), H. Dette (University of Bochum), J. Einmahl (Tilburg University), P. Hall (Australian National University), N.L. Hjort (University of Oslo), A. Kneip (Mainz University), O. Linton (London School of Economics), B. Park (Seoul National University), R. Sickles (Rice University), P. Wilson (University of Texas, Austin).

- WP2 : Research activities for this work package have been conducted in collaboration with (among others) : M. Bertero (Genoa), R. Dahlhaus (University of Heidelberg), I. Daubechies (Princeton), M. Forni (University of Modena), J. Jurečková (Charles University, Prague), A. Klein (University of Amsterdam), M. Lippi (La Sapienza, Rome), Z. Lu (Academy of Sciences, Beijing, and London School of Economics), H. Oja (University of Tampere), H. Ombao (University of Illinois at Urbana-Champaign), L. Sala (University Bocconi, Milan), L.T. Tran (Indiana University, Bloomington), B. Werker (University of Tilburg).
- WP3 : Research cooperations are ongoing with R. Cao (University of La Coruña, Spain), P. Markel (Minot State University, USA), I. McKeague (Columbia University), J. Swanepoel (North-West University, Potchefstroom, South Africa).
- WP4 : S. Acton (Rochester Institute of Technology), P. Eilers (University of Leiden), E. Ip (Wake Forest University), H. Kuechenhoff (University of Munich), J. Nezlek (College William & Mary), E. San Martin (P.U.C. Chile), M. Wilson (U.C. Berkeley).
- WP5 : P. Brito (Porto, Portugal), E. Diday, Y. Lechevallier (Paris, INRIA and Université Dauphine), J. J. Lee (Seoul), A. Gelman (Columbia University), H. Imai (Sapporo, Japan), H.A.L. Kiers (University of Groningen), K. Pärna (Tartu, Estonia), J.-P. Rasson (University of Namur), M. Vichi (La Sapienza University, Rome).
- WP6 : Research activities on incomplete data have been conducted in collaboration with, among others, R. Carroll (Texas A&M University), M. G. Kenward (London School of Hygiene and Tropical Medicine), C. Mallinckrodt (Eli Lilly & Company, Indianapolis), S. Lipsitz, P. Williams and G. Fitzmaurice (Harvard School of Public Health).

5. *Organization of international symposia.* Apart from the international workshops the network organizes on a yearly basis (see Section 3.1.1 for more details), members of the network had important responsabilities in the organization of some international symposia. We list here some examples.

   - Emmanuel Lesaffre organized the ‘First International Dental-statistical meeting’ 21-23 April 2004. He will also organize a Satellite Meeting of the IBC2006 meeting in Montreal.
   - Paul De Boeck organized the ‘Workshop on psychometrics and educational measurement’, Leuven, July 2003, the ‘Workshop on formal modeling of personality and affective processes’, and the ‘International conference of the Dutch research school IOPS’ (psychometrics and sociometrics), December 2005.
   - UCL and ULB jointly organized the ‘XXXIV Journées de Statistique’, Annual Meeting of the SFdS (Statistical Society of France) held in Belgium, May 2002. Léopold Simar (UCL) was chair of the organizing committee, and Marc Hallin (ULB) was chair of the scientific committee.
   - Léopold Simar was chair of the Bernoulli Section Program Committee and Member of the Coordination Program Committee of the 55th Session of the International Statistical Institute (ISI), World Congress held in Sydney, April 2005.

