Łagów Lubuski, 10-14 June 2013

INTERNATIONAL WORKSHOP

mODa 10

Model-Oriented Data Analysis and Optimum Design

WORKSHOP PROGRAMME

mODa Board

- **Anthony C. Atkinson**, London School of Economics
- **Barbara Bogacka**, Queen Mary, University of London
- **Valerii V. Fedorov**, Quintiles, Morrisville
- **Alessandra Giovagnoli**, University of Bologna
- **Joachim Kunert**, Technical University of Dortmund
- **Jesus López-Fidalgo**, University of Castilla-La Mancha
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- **Dariusz Uciński**, University of Zielona Góra
- **Henry P. Wynn**, London School of Economics
- **Anatoly A. Zhigljavsky**, University of Cardiff

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- **Dariusz Uciński**

Contents

Scientific Programme

Sunday 9 June	14:30- 21:30	**Registration**
	18:30 - 22:30	**Welcome Buffet in Spa Morena**
Monday 10 June	07:00 - 08:45	Breakfast
	09:00 - 09:30	Welcome from the Organizers
	09:30 - 10:00	**A. Pázman** Extended optimality criteria for optimum design in nonlinear regression
	10:00 - 10:30	**E. Rafajłowicz** D-optimum input signals for systems with spatio-temporal dynamics
	10:30 - 11:00	Coffee Break
	11:00 - 11:30	**A.C. Atkinson** Robust experimental design for choosing between models of enzyme inhibition
	11:30 - 12:00	**R.L.J. Coetzer** Optimal designs for multiple-mixture by process variable experiment
	12:00 - 12:30	**V. Casero-Alonso** Experimental designs for different approaches of simultaneous equations
	13:00 - 14:30	Lunch
	15:00 - 15:30	**A. Zhigljavsky** Optimal experimental design for correlated observations: Old results and recent advances
	15:30 - 16:00	**A. Pepelyshev** Optimal design for multivariate models with correlated observations
	16:00 - 16:30	**V. Lacko** On efficiency of designs for processes of Ornstein-Uhlenbeck type
	16:30 - 17:00	Coffee Break
	17:00 - 17:30	**A. Dean** A-optimal and A-efficient designs for discrete choice experiments
	17:30 - 18:00	**H. Großmann** Differences between analytic and algorithmic choice designs for pairs of partial profiles
	18:00 - 18:30	**M. Crabbe** Fast algorithms to generate individualized designs for the mixed logit choice model
	19:00 - 20:30	Dinner
	21:00 - 22:00	**Smooth jazz concert**

Tuesday 11 June	07:00 - 08:45	Breakfast
	09:00 - 09:30	**L. Deldossi** Objective Bayesian model discrimination in follow-up experimental design
	09:30 - 10:00	**E. Skubalska-Rafajłowicz** Random projections in model selection and related experiment design problems
	10:00 - 10:30	**B.T. Magnusdottir** c-optimal designs for the bivariate Emax model
	10:30 - 11:00	Coffee Break
	11:00 - 11:30	**V. Fedorov** Elemental information matrices in the design of dose-response studies with time-to-event end points
	11:30 - 12:00	**V. Dragalin** Optimal design of experiments for delayed responses in clinical trials
	12:00 - 12:30	**W.F. Rosenberger** Adaptive Bayesian design with penalty based on toxicity-efficacy response
	13:00 - 14:30	Lunch
	15:00 - 15:30	**A. Biswas** Optimal sample proportion for a two-treatment clinical trial in presence of surrogate endpoints
	15:30 - 16:00	**J.A. Moler** Randomization based inference for the drop-the-loser rule
	16:00 - 16:30	**A. Ghiglietti** Randomly reinforced urn designs whose allocation proportions converge to arbitrary prespecified values
	16:30 - 17:00	Coffee Break
	17:00 - 17:30	**J. López-Fidalgo** Optimal design for accelerated failure time models
	17:30 - 18:00	**C.H. Müller** D-optimal designs for lifetime experiments with exponential distribution and censoring
	18:00 - 18:30	**S. Biedermann** Optimal designs for full and partial likelihood information
	19:30 - 00:00	**Banquet at the Castle of the Order of St. John**

Wednesday 12 June	07:30 - 09:15	Breakfast
	09:30 - 10:00	**S. Leonov** Approximation of the Fisher information matrix for nonlinear mixed effects models in population PK/PD studies
	10:00 - 10:30	**T. Mielke** Sample size calculation for diagnostic tests in generalized linear mixed models
	10:30 - 11:00	**T. Waite** Random designs for robustness to functional model misspecification
	11:00 - 11:30	Coffee Break
	11:30 - 12:00	**N. Flournoy** Optimal design for the bounded log-linear regression model
	12:00 - 12:30	**W. Bischoff** Checking linear regression models taking time into account
	12:30 - 13:00	**F. Rapallo** From Markov moves in contingency tables to linear model estimability
	13:00 - 14:30	Lunch
	14:45 - 15:30	**B. Jones** Introduction to optimal design in JMP
	16:00	**Departure to Zielona Góra**
	18:00 - 19:00	**Concert at the Zielona Góra Philharmonic Hall**
	19:00 - 20:00	**Guided tour of Zielona Góra**
	20:00 - 22:00	**Conference dinner at the Zielona Góra Palm House**
	23:30	**Arrival to Łagów Lubuski**

Thursday 13 June	07:30 - 09:15	Breakfast
	09:30 - 10:00	**N. Youssef** Comparing optimal designs of computer experiments for estimating covariance parameters
	10:00 - 10:30	**M. Hainy** Approximate Bayesian Computation Design (ABCD), an introduction
	10:30 - 11:00	**D. Ginsbourger** Kernels and designs for modelling invariant functions: From group invariance to additivity
	11:00 - 11:30	Coffee Break
	11:30 - 12:00	**H. Nyquist** Convergence of an algorithm for constructing minimax designs
	12:00 - 12:30	**L. Wänström** Construction of minimax designs for the trinomial spike model in contingent valuation experiments
	12:30 - 13:00	**B. Jones** An efficient algorithm of generating space-filling designs with linear inequality constraints on the design region
	13:00 - 14:30	Lunch
		Meeting of the mODa Board
	15:00 - 15:30	**H. Holling** Optimal design for count data with binary predictors in item response theory
	15:30 - 16:00	**J. Kunert** Optimal crossover designs with interactions between treatments and experimental units
	16:00- 16:30	**K. Mylona** Bayesian optimal design of blocked and split-plot experiments for fixed effects and variance component estimation
	16:30 - 17:00	Coffee Break
	17:00 - 17:30	**Poster Highlights**
	17:30 - 18:30	**Poster Session**
	19:30 - 23:00	**Farewell Reception**

Friday 14 June	07:00 - 08:45	Breakfast
	09:00 - 09:30	**R. Harman** Barycentric algorithm for computing approximate D-optimal designs with simultaneous size and cost constraints
	09:30 - 10:00	**G. Sagnol** Computing exact D-optimum designs by mixed integer second order cone programming
	10:00 - 10:30	**M. Prus** Optimal designs for the prediction of individual effects in random coefficient regression
	10:30 - 11:00	Coffee Break
	11:00 - 11:30	**R.A. Bailey** Quasi-Latin designs for experiments in rectangles
	11:30 - 12:00	**K. Filipiak** On the universal optimality of circular uniform weakly neighbor balanced designs under the model with residual effects
	12:00 - 12:30	**A. Markiewicz** On optimality of neighbor designs under interference models
	12:30 - 14:00	Lunch
		End of the conference

List of Posters

- **M. Amo Salas**
  D-optimality for time series models
- **M. Borrotti**
  Maximum entropy design in high dimensions by composite likelihood modeling
- **E. Delgado Márquez**
  Optimum experimental design in the transport of materials in granular form
- **R. Dorta-Guerra**
  Bayesian optimal factorial designs for binary response models
- **L. Filová**
  The RL heuristic for computing optimal designs of experiments
- **R. Fontana**
  Algorithms for minimum-size design generation: Orthogonal fractional factorial designs and optimal designs
- **D. Ginsbourger**
  Estimating and quantifying uncertainties on level sets using the Vorob'ev expectation and deviation with Gaussian process models
- **R. Martín-Martín**
  Multiplicative algorithms for the construction of optimum designs of experiments for discriminating between two rival models
- **H. Maruri-Aguilar**
  Smooth models for computer experiments
- **C. May**
  A convergent algorithm for finding KL-optimum designs and related properties
- **W.G. Müller**
  Optimal designs for regression models with a constant coefficient of variation
- **E. Perrone**
  Design of experiments for copula models
- **E. Riccomagno**
  Optimal experimental design in marine robotics?
- **J.M. Rodríguez-Díaz**
  Optimal designs for compartmental models with unknown/non-constant transfer coefficients
- **P.C. Trandafir**
  New perspective of the optimal design for the Rasch models
- **D. Uciński**
  On the functional approach to locally D-optimum design for multiresponse models

Abstracts: Oral Presentations

10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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Robust experimental design for choosing between models of enzyme inhibition

Anthony C. Atkinson and Barbara Bogacka

Abstract Models for enzyme inhibition form a family of three parameter extensions of the Michaelis-Menten model to two explanatory variables, the concentrations of enzyme and inhibitor. The precise mechanism of inhibition is often unclear; two important mechanisms are competitive and non-competitive inhibition.