- Marc Hallin was Chair of the Program Committee of the XIth Annual Meeting of the Belgian Statistical Society, la-Roche-en-Ardenne, October 2003.
- Members of LUC and KUL organized the 18th International Workshop on Statistical Modelling, Leuven, 7 - 11 July, 2003.
- Members of LUC and KUL organized the Theme Conference of the Royal Statistical Society, Statistical Genetics and Bioinformatics, LUC, 14 - 17 July, 2003.
- Paul Janssen (LUC), together with Noël Veraverbeke (LUC) and Luc Duchateau (Ghent) organized the workshops 'Current trends and recent advances in Applied Biometry' (Nairobi, Kenya, 30 August - 3 September 2004 and Addis Ababa, Ethiopia, 24 - 27 August, 2005).
- Anestis Antoniadis (UJF) has organized and presided the international conference 'Wavelets and Statistics: watering the seed', partially supported by INRIA, held in Villard de Lans from 4 to 7 September 2003.
- Rainer von Sachs (UCL), together with E. Paparoditis and T. Sapatinas (University of Cyprus) organized an international workshop on "Recent Advances in Time Series Analysis", June 9-12, 2004, Protaras, Cyprus.

4.3 Durability of the IAP

4.3.1 Justification for a continuation

The need for a continuation of the existing research network can be motivated by means of many arguments :

- Statisticians, due to the interdisciplinary nature of their expertise and teaching duties, are typically scattered among faculties, schools, departements, etc. More than any other fields, they need help in order to meet and share their knowledge and experience. This network is a vital opportunity for the main statistical groups of Belgian universities to exist as a community.
- Despite its relatively small size, the network is doing very well on the international scene, as in explained in Section 4.2. For instance, the prize for the best thesis from the French Society was twice in a row assigned to a member of the network, papers are often published in top journals in their field, PhD student are often offered academic positions after graduating, etc.
- In practical settings problems come together. For instance, in the analysis of the dental data from the Signal Tandmobiel Study different aspects need to be considered at the same time. As an example, misclassification of the caries status in conjunction with interval censoring necessitates the examination of misclassification problems in survival models with interval censoring. What typically needs to be done is the integration of different methodologies to tackle practical complex research questions. The existence of a research network in which expertise on these various research topics is present, is therefore desirable.

- The network has proven to be successful in its research output (papers, books, proceedings, invited and contributed presentations, seminars). Further, it is very internationally active, in a large variety of ways, including but not restricted to, inviting scholars and paying scientific visits, giving courses abroad at universities, companies, and governmental agencies, etc. As such, it is recognized as a strong international partner, for a number of areas even as a world leader.

- The network has further ensured that Belgium is on the map from a statistical point of view. The network partners have intensive collaborations, and bring together theoretical and applied expertise across a variety of areas. This is a very strong asset worth of further support.

- The methodology used in different areas of statistics (genetics, time series, econometrics, etc.) is often similar in nature. It is therefore important to have a network in order to combine forces and to look at statistical problems from different angles.

- As illustrated in Section 2, many cross-links exist between the 7 partners and between the 6 work packages of the network, for example :

  - The collaboration between LUC, KUL-1, and KUL-2 is a natural and desirable collaboration because the three groups work on generalized linear and nonlinear mixed models and mixture extensions, estimation of these models, strategies to deal with missing data, etc.
  - The collaboration between UCL and KUL-1 is of high importance for extensions to nonparametric approaches for the models the KUL-1 group investigates (mainly functional estimation of random effect densities and change-point models).
  - The collaboration between KUL-1, ULB and LUC is very useful for the time dimension the KUL-1 group wants to include in their research.
  - etc.

  We refer to Section 2 for more examples.

4.3.2 Adaptation of the current organization

Overall, the network has been very successful so far and one would like to continue with the same general architecture. The actual Belgian partners wish to continue with UCL staying the network coordinator. As to the European partners, the successful collaboration with UJF would like to be continued. On the other hand, in view of the expected retirement of H. Bock, a replacement of the RWTH partner seems advisable. Inclusion of the University of Groningen (Department of Sociology), could be beneficial to the network, given the solid background of the statistics group of that department, in particular with regard to mixed models. The inclusion of other European and/or Belgian partners will be investigated. The intention is to select a total of about 3-4 European partners.

5 Output

5.1 Most relevant publications

The following list contains a selection of the most relevant publications, written by members of the IAP-network.

- Antoniadis, A. and Gijbels, I. (2002), Detecting abrupt changes by wavelet methods. *Journal of Nonparametric Statistics.* **14**, 7–29.

- Daubechies, I., Defrise, M., and De Mol, Chr. (2004). An iterative thresholding algorithm for linear inverse problems with a sparsity constraint. *Communications in Pure and Applied Mathematics* **57**, 1413-1457.

- De Boeck, P., and Wilson, M. (Eds.) (2004). *Explanatory item response models: A generalized linear and nonlinear approach.* New York: Springer-Verlag (with chapters from members of the LUC and KUL-2 team).

- Duchateau, L. and Janssen, P. (2004). Penalized partial likelihood for frailties and smoothing splines in time to first insemination models in dairy cows. *Biometrics*, **60**, 608–614.

- Forni, M., Hallin, M., Lippi, M., and Reichlin, L. (2005). The generalized dynamic factor model: one-sided estimation and forecasting. *Journal of the American Statistical Association*, to appear.

- Gelman, A., Van Mechelen, I., Verbeke, G., Heitjan, D.F., and Meulders, M. (2005). Multiple imputation for model checking: Completed-data plots with missing and latent data. *Biometrics*, **61**, 74–85.

- Ghidey, W., Lesaffre, E. and Eilers, P. (2004). Smooth random effects distribution in a linear mixed model. *Biometrics*, **60**, 945–953.

- Hall, P. and Simar, L. (2002). Estimating a changepoint, boundary, or frontier in the presence of observation error. *Journal of the American Statistical Association*, **97**, 523–534.

- Hallin, M. and Paindaveine, D. (2004). Rank-based optimal tests of the adequacy of an elliptic VARMA model. *Annals of Statistics* **32**, 2642-2678.

- Molenberghs, G. and Verbeke, G. (2005). *Discrete Longitudinal Data.* New York: Springer-Verlag.

- Van Keilegom, I. and Veraverbeke, N. (2002). Density and hazard estimation in censored regression models. *Bernoulli*, **8**, 607–625.

- Van Mechelen, I., Bock, H.-H., and De Boeck, P. (2004). Two-mode clustering methods: A structured overview. *Statistical Methods in Medical Research*, **13**, 363–394.

5.2 Appeal of the IAP

5.2.1 Visibility and appeal of the IAP

In order to make the IAP network well visible to the scientific community and in order to be considered as an active, productive and stimulating research network, we have taken the following initiatives :

- *Logo.* A logo has been created. It can be found on the front page of this report, as well as on the web page of the network (`www.stat.ucl.ac.be/IAP`). It has been designed by the young researchers of the UCL-team and includes a number of hidden statistical concepts.
- *Web site.* An extensive web site has been set up, which contains information about e.g. call for applications, description of the project, list of personnel working under the IAP project, member lists,... See Section 3.3 for more information.
- *Technical Reports and Publications Series.* Two series, available via the website, report on scientific results obtained within the IAP-statistics network: the Technical Report Series and the Publications Series. See Section 3.3 for more details.
- *Email lists.* A regularly updated list containing all email addresses of members of the network is used to disseminate information about short courses, visitors, call for applications, ... In addition, this information can be found on the web page.
- *Other ways to make the IAP visible.* Announcements of pre/post-doc positions of the IAP network are widely spread via numerous email lists all over the world. The activities of the network are also mentioned in B-Stat News, the official journal of the Belgian Statistical Society.