The two models, which have a similar structure may be combined in a single four-parameter model with parameter of combination λ. Locally Ds-optimum designs for λ provide a method of discriminating between the models. However, these locally optimum designs depend on the values of two of the parameters in the combined model. We find the minimum and average efficiencies of these designs over a set Θ of parameter values.

The highest value of minimum efficiency of a locally optimum design over Θ is 31.53%, with average efficiency 69.11%. For this and similar designs, which are locally optimum for central values of Θ, the minimum efficiency occurs at extreme parameter values. This suggests that a combination of locally optimum designs for central and extreme points in Θ will have improved minimum efficiency.

We find the properties of equally-weighted combinations of all pairs of locally optimum designs. The design with the highest minimum efficiency, 47.78%, has an average efficiency of 56.43%. Other designs have higher average efficiency, but a lower minimum value. Plots of the two efficiencies for the pairs of designs reveal which designs lie on the efficiency frontier. The trade-off between the two efficiencies leads to the selection of the design with the maximum value of one efficiency, given the other is fixed.

Because of the structure of the locally optimum designs, the equally weighted combinations of two designs only have six points of support. A plot shows how the structure of the six-point design with highest minimum efficiency suggestively relates to those of the locally optimum designs.

Key words: design efficiency, locally optimum design, maximin design, Michaelis-Menten model

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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Quasi-Latin designs for experiments in rectangles

Rosemary A. Bailey

Abstract Yates [4] and Rao [3] generalized Latin squares to quasi-Latin squares. A factorial set of treatments is applied to the cells of a square array in such a way that no treatment occurs more than once in any row or column and that the partial confounding with rows and with columns corresponds to standard factorial effects. Healy [2] extended the idea to 2^n experiments in a rectangle whose dimensions are both powers of 2. In recent joint work with Brien, Thao and Tolund [1], I have substantially extended these methods to deal with various sizes of rectangles, or collections of rectangles, which commonly occur in experiments in glasshouses. The user has considerable freedom over the choice of confounding patterns.

Key words: factorial design, row–column design, experimental design

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
10–14 June 2013, Łagów Lubuski, Poland

Optimal designs for full and partial likelihood information

Maria Konstantinou, **Stefanie Biedermann** and Alan Kimber

Abstract Survival data are often modelled through Cox's proportional hazards model, see, e.g., [1], including covariates. We develop a general framework for designing such experiments. We first derive an expression for the asymptotic covariance matrix of Cox's partial likelihood estimator for the coefficients of the covariates. Our approach is then illustrated through an application to the special case of only one covariate, where we find a necessary condition for design optimality.

There are only two papers in the literature so far considering optimal designs for Cox's model, i.e. [2] and [4]. Our results generalise those by [2] in several directions. We derive minimum variance designs for different censoring mechanisms, and both discrete and interval design spaces, and compare these designs with the corresponding designs found using the full likelihood information; see [3]. We demonstrate numerically and analytically that the latter designs are highly efficient for estimation in the partial likelihood model, in particular in the situation of heavy censoring. We also compare our results with those reported in [4], and explain the differences.

Key words: censoring, Cox's proportional hazards model, partial likelihood

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Checking linear regression models taking time into account

Wolfgang Bischoff

Abstract Linear regression models are usually checked by a lack-of-fit (LOF) test to be sure that the model is at least approximately true. In many practical cases data can only be sampled sequentially. Such a situation can appear in industrial production when goods are produced one after the other. So as time goes by, the mean may also depend on time, i.e., the mean is not only a function of the covariates, but it may be also a function of time. This dependence over time is difficult to detect by a conventional LOF test. Tests based on the residual partial sum process are then more suitable. Therefore, in such a situation we suggest applying both an LOF test, e.g., the F-test, and a test based on the residual partial sum process, e.g., a test of Kolmogorov type. When the linear regression model is not rejected by either test, least squares estimation can be used to estimate the parameters of the linear regression model. For the situation just discussed, we are here interested in a design with which we can efficiently run the two tests and estimate the linear model. Usually, classical optimal designs and LOF-optimal designs do not have these properties.

Key words: model checks with respect to covariates and time, F-test, test of Kolmogorov type, residual partial sum process, D-optimal design, uniform design, LOF-optimal design, D-optimal 1/2-LOF efficient design

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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Optimal sample proportion for a two-treatment clinical trial in presence of surrogate endpoints

Atanu Biswas, Buddhananda Banerjee and Saumen Mandal

Abstract The use surrogate endpoints is a very popular practice in medical research when availability of true endpoints is less due to cost and/or time constraint. Here we obtain optimal proportion of allocation among the two competing treatments based on both true and surrogate endpoints. As the optimum true-surrogate sample proportion by minimizing the variance of estimated parametric function, e.g. treatment difference, lies in boundary, we obtain cost optimized choices for these parameters. These are further used in a two stage optimization for the proportion of allocation to the treatments.

Key words: surrogate endpoint, optimal allocation, two stage optimization

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Experimental designs for different approaches to simultaneous equations

Víctor Casero-Alonso and Jesús López-Fidalgo

Abstract Models with simultaneous equations are considered. These models are widely used in experimental economics and business, among many other fields. In particular, a model with two equations is considered in this work. One of the explanatory variables (exogenous) of the first equation is the response variable (endogenous) of the second equation. In the second equation there is a controllable variable, which is being designed. If the second equation is plugged into the first one the designable variable is now in both equations. These are two different models producing different maximum likelihood estimators and therefore information matrices and optimal designs. D-optimal and c-optimal designs for both approaches are computed and compared, both in a discrete and a continuous design space. The different cases of completely known correlation and a correlation dependent of estimable coefficients are considered and compared. A sensitivity analysis is performed to have an idea of the risk in choosing wrong nominal values of the parameters. In the discrete design space case bounds for the weight of the D–optimal design and for D-efficiency are obtained.

Key words: approximate design, D–optimal designs, c–optimal designs, simultaneous equations models, structural equations models.

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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Optimal designs for multiple-mixture by process variable experiments

Roelof L. J. Coetzer and Linda M. Haines

Abstract Experiments for mixtures have been extensively investigated. Models and attendant designs for settings involving crossed mixtures and, separately, mixture-of-mixtures are well documented [1]. In industry, however, experiments involving multiple mixtures, i.e., both crossed mixtures and mixtures-of-mixtures, together with process variables, which may change the effect of the blending properties of the mixture components on the response of interest, occur frequently. The mixture variables are typically subject to lower and upper constraints. In this talk response surface models in more than two sets of mixture variables, including multiple-mixtures and sub-compositions, in combination with process variables, are developed and the corresponding *D*-optimal designs are constructed. The work is motivated by an industrial problem where the amount of gas produced in a coal gasification plant depends crucially on the distribution of the size of the coal particles, on the composition of the coal feed and of the ash, which is a sub-component of the coal, and on a number of process variables [2]. The model building process which proceeds stepwise, and is mirrored in design construction, is illustrated by means of the coal gasification process. The approach can be readily extended to large-scale industrial experiments but some care in obtaining designs for individual mixtures is clearly required.

Key words: multiple mixture experiments, process variables, *D*-optimal designs

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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Fast algorithms to generate individualized designs for the mixed logit choice model

Marjolein Crabbe, Deniz Akınç and Martina Vandebroek

Abstract The mixed logit choice model has become the common standard to analyze choice behavior. Efficient design of the corresponding choice experiments is therefore indispensable to obtain precise knowledge of consumers' preferences. Accounting for the individual-specific coefficients in the model, this research advocates an individualized design approach. Individualized designs are sequentially generated for each person separately, using the answers from previous choice sets to select the next best set in a survey. In this way they are adapted to the specific preferences of an individual and therefore more efficient than an aggregate design approach. In order for individual sequential designs to be practicable, the speed of designing an additional choice set in an experiment is obviously a key issue. This paper introduces three design criteria used in optimal test design, based on Kullback-Leibler information, and compares them with the well-known $\mathscr{D}$-efficiency criterion to obtain individually adapted choice designs for the mixed logit choice model. Being equally efficient to $\mathscr{D}$-efficiency and at the same time much faster, the Kullback-Leibler criteria are well suited for the design of individualized choice experiments.

Key words: discrete choice, mixed logit, individualized design, $\mathscr{D}$-efficiency, Kullback-Leibler information

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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A-optimal and A-efficient designs for discrete choice experiments

Fangfang Sun and **Angela Dean**

Abstract Discrete choice experiments are used widely in areas such as marketing, city planning, and medical care, etc., for the purpose of determining consumer preference to products and services. In a "forced choice" experiment, respondents are shown "choice sets" of "options" or "profiles". The profiles represent a selection of products or services and are made up of a number of attributes (factors) at various levels and are similar to "treatment combinations" in a factorial experiment. Each respondent is asked to select their most preferred profile from each choice set. Information about the choices made can be used to infer the effects of the individual attribute levels on consumer preference as well as interactions. In turn, this attribute information can be used in the future to design new products more tailored to the population requirements.

In this talk, the multinomial logit model (MNL) is used to model the probability that a particular option is chosen from a given finite choice set. The systematic component of the utility of each option is modelled in terms of parameters representing the main effects and interactions of the attributes. An A-optimal design is one which minimizes the variance of the contrasts of interest of these parameters.

Since the MNL model is a non-linear model, the optimal design despends upon the parameter values. A common approach is to construct designs for the particular case of equally attractive options. For this case, a lower bound is derived for the A-value of a discrete choice design. Some examples of designs acheiving the lower bound are given. For situations when the bound cannot be achieved, and when a complete search for the optimal design is not feasible, the model is linearized and a "factor loading" approach is taken to suggest options that should be included in a choice set. It is shown that this approach leads to highly A-efficient designs. This approach can be extended to construction of designs under the assumption of unequally attractive options.

Key words: A-optimal, discrete choice experiment, efficiency bound, factor analysis, multinomial logit model

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Objective Bayesian model discrimination in follow-up experimental design

Guido Consonni and **Laura Deldossi**

Abstract Occasionally, screening designs do not lead to unequivocal conclusions regarding which combinations of factors (models), are active. From a Bayesian viewpoint, this means that the posterior distribution on model space will be fairly evenly spread out over a few models. In these circumstances, a follow-up design is needed, the objective being of choosing extra runs in order to solve, or at least alleviate, this ambiguity.

In order to achieve this aim we compute, for each model, the posterior predictive distribution for the extra runs, and evaluate the Kullback-Leibler (KL) divergence between all pairs of predictive distributions. Finally, all KL-divergences are averaged using weights given by the product of the corresponding pairs of posterior model probabilities. This average defines a model discrimination criterion, see [6], which we maximize over all possible designs for the extra runs.

Adopting an objective Bayes perspective, we make use of a multiplicity-correction prior on model space, together with a robust objective model choice prior on model specific parameters to obtain the posterior probability of each candidate model. On the other hand, the predictive distributions under each model are obtained using standard noninformative estimation priors.

Our analysis produces closed form expressions for the Bayes factors, and the allied posterior model probabilities, as well as for the model discrimination criterion. This, in turn, allows an efficient implementation of the optimization algorithm. When applied to real data, our method, which is fully automatic, produces results which compare favorably to previous analyses based on subjective weakly informative priors.

Key words: model discrimination, objective Bayes, Kullback-Leibler divergence

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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Optimal design of experiments for delayed responses in clinical trials

Vladimir Dragalin

Abstract The efficiency of optimal design of experiments when the primary endpoint is immediate is well documented. Often, however, in practice of clinical trials there will be a delay in the response of clinical interest. Since few patients will have experienced the endpoint in the early stages of a trial there may be little information that can be used in making a decision to modify the trial's course. But almost always, the clinical efficacy endpoint will be measured at early time points and these measurements might be correlated with, and predictive, for the primary long-term endpoint. The focus of the definitive analysis is still the primary clinical endpoint and not these short-term endpoints. The latter may be used just as necessary condition of potential treatment effect and can enhance the interim decision of dropping a treatment arm or changing the treatment allocation. The research questions are: what is the optimal number of measurements per patient and what are the optimal time intervals between these measurements? A major benefit of modeling relationships between early and late endpoints is that it makes for stronger interim assessments of long-term endpoints and therefore improves the efficiency of adaptive designs.

We introduce the model for the primary endpoint as a parsimonious sigmoid Emax dose-response model. This model has been used in many publications on adaptive dose ranging designs. We consider also a parametric model for the time-profile of the repeated measurements per patient. Locally optimal designs and information matrices for these special non-linear mixed effects models are defined. A cost for repeated measurements is proposed and the optimality criterion is maximized taking into account both the cost for patient recruitment and the cost incurred in taking a single measurement. Additional technical details in implementing the adaptive version of the optimal designs in this situation are presented.

Key words: adaptive design, clinical trial, delayed response, interim analysis, optimal design of experiments

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Elemental information matrices in the design of dose-response studies with time-to-event end points

Valerii Fedorov and Xiaoqiang Xue

Abstract For the clinical trials, in which the time to the treatment-related event is the primary end point, the study is often terminated before the event is observed for all participating subjects. For instance, subjects enter the study at random moments after the study is open but a trial ends at either a pre-determined time or when a pre-determined number of events is observed. The random censoring model is a natural choice for that type of clinical trials. One of the basic steps in optimal design is to find the elemental information matrix. In this presentation we consider the derivation of elemental information matrices for enrollment times that have Gamma and Beta distributions and focus on the exponential time-to-event distribution.

Key words: clinical trials, random censoring model, elemental information matrix

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On the universal optimality of circular uniform weakly neighbour balanced designs under the model with residual effects

Katarzyna Filipiak

Abstract In the class of circular repeated measurements designs [3] and [2] showed that circular balanced uniform designs are universally optimal under the model with residual effects. Our aim is to extend these results by proving the universal optimality of circular weakly neighbour balanced uniform designs under the model with residual effects. Circular weakly neighbour balanced designs were defined and characterized as universally optimal under an interference model in [1]. These designs have a nice property that they require a much lower number of experimental units. We also give a construction method of such designs.

Key words: repeated measurement design, universal optimality, uniform design, circular weakly neighbor balanced design

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Optimal design for the bounded log-linear regression model

HaiYing Wang, Andrey Pepelyshev and **Nancy Flournoy**

Abstract Wang and Flournoy [1] developed estimation procedures for a log-linear regression model which has bounded response with unknown bounds on its domain and non-homogeneous variance, as an alternative to the four parameter logistic model. In the present paper, we theoretically obtain that for the bounded log-linear regression model with five unknown parameters, an optimal design that minimizes an information based criterion consists at most five design points including the two boundary points of the design space. For a regular model, five is usually the lower bound of the number of design points required for estimability if a model has five unknown parameters, but for our model it is an upper bound. Specifically, the *D*-optimal design does not depend on the two parameters representing the boundaries of the response but it does depend on the variance of the error. Furthermore, if the error variance is known and bigger than a constant, we prove that the *D*-optimal design is the two-point design supported at boundary points of the design space with equal weights. This gives an example where the number of design points is less than the number of unknown parameters but all the parameters are still estimable. Numerical examples and simulation results are provided.

Key words: bioassay, D-optimality, non-linear model, non-regular model, optimal design

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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Randomly reinforced urn designs whose allocation proportions converge to arbitrary prespecified values

Andrea Ghiglietti and Anna Maria Paganoni

Abstract There are many randomization procedures in clinical trials in which the proportion of patients allocated to treatments converges to a fixed value. Some of these procedures are adaptive and the limiting proportion can depend on the treatments' behaviors. We focus on a particular class of adaptive designs, described in terms of randomly reinforced urn models that were studied and extended to the case of continuous responses by [3]. In that work it was proved that the probability to allocate units to the best treatment converges to one as the sample size increases. We construct a new randomly response urn design able to target fixed asymptotic allocations that are function of treatments' performances. The model and the main convergence theorem are presented in [1]. We prove asymptotic results for the process of colors generated by the urn and for the process of its compositions, concerning almost sure convergence and the convergence rates [2]. Applications to sequential clinical trials and connections with response-adaptive design of experiments are considered, as well as simulation studies concerning the power function of a testing hypothesis procedure that naturally arises from this statistical framework are detailed.

Key words: response adaptive designs, randomly reinforced urns, asymptotic power

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Kernels and designs for modelling invariant functions: From group invariance to additivity

David Ginsbourger, Nicolas Durrande, and Olivier Roustant

Abstract We focus on kernels incorporating different kinds of prior knowledge on functions to be approximated by Kriging. A recent result on random fields with paths invariant under a group action [4] is extended to combinations of composition operators. This generalisation allows, e.g., to characterise the class of positive definite kernels leading to random fields with additive paths [2, 3]. A discussion follows on implications on design of experiments, and it is shown numerically in the case of additive kernels that so-called "axis designs" and their equivalent class for Kriging outperfom latin hypercubes [1] in terms of the IMSE criterion [5].

Key words: design of computer experiments, Gaussian processes, Kriging

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Differences between analytic and algorithmic choice designs for pairs of partial profiles

Heiko Großmann

Abstract Choice experiments are widely used for measuring how the attributes of goods or services influence preference judgments. To this end, a suitable experimental design is used to combine attribute levels into options or profiles and to further arrange these into choice sets. Often incomplete descriptions of the options, which are known as partial profiles, are used in order to reduce the amount of information respondents need to process. For the situation where the choice sets are pairs, where only the main effects of the attributes are of interest and where the attributes fall into two groups such that all attributes within a group have the same number of levels, optimal designs which were obtained analytically are compared with algorithmically generated designs. For the situations considered, there are sometimes substantial differences between the efficiencies of the two types of design.