5.2.2 New marks of interest

The IAP network has, over the past three and a half years, built up an important international reputation and recognition. Some examples are :

- Regulatory authorities, such as the US Food and Drug Administration, have shifted or are shifting away from their more conventional recommendations to perform complete case analysis and last observation carried forward for incomplete longitudinal clinical trials, to direct likelihood methods, multiple imputation, and their Bayesian counterparts. Moreover, sensitivity analysis is more and more a part of the required modes of analysis for registration clinical trials. WP6 has strongly contributed to this effort and members of the team have been invited to participate in the writing of a White Paper on the handling of incomplete data in clinical trials by the FDA. The work package has a strong involvement in similar discussions with the European and British regulatory authorities as well.
- The work on longitudinal and incomplete data, disseminated through a wide variety of research papers and the books by Verbeke and Molenberghs (2000, 2005) and the short courses based there upon, has reached several thousands of colleagues and students (with over 4000 copies of the books sold and several thousands of students having attended short courses).

- The concerted efforts on surrogate markers, of which the book by Burzykowski, Molenberghs, and Buyse (2005) is a key testimony, has had a strong impact, worldwide, on the way of thinking about surrogate marker and surrogate endpoint evaluation. This effort is accompanied by a variety of lectures and short courses worldwide, and several research papers.
- The Central Bank in Frankfurt now uses the dynamic factor model developed in WP 2.
- Our network has an increasing international visibility. The number of candidates for the pre- and post-doc positions within the network shows this. As an example, for the last post-doc position at UCL, a total of 17 candidates applied (almost all non-Belgian).
- The pre- and postdoctoral researchers working under the IAP come from a variety of countries :
  - Predoctoral researchers : Argentina (1), Belgium (4), Czech Republic (2), Germany (1), Hungary (1), Italy (1), Poland (2), Romania (1), Ukraine (1), United Kingdom (1)
  - Postdoctoral researchers : Belgium (2), China (1), France (2), Marocco (1), South-Korea (1), Ukraine (1)
- Some of the partners of the network are active in other international research networks. See Section 4.2.2.1 for more details.
- A number of prestigious researchers have visited the partners of the network for giving short courses and seminars, participating to workshops and meetings, working on joint research projects,.... We refer to Sections 3.1.1, 3.1.2, 3.1.3 and 3.1.5 for more details.

5.3 PhDs and postdoc trainings

The following table summarizes the number of PhD students and postdocs that were trained in the network. The numbers in the table represent the average number **per year**.

Partner	PhD		Postdoc	
	IAP	not IAP	IAP	not IAP
UCL	3	11	3	1
KUL-1	3	7	1	6
KUL-2	3	8	0	0
LUC	0	3	1	4
ULB	2	10	0	1
RWTH	1	3	0	1
UJF	0	2	0	0
Total	12	44	5	13

The added value the network offers to the careers of PhD and postdocs can be described as follows :

- Thanks to the IAP network, there is a better exchange of ideas between students of the different partners. This can be explained by the fact that they meet each other more regularly than before the existence of the network (at workshops, meetings, joint seminars, short courses,...). Fruitful scientific interactions are the result of this.
- The short courses offer a unique chance to the young researchers to learn from specialists in the field about areas they are less familiar with. It is an efficient way to broaden their view on statistics.
- The 'Young Researchers Day', yearly organized by the PhD students of the UCL partner, is attended by many of the PhD students of the other partners. It stimulates interactions and connections between them. See Section 3.1.2 for more details about this meeting.
- In the light of the creation of big doctoral schools, as required by the FNRS (National Science Foundation of the French speaking community) from next academic year on, the partners from UCL and ULB are the leading forces behind a project to create a doctoral school in statistics and actuarial sciences, that will incorporate a number of universities in the French speaking part of Belgium, and a number of associate partners in the Flemish part and abroad. This doctoral school will stimulate even more the exchange of information between researchers of the network.
- At a one-week meeting at UC Berkeley, PhD students, postdocs and staff from KUL-1, KUL-2 and LUC met to discuss the use of generalized linear and nonlinear mixed models in psychometrics.
- In the series of weekly seminars at KUL-1, a number of joint seminars between KUL-1 and KUL-2 have been organized, to stimulate interaction between the members of the two groups, and especially the young researchers.

5.4 New research teams

Not relevant.

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