Key words: choice experiments, paired comparisons, partial profiles, optimal design

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Approximate Bayesian Computation Design (ABCD), an introduction

Markus Hainy, Werner G. Müller and Henry P. Wynn

Abstract We propose a new technique of generating optimal designs by means of simulation in situations where the probability model is not easily available. The method combines ideas from approximate Bayesian computation (ABC), see e.g. [1], and optimal design of experiments. It allows great flexibility in the employed criteria and models. The criteria depend on the posterior distribution of the parameters, hence the need to approximate the posterior distribution by using ABC techniques.

We illustrate the idea by a simple expository example for which we also assess the approximation quality at different points in the design space by varying the precision of the ABC approximation.

Key words: simulation-based design, approximate Bayesian computation, intractable likelihood

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Barycentric algorithm for computing approximate D-optimal designs with simultaneous size and cost constraints

Radoslav Harman

Abstract Consider a linear regression model with uncorrelated errors and a finite experimental domain $\mathscr{X}$. Let $c(x)$, $x \in \mathscr{X}$, be coefficients proportional to the costs associated with trials in individual design points. In the talk, we will describe a monotonically convergent "barycentric" algorithm for computing approximate *D*-optimal experimental designs in the class Ξ_c of all designs ξ that satisfy both the size constraint $\sum_{x\in\mathscr{X}} \xi(x) = 1$ and the total cost constraint $\sum_{x\in\mathscr{X}} c(x)\xi(x) \leq 1$. The algorithm is derived by a systematic approach from the multiplicative algorithm for computing approximate *D*-optimal designs on the convex hull of a finite set of positive semidefinite matrices (e.g., [1]).

Key words: D-optimal design, multiplicative algorithm, barycentric algorithm, size constraints, cost constraints

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Optimal design for count data with binary predictors in item response theory

Heinz Holling, Ulrike Graßhoff and Rainer Schwabe

Abstract The Rasch Poisson counts model allows for the analysis of mental speed which represents a basic component of human intelligence. An extended version of the Rasch Poisson counts model, which incorporates covariates in order to explain the difficulty, provides a means for modern rule-based item generation. After a short introduction into the extended Rasch Poisson counts model we will develop locally D-optimal calibration designs for this model. Therefore, the Rasch Poisson counts model is embedded in a particular generalized linear model. Finally, the robustness of the derived designs will be investigated.

Key words: Rasch Poisson counts model, generalized linear model, optimal design

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An efficient algorithm of generating space-filling designs with linear inequality constraints on the design region

Bradley Jones and Ryan Lekivetz

Abstract Latin Hypercube designs (LHD) are in standard use as plans for deterministic computer experiments. However, these designs depend on the ability of the investigator to set each factor independently of all the others. To be specific, the implied design region for an LHD is a hypercube. However, there are cases where some parts of such a design region may be inaccessible or even nonsensical. In such cases it is useful to be able to produce a design that is both space-filling while obeying linear inequality constraints on the design region.

In this talk we present an efficient algorithm for generating space-filling designs in an arbitrary k-dimensional polytope. We first generate a random sample of a large number of points inside the polytope. Then we use a fast clustering algorithm to create n clusters of points where n is the desired number of design points. The design is then composed of the cluster centroids of each of the clusters.

This construction approach leads to some desirable properties. Using cluster centroid forces the design points away from each other in the space of the design. Using a random sample of points results in designs that do not replicate in projection. When applied to design regions without constraints, this design approach yields designs that are nearly orthogonal.

We supply several examples including designs on a simplex. We also compare our designs to maximin LHDs for various measures of space-fillingness.

Key words: clustering, polytope sampling, space-filling

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Optimal crossover designs with interactions between treatments and experimental units

Joachim Kunert, Andrea Bludowsky and John Stufken

Abstract The paper considers a model for crossover designs with carryover effects and a random interaction between treatments and experimental units. Under this model, two observations of the same treatment on the same unit are correlated and therefore provide less information than two observations of the same treatment on different units. This removes a weakness of the traditional model.

The introduction of the interaction, however, makes the determination of optimal designs much harder than in the traditional model. Generalizing the results of [1], the present paper uses Kushner's method, see [2], to determine optimal approximate designs. We restrict to the case where the number of periods is less or equal to the number of treatments.

We determine the optimal designs in the important special cases that the number of periods is 3, 4 or 5. It turns out that the optimal designs depend on the variance of the random interactions and in most cases are not binary. However, we can show that neighbor balanced binary designs are highly efficient, regardless of the number of periods and of the size of the variance of the interaction effects.

Key words: universal optimality, carryover effects, treatment effects

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On efficiency of designs for processes of Ornstein-Uhlenbeck type

Vladimír Lacko

Abstract Recently a number of published papers dealt with optimization of experiments for processes governed by specified variants of a linear stochastic differential equation of the form

$$\mathrm{d}X(t) = [a(t)X(t) + b(t)]\mathrm{d}t + \sigma(t)\mathrm{d}W(t), \quad X(0) = X_0 \text{ fixed}, \quad t \geq 0, \qquad (1)$$

see, for instance, [1, 2, 3].

For a given sampling design $t_1, \ldots, t_n$, $0 < T_* \leq t_1 < \ldots < t_n \leq T^*$, we formulate the model (1) in terms of nonlinear regression with correlated Gaussian observations. Optimization of such experiments can be challenging. Therefore, instead of computation of optimal designs, we assess the quality of a finite-point design with respect to the observation of the full trajectory. We show that the conclusions hold true also for an extended class of more complicated processes. We demonstrate the results on a Gompertz model with applications in mammography scheduling in the case of tumour detection.

Key words: stochastic differential equation, experimental design, Fisher information, Gompertz model of tumour growth

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Approximation of the Fisher information matrix for nonlinear mixed effects models in population PK/PD studies

Sergei Leonov and Alexander Aliev

Abstract We discuss different types of approximations of the individual Fisher information matrix used in population optimal design software tools and describe a Monte Carlo option in the PkStaMp library which constructs optimal sampling schemes for population pharmacokinetic (PK) and pharmacodynamic (PD) studies.

Key words: population PK/PD model, optimal sampling scheme, nonlinear mixed effects

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
10–14 June 2013, Łagów Lubuski, Poland

Optimal design for accelerated failure time models

R. Del-Campo, **J. Lopez-Fidalgo** and M.J. Rivas-Lopez

Abstract Proportional Hazards (PH) models have been widely used to analyze survival data. An important drawback is that the restrictions for this model are satisfied just for a few probability distributions. Accelerated Failure Time (AFT) models are an alternative to the PH model with more relaxed conditions. AFT models focus on the direct effect of the explanatory variables on the survival time instead of hazard function as in the PH models. This characteristic allows for an easier interpretation measuring directly the effect of the correspondent covariate on the survival time. AFT models has not been used much for analyzing clinical trial data, although it is fairly common in the field of manufacturing.

Let $x = (x_1, x_2, \ldots, x_p)$ be the vector of covariates. The model is written mathematically as

$$S(t|x,\theta) = S_0(t/\eta(x,\theta)),$$

where S_0 is the *baseline survival function* and $\eta(x,\theta)$ is an *acceleration factor*, which speeds up the effect of the survival time in the survival function. The acceleration factor is typically the exponential of a linear relationship,

$$\eta(x,\theta) = \exp(\theta_1 x_1 + \theta_2 x_2 + \cdots + \theta_p x_p).$$

Under an AFT model the covariate effects are assumed to be constant and multiplicative on the time scale, that is, the covariate impacts on survival by a constant factor (acceleration factor).

Optimal designs are computed for this model.

Key words: accelerated life models, optimal design, survival analysis

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c-optimal designs for the Bivariate Emax model

Bergrun Tinna Magnusdottir

Abstract In this presentation we explore locally c-optimal designs for non-linear, bivariate response models. A General Equivalence Theorem (GET) is provided and we discuss the influence from model and (co)variance parameters on the designs. The focus is on designs for dose finding studies.

Finding a suitable dose is among the most difficult tasks during clinical development of a new drug. In early phases dose finding studies usually focus on finding a safe dose. Safety variables are thus of main interest. In later phases the focus is shifted towards efficacy. Typically a primary efficacy variable is defined and modeled. Various dose-response models have been suggested. For continuous responses among the most successful ones is the Emax model. In this presentation both efficacy and safety are considered simultaneously and the Emax model is extended to a model with a bivariate response, one response being a primary efficacy variable and one being a primary safety variable. This model is referred to as the Bivariate Emax model. In this presentation we explore locally c-optimal designs for the Bivariate Emax model and a simplified version of it. More specifically we explore locally c-optimal designs that minimize the asymptotic variance for the estimate of the dose that maximizes the patient's utility. The utility is a function of the efficacy and safety variables and referred to as the Clinical Utility Index (CUI).

Theorems and tables that can be used for constructing some locally c-optimal designs for the Bivariate Emax model and the simplified version of it are provided. Special focus is on the influence the covariance structure has on the locally c-optimal designs. For the Bivariate Emax model it is concluded that when the correlation between the primary efficacy and the primary safety variable is sufficiently small two point locally c-optimal designs can be found, else an extra design point is needed.

Key words: c-optimal designs, dose-finding, efficacy and safety, bivariate Emax model, clinical utility index

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On optimality of neighbor designs under interference models

Augustyn Markiewicz

Abstract The concept of neighbor designs was introduced and defined by Rees (1967) who gave also some methods of their construction. Henceforth many methods of construction of neighbor designs as well as of their generalizations are available in the literature. However there are only few results on their optimality. Therefore the aim of the talk is to give an overview of study on this problem. It will include some recent results on optimality of specified neighbor designs under various linear models. or example we study optimality of circular weakly neighbor balanced designs. Under the interference model universal optimality of such designs with additional property being uniform on the blocks is proved in Filipiak and Markiewicz (2012).

Key words: neighbor designs, circular balanced design, universal optimality

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10–14 June 2013, Łagów Lubuski, Poland

Sample size calculation for diagnostic tests in generalized linear mixed models

Tobias Mielke and Rainer Schwabe

Abstract Intra-cluster correlations have to be taken into account for calculating the stochastic behavior of estimators in diagnostic studies with repeated measurements in individuals. One approach of inducing the intra-cluster correlation is provided by generalized linear mixed models. The inverse of the Fisher information matrix as the asymptotic covariance of the maximum likelihood estimator is in these models of interest for determining the required sample size in statistical tests. Approximations of the Fisher information matrix are needed, as the likelihood function in mixed effects models generally contains integrals which cannot be simplified in a closed formula. Experimental designs are hence usually based on certain approximations, what might limit their efficiency with respect to the true model. The influence of different approximations of the Fisher information matrix on the needed sample size for proving non-inferiority in diagnostic studies will be demonstrated in this presentation.

Key words: generalized linear models, mixed effects models, Fisher information, sample size calculation, non-inferiority tests

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Randomization based inference for the drop-the-loser rule

Nancy Flournoy, Arkaitz Galbete, **José Antonio Moler** and Fernando Plo

Abstract In the framework of clinical trials, legal and ethical restrictions make a population model unrealistic for sampling, see [3]. Randomization tests, see [2], are a viable alternative to classical inference. Their theoretical properties depend heavily on the random rule used to allocate patients in treatments, so that ad-hoc theoretical studies are necessary for each allocation design. In this paper, we obtain theoretical results for randomization tests when the drop-the-loser rule is used, see [1].

Key words: clinical trial, adaptive design, randomization-based inference

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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D-optimal designs for lifetime experiments with exponential distribution and censoring

Christine H. Müller

Abstract The approach of Kiefer-Wolfowitz [1, 2] is used to construct optimal designs for lifetime experiments with exponential distribution and censoring. The determinant of the asymptotic covariance matrix of the maximum likelihood estimator [3] is used as the design criterion. If the expected life time is simply reciprocal to the stress, then the optimal design does not depend on the unknown parameter and the censoring. However, the situation is more complicated for the more frequent assumption that the logarithm of the expected lifetime is linear in the stress. Conditions are given here where the locally D-optimal designs for experiments with censoring coincide with those in the classical approach of linear regression with normally distributed errors and without censoring. In particular, this is the case when the censoring variable is not too small and the slope of the regression is not too large.

Key words: lifetime experiment, exponential distribution, D-optimal design

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10–14 June 2013, Łagów Lubuski, Poland

Bayesian optimal design of blocked and split-plot experiments for fixed effects and variance component estimation

Kalliopi Mylona, Peter Goos and Bradley Jones

Abstract Many industrial experiments involve one or more restrictions on the randomization. The most commonly used experimental designs in those cases are blocked designs and split-plot designs, where the experimental runs are performed in groups. In general, modeling data from blocked and split-plot response surface experiments requires the use of generalized least squares and the estimation of two variance components. The literature on the optimal design of blocked and split-plot response surface experiments, however, focuses entirely on the precise estimation of the fixed factor effects and completely ignores the necessity to estimate the variance components as well. To overcome this problem, we propose a new Bayesian optimal design criterion which focuses on both the variance components and the fixed effects. A novel feature of the criterion is that it incorporates prior information about the variance components through log-normal or beta prior distributions. In our algorithm for generating optimal blocked and split-plot designs, we implement several lesser-known but computationally efficient quadrature approaches for the numerical approximation of the new optimal design criterion.

Key words: blocked design, Gaussian quadrature, restricted maximum likelihood (REML), split-plot design, variance component estimation

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Convergence of an algorithm for constructing minimax designs

Hans Nyquist

Abstract An optimum design of an experiment minimizes a criterion function of the information matrix. When using nonlinear models, optimal designs generally depend on unknown parameters so that it is not possible to construct an optimum design. There are several approaches to deal with this problem. One approach is using optimum in average designs, sometimes referred to as Bayesian designs. In this approach a prior distribution over several parameter values is used to form a weighted criterion function which is minimized. Another approach is using minimax designs, which minimizes the maximum of the criterion function as the parameters are varied over a specified subset of the parameter space. Unfortunately, construction of minimax designs has shown to be numerically intractable in many applications. The H-algorithm is a new iterative algorithm that utilizes the relation between minimax designs and optimum in average designs based on a particular prior distribution called the least favorable distribution. If a least favorable distribution was known it would also be possible to construct a minimax design. Unfortunately, a least favorable distribution is rarely known. However, there exist characterizations of least favorable distributions and therefore, it is also possible to find prior distributions that are closer to a least favorable distribution. In each iteration of the H-algorithm, one first searches for a prior distribution that is closer to the least favorable distribution and then finds the optimum in average design with respect to this prior. In this presentation we describe the H-algorithm in more detail, the convergence of the algorithm is discussed, and its application is illustrated in numerical examples. It is found that the conditions for convergence are mild and that it is fairly easy to apply the algorithm.

Key words: minimax designs, optimum on average designs, least favorable distribution

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Extended optimality criteria for optimum design in nonlinear regression

Andrej Pázman and Luc Pronzato

Abstract Among the major difficulties that one may encounter when estimating parameters in a nonlinear regression model are the non-uniqueness of the estimator, its instability with respect to small perturbations of the observations and the presence of local optimizers of the estimation criterion. Even when the design relies on small-sample properties of the estimator, a non-overlapping assumption is used (see [1, p. 66, 157]) which permits to avoid the aforementioned difficulties. Also, taking the (intrinsic and parameter-effects) curvatures of the model into account, e.g. as in [2], is not sufficient since curvatures are local measures of nonlinearity while it is the global behavior of the expectation surface that is responsible for those difficulties.

We show that these estimability issues can be taken into account at the design stage, through the definition of suitable design criteria. Extensions of E, c and G-optimality criteria will be considered, which, when evaluated at a given θ^0 (local optimal design), account for the behavior of the model response $\eta(\theta)$ for θ far from θ^0. In particular, they ensure some protection against close-to-overlapping situations where $\|\eta(\theta) - \eta(\theta^0)\|$ is small for some θ far from θ^0. These extended criteria are concave, their directional derivative can be computed and necessary and sufficient conditions for optimality (Equivalence Theorems) can be formulated. They are not differentiable, but a relaxation based on maximum-entropy regularization is proposed to obtain concave and differentiable alternatives. When the design space is finite and the set of admissible θ is discretized, their optimization forms a linear programming problem.

Key words: estimability, overlapping, maximum-entropy regularization

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Optimal design for multivariate models with correlated observations

Andrey Pepelyshev

Abstract Consider the common linear regression model

$$y(x) = \theta_1 f_1(x) + \ldots + \theta_m f_m(x) + \varepsilon(x), \quad x \in X \subset \mathbb{R}^d \tag{1}$$

where functions $f_1(x), \ldots, f_m(x)$ are linearly independent and continuous, a random error field $\varepsilon(x)$ has the zero mean with the covariance kernel $K(x,x') = \mathrm{E}[\varepsilon(x)\varepsilon(x')]$, parameters $\theta_1, \ldots, \theta_m$ are unknown and the explanatory variable x varies in a compact design space X. Suppose that N observations $y_1, \ldots, y_N$ can be taken at experimental conditions $x_1, \ldots, x_N$ to estimate the parameters in the model ().

To study the design problem of estimating θ in the case of multivariate models with correlated observations, the methodology proposed in [1, 2] can be applied. The numerical procedure of constructing asymptotic optimal and exact designs is proposed. It is shown that exact N-point designs generated from these asymptotic designs for any desired N have a very good efficiency. The performance of the procedure is illustrated in the case of spatial models.

Key words: correlated observations, asymptotic optimal design, spatial design

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10–14 June 2013, Łagów Lubuski, Poland

Optimal designs for the prediction of individual effects in random coefficient regression

Maryna Prus and Rainer Schwabe

Abstract Random coefficient regression models, which incorporate variations between individuals, are getting more and more popular in many fields of application, especially in biosciences. Besides the estimation of population parameters describing the mean behavior across all individuals (i) the prediction of the individual response as well as of (ii) the individual deviations from the population mean response has attracted larger interest.

For the determination of optimal designs for estimating the population parameters some analytical and practical results may be found in the literature. We propose optimal designs for (i) as well as (ii) in random coefficient models. If the mean population parameters are unknown, which is typically the case, the mean squared error for (i) and (ii) do not coincide and the design optimization leads to substantially different results. For simplicity, we consider the case where all individuals are treated in the same way. If the population parameters were known, Bayesian optimal designs would be optimal (see [1]). While the optimal design for the prediction of the individual responses differ from the Bayesian optimal design proposed in the literature (see [2]), the latter designs remain optimal if only the individual deviations from the mean response are of interest. The obtained theoretical results will be illustrated by a simple example.

Key words: random coefficient regression, individual parameters, individual deviations, prediction, unknown population mean, individual designs

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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D-optimum input signals for systems with spatio-temporal dynamics

Ewaryst Rafajłowicz and Wojciech Rafajłowicz

Abstract Our aim is to provide optimality conditions for optimal input signals that are D-optimal for parameter estimation in linear systems described by partial differential equations. They are derived from the variational approach that provides constructive optimality conditions. We also reveal the space-time structure of optimal input signals. We also derive optimality conditions for input signals for identifying parameters in systems described by ordinary differential equations.

Several results on topics similar to those considered here can be found in [3], where the so called frequency-domain synthesis is discussed. In this talk we provide results that differ from that presented in [4] in the following respect: here, we obtain the optimality conditions directly, using the variational approach. As result, we can provide a simple algorithm for input signal calculation when one parameter is estimated that is based on solving an algebraic eigenvalue problem.

The accompanying problem of sensor allocation [2] has received much attention in recent years (see [5] and [1] for interesting results on moving sensors trajectories).

Key words: optimal input signal, D-optimality, variational approach

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
10–14 June 2013, Łagów Lubuski, Poland

From Markov moves in contingency tables to linear model estimability

Roberto Fontana, **Fabio Rapallo** and Maria Piera Rogantin

Abstract Saturated fractions play an important role in Design of Experiments. Given a model, saturated fractions have the minimal number of points allowing the estimation of all parameters of the model. Using Algebraic Statistics, we characterize saturated fractions of a factorial design in terms of the circuits of the design matrix and we define a criterion to actually check whether a given fraction is saturated or not, avoiding the computation of the determinant of the corresponding design matrix.

Algebraic Statistics is a discipline encompassing the application of Combinatorics and Polynomial algebra to Statistics. Its most prominent results concern essentially the analysis of contingency tables and Design of Experiments. In this work, we merge such two approaches. First, we identify a factorial design with a contingency table whose entries are the values of the indicator function of the fraction, i.e., they are equal to 1 for the fraction points and 0 otherwise. This implies that a fraction can also be considered as a subset of cells of the table. Second, we apply tools from Algebraic Statistics to characterize the saturated fractions of factorial designs.

The definition of circuits is the core of our algorithm, and it has already been considered in the framework of contingency tables for the definition of robust procedures for outliers detection, but limited to two-way tables. The circuits are a special class of Markov moves associated with the design matrix of the model.

This presentation is mainly focused on the theoretical characterization of saturated fractions. Nevertheless, we also discuss some applications, especially to simulated designs.

Key words: circuits, estimability, linear models, simulation

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10–14 June 2013, Łagów Lubuski, Poland

Adaptive Bayesian design with penalty based on toxicity-efficacy response

William F. Rosenberger and Lei Gao

Abstract The penalized local D-optimal design is introduced by Dragalin and Fedorov (2006). We extend the method to the Bayesian realm for the bivariate Gumbel model. Then we conduct a simulation study to compare our method with the trade-off methods of Thall and Cook (2004). Various measures are employed to present a thorough understanding of both the methods. Our method is more favorable in terms of consistency across simulations and information gain.

Key words: adaptive designs, efficacy-toxicity responses, penalty function

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10th International Workshop on *Model-Oriented Data Analysis and Optimum Design*
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Computing exact D-optimum designs by mixed integer second order cone programming

Guillaume Sagnol and Radoslav Harman

Abstract Consider a design space X with $s < \infty$ elements, and positive semidefinite $m \times m$ matrices $H_1, ..., H_s$ representing the information that can be gained from the trials in individual design points. Let the experimental design be represented by an s-dimensional vector $\mathbf{w}$ of weights, and assume that the quality of $\mathbf{w}$ is measured by the criterion of D-optimality defined as

$$\Phi_D(\mathbf{w}) = \det^{1/m}\left(\sum_{i=1}^{s} w_i H_i\right).$$

In this talk we will show that the function Φ_D is *second-order cone representable*, i.e. its hypograph can be represented by a set of second order cone inequalities. As a result, the method of *second order cone programming* (SOCP) can be used to compute approximate D-optimal designs with any system of linear constraints on the weight vector $\mathbf{w}$. More importantly, the proposed characterization of Φ_D allows us to compute exact optimal designs, i.e. to solve design problems in which the weights are constrained in the integral domain. This is possible thanks to high quality branch-and-cut solvers that are specialized to solve *mixed integer second order cone problems* (MISOCP), i.e. second order cone optimization problems in which some of the variables are constrained in the integral domain. In contrast, the previous *maxdet programming* method relies on semidefinite programming (SDP), and there is currently no reliable solver handling SDP with integer variables.

We will provide experimental results showing that (i) For continuous problems with constraints on the weights, the SOCP method is numerically more stable than the previous approach of maxdet programming; (ii) The MISOCP approach can find a provably optimal design for many models where the KL-exchange algorithm misses the optimum; (iii) The MISOCP method finds exact optimal designs much faster than the raw branch-and-bound approach originally proposed by Welch.

Key words: D-optimal designs, exact designs, mixed integer second order cone programming

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Random projections in model selection and related experiment design problems

Ewa Skubalska-Rafajłowicz and Ewaryst Rafajłowicz

Abstract The idea of using random projections for model selection purposes was introduced by the first author in [2] in the context of usually even larger models arising in identification of nonlinear time series.

In this talk, our aim is to propose a method for selecting terms to be included into a regression model, when part of primary candidates are specified (e.g., the main effects) and to discuss problems of experimental design that arise in such cases. Our problem statement is the closest in spirit to the one in Chapter 20 of [1]. A distinctive feature of our problem statement is a deficit in admissible number of experiments compared with a much larger number of candidate terms. The proposed approach is based on applying a large number of random projections of candidate terms in order to sift out spurious terms. The corresponding experiment design problem is stated and solved for a linear regression with a (possibly very large) number of interactions. The results of simulations are also reported. The results are confined to D-optimal designs, but the general idea conveys smoothly to other criteria.

Details of random projections for selecting a regression terms are presented in [3], where a semi-heuristic explanation of why it works is given. In this talk we provide only the main idea that is necessary for stating the problem of experimental design.

Key words: random projections, regression, model selection, experimental design

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Random designs for robustness to functional model misspecification

Tim Waite and Dave Woods

Abstract Optimal design usually begins by assuming that at least one prespecified parametric model is correct, perhaps with several possible alternatives in mind. In practice, we are never certain that this holds. We consider response surface problems where the model mean is of the form $\mu(x) = f(x;\theta) + \psi(x)$, with $f(x;\theta)$ a linear model approximation to the truth, and ψ the *discrepancy*.

The most realistic approaches to this problem develop optimal designs robust to discrepancy functions from an infinite-dimensional class, $\mathscr{H}$, where either (i) it is a priori possible to derive a bound applying to all $\psi \in \mathscr{H}$, or (ii) only the L^2-norm of ψ is bounded over $\mathscr{H}$. If we adopt the broader class (ii), then every finitely-supported design has infinite 'worst-case' (over possible ψ) integrated mean-square prediction error (IMSEP). To overcome this, authors choosing assumption (ii) have proposed infinitely-supported designs defined by density functions on the design space. Implementation of such 'designs' is troublesome, since in practice we require a finite approximation, which will again have infinite worst-case IMSEP.

We demonstrate a new approach in which stochastic strategies, or *designers*, are used to generate finite designs. The essential idea is to perturb the design points by adding a tunable amount of uniform jitter. If we also average over the random choice of design, then the worst-case IMSEP is finite. We develop a class of designers for which the worst-case IMSEP is analytically and computationally tractable. Algorithms for the selection of efficient designers are considered, and the inherent bias-variance trade-off is illustrated.

Key words: approximate model, experimental design, robustness, random design

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10–14 June 2013, Łagów Lubuski, Poland

Construction of minimax designs for the trinomial spike model in contingent valuation experiments

Ellinor Fackle-Fornius and **Linda Wänström**

Abstract This paper concerns design of contingent valuation experiments when interest is in knowing whether respondents have positive willingness to pay and if so, if they are willing to pay a certain amount for a specified good. A trinomial spike model is used to model the response. Locally D- and c-optimal designs are derived and it is shown that any locally optimal design can be deduced from the locally optimal design for the case when one of the model parameters is standardized. It is demonstrated how information about the parameters, e.g. from pilot studies, can be used to construct minimax and maximin efficient designs, for which the best guaranteed value of the criterion function or efficiency function is sought under the assumption that the parameter values are within certain regions. The proposed methodology is illustrated in an application where the value of environmentally friendly produced clothes is evaluated.

Key words: locally optimal design, minimax design, maximin efficient design, H-algorithm, contingent valuation

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10–14 June 2013, Łagów Lubuski, Poland

Comparing optimal designs of computer experiments for estimating covariance parameters

Noha Youssef and Henry Wynn

Abstract The Gaussian process (GP) model is commonly used to model the output of a computer experiment. The GP is defined by its covariance structure. The study aims at comparing two different designs for estimating the covariance function parameters. The first design is obtained via the Partial Maximum Entropy Sampling (PMES) design criterion. In order to use this criterion, [1] suggests approximating the process itself by the Karhunen-Loeve (K-L) expansion. As a result, the covariance function is also approximated using the same expansion. The covariance parameters are then embedded in the model as mean parameters. The PMES criterion maximises the information for a subset of the mean parameters which correspond to the covariance parameters.
The second design uses the log determinant of the inverse Fisher information matrix as its design criterion for estimating the covariance parameters as proposed by [2]. Both criteria work on different approximations for the actual covariance structure.
In this study, the Bayesian approach is adopted for constructing both designs. The exchange algorithm is used to search for the optimal design. Different accuracy measures of predictions are calculated to assess the performance of the two different optimal designs.

Key words: computer experiments, experimental design, Karhunen-Loeve expansion, Fisher information matrix, entropy

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Optimal experimental design for correlated observations: Old results and recent advances

Anatoly Zhigljavsky

Abstract In this talk, I will review some results on optimal experimental design for regression models with correlated observations. The talk is based on recent publications [1, 2, 3]. My collaborators in this research are Holger Dette (Bochum) and Andrey Pepelyshev (St.Petersburg-Aachen-Cardiff).

The common linear regression model $y(x) = \theta^T f(x) + \varepsilon(x)$ is considered, where $f(x) = (f_1(x), \ldots, f_m(x))^T$ is a vector of base functions, $\theta = (\theta_1, \ldots, \theta_m)^T$ is a vector of unknown parameters, $\varepsilon(x)$ denotes a random error process, and x is the explanatory variable, which varies in a compact design space $\mathscr{X} \subset \mathbb{R}^d$. We assume that N observations, say $y_1, \ldots, y_N$, can be taken at experimental conditions $x_1, \ldots, x_N$ to estimate the parameters θ. Suppose that $\varepsilon(x)$ is a stochastic process with $\mathrm{E}[\varepsilon(x)] = 0$, $\mathrm{E}[\varepsilon(x)\varepsilon(x')] = K(x,x')$, $x, x' \in \mathscr{X}$, where $K(x,x')$ is a covariance kernel. Different variations of the optimal design problem will be discussed and some of them even solved. These variations differ in various assumptions about the design space $\mathscr{X}$, the covariance kernel $K(x,x') = E[\varepsilon(x)\varepsilon(x')]$, and also in different sets of designs and the estimates of the unknown parameters used.

Results for the case of one-parameter models are rather complete. These results are reviewed first. We then discuss the general case of multi-parameter models and consider general optimality theorems and numerical algorithms for construction of optimal designs. We then explain the classical Bickel-Herzberg approach and its extension for the case of a long-range dependent error process.

Key words: experimental design, correlated observations, correlation kernel, universally optimal design

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Abstracts: Poster Presentations

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D-optimality for time series models

Mariano Amo-Salas and Jesús López-Fidalgo

Abstract Time series models are a sort of nonlinear models where the observations are not independent and the function which defines this correlation depends on the mean of the model. In this work, these models are studied from the framework of Optimal Experimental Design in order to obtain the best moments to perform experiments. The model and the covariance function are expressed in a suitable form to apply the usual techniques of Optimal Experimental Design. The expression of the Fisher information matrix is provided for estimating the parameters of the model when they appear in the covariance function. Optimal designs for the simplest models are computed for different nominal values of the nonlinear parameter and their efficiencies are compared. Finally, more complex models are proposed.

Key words: AR(1), D-optimality, covariance matrix

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Maximum entropy design in high dimensions by composite likelihood modeling

Davide Ferrari and **Matteo Borrotti**

Abstract In maximum entropy sampling (MES) [2], a design is chosen by maximizing the joint Shannon entropy of parameters and observations. However, when the conditional parametric model of the response is contains a large number of covariates, the posterior calculations in MES can be challenging or unfeasible. In this work, we consider the use of composite likelihood modeling [1, 3] to break down the complexity of the full likelihood and code the original optimization problem into a set of simple partial likelihood problems. We study the behavior of the composite likelihood sampling approach as the number of design variables grows using both asymptotic analysis and numerical simulations.

Key words: high dimensional experiments, maximum entropy sampling, composite likelihood model

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Optimum experimental design in the transport of materials in granular form

Mariano Amo Salas, **Elvira Delgado Márquez**, Jesús F. López Fidalgo

Abstract Materials in granular form are widely used, having a great importance in the chemical, food, agricultural and pharmaceutical industries. During the discharge of a two-dimensional silo, the flow of grains through an orifice is arrested if the size of the outlet is not large enough. In the outpouring of grains, jamming occurs due to the formation of an arch at the outlet. After a jam, an input of energy (blowing, shaking or tapping) is necessary to break the blocking arch and restart the flow. Then, the grains fall until a new arch is formed.

The model that describes the flow of grains from a two-dimensional silo and the costs of experimentation is studied in this work from the perspective of the Optimum Experimental Design. The D-optimal designs for the sizes of the outlet are computed and their efficiencies are provided. A sensitivity test is performed for different values of the size of the outlet optimal.

Key words: D-optimality, materials in granular form, Fisher information matrix.

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Bayesian optimal factorial designs for binary response models

Roberto Dorta-Guerra, Enrique González-Dávila and Josep Ginebra

Abstract An alternative and, in a sense, a more realistic approach to designs for generalized linear models is to introduce a prior distribution on the parameters rather than a single guess. Some authors as Charloner and Larntz (1989), Atkinson, et al. (1993) and Letsinger (1995), have studied the Bayesian designs for binary response models. On the other hand factorial designs are very used as screening designs at the preliminary stages of an investigation when the outcome is continuous. These designs are either optimal or close to optimal among all experiments with the same sample size, for a broad class of experimental regions and for most sensible design optimality criterion, including the determinant of the information matrix. In this work we have studied the optimal factorial designs from the Bayesian point of view for binary response models.

Key words: factorial designs, binary response models, Bayesian designs

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The RL heuristic for computing optimal designs of experiments

Lenka Filová and Radoslav Harman

Abstract We propose a new greedy-type incremental heuristic for computing efficient exact designs of experiments. The proposed method is versatile in the sense that it can be used with any optimality criterion and various non-standard restrictions on the design weights. We have tested the method on computing optimal designs for block models with $b = 10$ blocks of size two and $v = 9, \ldots, 45$ treatments (see [2] for an application to microarray experiments) and the quadratic 3^3 factorial response surface model with $N = 10, \ldots, 20$ runs (see [4] for exact D-optimal designs). We compared the results to those of the KL exchange algorithm (cf. [1], Section 12.6) and the efficient rounding algorithm [3].

Key words: optimal design, exact design, heuristic algorithm, block design, quadratic model

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Algorithms for minimum-size design generation: Orthogonal fractional factorial designs and optimal designs

Roberto Fontana

Abstract This contribution studies algorithms for finding minimum size designs that belong to two classes: orthogonal fractional factorial designs and optimal designs. Minimum size designs are frequently used in many fields of application, including medicine, engineering and agriculture when the cost of each run is high.

In the first part of the work we focus on minimum size Orthogonal Fractional Factorial Designs (OFFDs) generation. We present an algorithm based on the joint use of polynomial counting function and complex coding of levels, [1]. The algorithm has been implemented in a software tool, written in SAS/IML, for the generation of minimum size OFFDs, [2]. It is worth noting that the algorithm puts no restriction either on the number of levels of each factor or on the orthogonality constraints and so it can be applied to a very wide range of designs, including mixed level orthogonal arrays.

In the second part of the work we study optimal *saturated* designs, mainly *D*-optimal designs. Widely used statistical software make available efficient algorithms for finding an optimal design according to the user's specifications. Nevertheless, these algorithms do not guarantee a *global* optimal design. Indeed, they start from an initial randomly chosen design and find a local optimal design. If the initial design is changed, the optimum found will, in general, be different. A natural question arises. Should we stop at the design found or should we run the algorithm again in search of a better design? This work uses very recent methods and software for discovery probability to support the decision to continue or stop the sampling.

Key words: orthogonal fractional factorial designs, optimal designs, algebraic statistics, discovery probability

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Estimating and quantifying uncertainties on level sets using the Vorob'ev expectation and deviation with Gaussian process models

Clément Chevalier, **David Ginsbourger**, Julien Bect and Ilya Molchanov

Abstract Several methods based on Kriging have been recently proposed for calculating a probability of failure involving costly-to-evaluate functions. A closely related problem is to estimate the set of inputs leading to a response exceeding a given threshold. Now, estimating such level set—and not solely its volume—and quantifying uncertainties on it are not straightforward. Here we use notions from random set theory to obtain an estimate of the level set, together with a quantification of estimation uncertainty. We give explicit formulae in the Gaussian process set-up and provide a consistency result. We then illustrate how space-filling versus adaptive design strategies may sequentially reduce level set estimation uncertainty.

Key words: Gaussian process modeling, excursion set, sequential design, uncertainty quantification, random set theory

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Multiplicative algorithms for the construction of optimum designs of experiments for discriminating between two rival models

R. Martín-Martín, R. Dorta-Guerra, L. Rodríguez-Aragón, B. Torsney

Abstract A properly designed experiment can help in discriminating between competing models. Atkinson and Fedorov [1] introduced the so-called T-optimality criterion which has an interesting statistical interpretation as the power of a test for the fit of a second model when the first one is true. Usually there is no closed form for the T-optimum design and it must be computed through an iterative procedure. We study a new approach to determining T-optimum designs based on the approach and multiplicative algorithms for computing optimal designs obtained by Torsney and Martín-Martín [2] . They described a new procedure to determine optimal designs. Such an approach involves transforming design point values to proportions of the design interval and choosing these proportions optimally to determine exact designs or choosing both these proportions and design weights optimally to determine approximate designs. In this work we provide a new algorithm combining the algorithm of Atkinson and Fedorov and the multiplicative algorithm. In addition, we illustrate its behavior for three real examples, two of them contained in the statistical literature.

Key words: model discrimination, T-optimality, multiplicative algorithm

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Smooth models for computer experiments

Ron Bates, Peter Curtis, **Hugo Maruri-Aguilar** and Henry Wynn

Abstract We present recent developments on our work on models for computer experiments. We are expending the technology on two directions. We first take advantage of orthogonal polynomial bases so that computations are stable and not prone to numerical inaccuracy. On a second direction, we are linking smoothness criteria to optimal design. The smoothness criterion aims to minimise

$$\Psi_2 = \theta^T K \theta$$

subject to interpolation restrictions. The optimal smoothness value achieved Ψ_2^* can be rewritten in terms of data vector y as $\Psi_2^* = y^T Q y$ and this enables us to search for the design using a criterion built upon desirable properties of the matrix Q.

Promising early results allow us to select design points such that the corresponding polynomial model will be smooth. We compare our results against designs built using traditional criteria.

Key words: regression, splines, kernel smoothing, non-parametric regression; computer experiments

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A convergent algorithm for finding KL-optimum designs and related properties

Giacomo Aletti, **Caterina May** and Chiara Tommasi

Abstract Among optimality criteria adopted to select best experimental designs to discriminate between different models, KL-optimality criterion is very general. A KL-optimum design is obtained from a minimax optimization problem on an infinite-dimensional space. In this paper some important properties of the KL-optimality criterion function are highlighted and an algorithm to construct a KL-optimum design is proposed. It is analytically proved that a sequence of designs obtained by applying iteratively this algorithm converges to the set of KL-optimum designs, provided that the designs are regular. Furthermore a regularization procedure is discussed.

Key words: model discrimination, Kullback-Leibler divergence, point-to-sets maps, ascendant functions

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Optimal designs for regression models with a constant coefficient of variation

Holger Dette and **Werner G. Müller**

Abstract In this paper we consider the problem of constructing optimal designs for models with a constant coefficient of variation. We explore the special structure of the information matrix in these models and derive a characterization of optimal designs in the sense of Kiefer and Wolfowitz (1960). Besides locally optimal designs, Bayesian and standardized minimax optimal designs are also considered. Particular attention is spent on the problem of constructing D-optimal designs. The results are illustrated in several examples where optimal designs are calculated analytically and numerically.

Key words: optimal design, heteroscedasticity, constant coefficient of variation, polynomial regression

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Design of experiments for copula models

Elisa Perrone and Werner G. Müller

Abstract In applications modeling dependencies by traditional covariance functions is often of limited use. Then stochastic dependence can easily and elegantly modeled by so-called copulas, functions with very special properties that have a strong connection with arbitrary marginal distributions (See[1]). The idea is to look into the relationship between the optimal design theory and the copula theory in order to find out what could be the best combination between the design model and the copula family. A first application of copulas to the optimal design theory was treated in [2]. In this work we investigate how the change of the copulas influences the optimal design obtained. We give a more general view of what could be the strengths and the weaknesses of this approach. Finally, we show some future perspectives and some interesting questions to answer to.

Key words: Copulas, Archimedean copulas, Optimal experimental design

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Optimal experimental design in marine robotics?

Massimo Caccia, **Eva Riccomagno** and Eleonora Saggini

Abstract This presentation is motivated by a recent collaboration between our two groups on definition of good experimental methodologies and practices in marine robotics. In particular the introduction of autonomous robots in civilian applications requires new technological regulations in an area where the risks are largely unknown and difficult to quantify.

Our collaboration includes a just-started project titled "Optimal design of experiments in marine robotics". It aims at providing real-time, adaptive and sequential algorithms to control and optimize the dynamics of the vehicle when e.g. performing a path-following task [1]. When the equations of the vehicle dynamic are known we plan to use local optimal DoE.

So far we have developed a simple method to estimate when the heading parameter is in steady state and hence the time point at which to give an input signal. This is based on correlogram for observations in adaptive moving windows and, for our specific applications, it performs well when compared with more refined online methods for signal extraction (e.g., in [2]) or modern variation of the Ljung-Box statistic (see, e.g., [3]).

Key words: marine robotics, local optimal experiments, path following

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10–14 June 2013, Łagów Lubuski, Poland

Optimal designs for compartmental models with unknown/non-constant transfer coefficients

Juan M. Rodríguez-Díaz, Guillermo Sánchez-León and Mayte Santos-Martín

Abstract Compartmental analysis has applications in clinical medicine, pharmacokinetics, internal dosimetry, nuclear medicine, ecosystem studies and chemical reaction kinetics. It can be described as the analysis of a system by splitting it into a finite number of component parts, which are called *compartments*. Compartments interact through the exchange of species. 'Species' may be, e.g., a chemical substance, a hormone, individuals in a population, etc. (see, e.g., [1] or [3]). The content in each compartment at time t is described by a system of ordinary differential equations (ODE), and for constant transfer coefficients between compartments this solution is given by a sum of exponential terms [2]. But very often some parameters of these biokinetic models are unknown, and in most of these cases that means that the analytical form of the solution cannot be obtained, which generally implies that optimal designs cannot be computed. In this work we propose a numerical procedure for obtaining optimal designs for compartmental models when they have not an analytical solution, and the ideas can be extend to other (non-compartmental) ODE systems without analytical solutions.

Key words: compartmental model, optimal design, ordinary-differential-equation system

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New perspective of the optimal design for the Rasch models

Paula Camelia Trandafir

Abstract The Rasch models are very common in social science research, particularly in the analysis of performance or attitudinal data in psychology, education, medicine, marketing and other fields where testing is relevant. A main characteristic of these models, concerns the separation of two kinds of parameters, one that describes qualities of the subject under investigation, and the other relates to qualities of the situation under which the response of a subject is observed.

In this work one overview of the optimal design for Rasch Model is made it, doing an in-depth analysis both to the several models of Rasch as to the methods and results of the experimental design point of view. Taking into account the positive and /or negative parts of the existing work, in this paper new alphabetical designs are presented. Also are shown new designs to discriminate between the models and at the time good design to estimate the parameters. As the final goal, the results obtained are compared with the experimental one used in the social science area and with the similar results bring in previous works from the optimal design field.

Key words: Rasch models, optimal design, discrimination design

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On the functional approach to locally D-optimum design for multiresponse models

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Abstract Optimal designs are usually found either in closed form or numerically. In addition to that, there is also the so-called "functional approach" introduced in a number of papers and the comprehensive monograph by Melas [1]. In this talk we use the latter in the context of experiments for a multiresponse chemical kinetic model described by ordinary differential equations. Specifically, we assume that the observations are of the form

$$y_i = \eta(t_i, \theta) + \varepsilon_i, \quad t_i = 1, \ldots, N, \tag{1}$$

where $\eta(t;\theta) = \big([A](t;\theta), [B](t;\theta), [C](t;\theta)\big)^{\mathsf{T}}$, $[A], [B]$ and $[C]$ are concentrations of three reactants which depend on an unknown vector parameter θ, $t_i \in T$, a time interval, $i = 1, \ldots, N$, ε_i stands for measurement noise, $\mathrm{E}\{\varepsilon_i\} = 0$, $\mathrm{E}\{\varepsilon_i \varepsilon_j^T\} = R\delta_{ij}$, δ_{ij} is the Kronecker delta, R being a given 3×3 matrix. At first, we characterize the number of support points in locally D-optimal designs. Then the support points and weights of the optimal design are treated as implicit functions of some auxiliary parameter. They are then represented by means of power series and then the problem reduces to numerical computation of a sufficiently large number of their most significant terms. Numerical examples provide evidence that this approach makes it possible to approximate locally optimal designs for the nonlinear model considered with quite high accuracy.

Key words: miltiresponce regression models, nonlinear models, locally D-optimum designs, functional approach

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