Optimal Design of Experiments – Theory and Application

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The Age of Maturity: Fifty Years of Methodology and Applications of Experimental Design in Russia.

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The beginning of experimental design in Russia was in 1960, when the Journal ‘Progress in Chemistry’ was published the review by Prof. V. Nalimov “Statistical Methods of Search the Optimal Conditions for Chemical Processes”. It was some analysis of foreign sources.

The period from 1960 to 2010 we are divide into three parts:

From 1960 to 1980,
From 1981 to 1991,
From 1992 to 2010.

On each part we are discuss methodological and applied aspects the investigations in area of experimental design: publications (books, review, some articles), organizational activities (scientific councils, conferences, seminars, and so on), education, and scientometrical investigations.

The first part was connected with development of some scientific groups in chemical and metallurgical organizations. They were publication of some tens applied articles. In this time experimental design was a part of chemical cybernetics. But just in the end of 1960s was created “invisible collective (college)” under the leadership of Prof. V. Nalimov and was beginning some development of theoretical and methodological problems of building designs on the base of some criterion of optimality. There were big growth of applied publications in chemistry, metallurgy and technics. It was start of big conferences and numerous seminars. It was the beginning of educational activities in this area.

On the second part by Nalimov’s school was developed logical fundamental of experimental design. Design of experiment was included in applied statistics as an independent part. In this time was published some catalogs for plans of experiments. For the beginning of 1980 was published some thousands of articles and more than 100 books with different applied problems.

On the third part scale for methodological and applied works in this area was significant smaller in connection with systematical crisis of Russian science.
Advances in cub models with application to the evaluation of natural parks in the dolomites

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The rating problem arises very often in statistical surveys, where respondents are asked to evaluate several topics of interest (products, services, treatments, etc.). In this framework, a new approach is represented by a class of mixture models (Covariates in the mixture of Uniform and shifted Binomial distributions, CUB models), proposed by Piccolo (2003), D’Elia and Piccolo (2005) and Iannario and Piccolo (2006). Together with parametric inference, a permutation solution to test for covariates effects, when a univariate response is considered, has been discussed in Bonnini et al. (2011), where the method has been proved to be well performing and competitive with respect to the asymptotic solution. In the present work we perform an extension of the simulation study to prove the good power behavior of the permutation solution also in other different situations. The method is also applied to real data regarding the analysis of the main reasons that drive tourists to choose Sesto/Alta Pusteria’s Dolomites (an area of the Trentino Alto Adige region in Italy) as resort for their holidays.

Keywords: Permutation test, CUB models, rating data, power study.
Optimal design of drug development programmes: some open research questions

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Design of experiments is of fundamental importance to drug development, where one single confirmatory clinical trial can involve significant investments in time and cost. Even more important, good designs can help bring useful new medicines to patients in need and, in other cases, help terminate the development of ineffective and intolerable drugs. Much research, in academia and industry, has been devoted to optimising clinical trial designs. In the 2000s, the most intensive research area has been adaptive designs. The Adaptive Design Scientific Working Group (ADSWG) has been influential in bringing new designs into industry practise and regulatory acceptance. A next step is ADSWG’s launch of an Adaptive Programme (AP) network, with 30+ members from industry and academia. The basic premise is to try to optimise a series of trials, rather than single experiments. For example, the optimality criterion for a dose-finding trial should be chosen to reflect how the results from that experiment will be utilised when designing the confirmatory trials. One formulation of the problem assumes a prior $\pi_1$ for all efficacy and safety parameters. Based on this prior, we are to optimise the phase II dose-finding study design, $N_2\cdot\xi_2$, that is both the total sample size and the relative distribution of observations on different doses. Data, $X_2$, from this trial together with $\pi_1$ lead to an updated prior, $\pi_2$, which can guide the phase III confirmatory trial design $N_3\cdot\xi_3$. We are to optimise both the phase II and phase III designs (the latter depending on data from the former) in terms of an expected utility, which reflects sampling costs as well as potential rewards. In the presentation, we will sketch this issue, give some results related to AP, and discuss the need for further research in the area.
Some construction of regular E-optimal spring balance weighing designs for even number of objects

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The optimality of designs plays a main role in the theory of the experiments. We consider experiment in that the result we can describe as linear combination of unknown measurements of objects with coefficients of this combination equal to 1 or 0. Now, weighing designs are applicable to a great variety of measurement problems: in weighing, lengths, voltages, resistances, concentrations of chemical mixtures. Presented paper deals with the estimation problem of individual weights of objects in spring balance weighing design that satisfy the criterion of E-optimality. We assume that we have several kinds of balances with different precisions. Here, the lower bound for the maximum eigenvalue of the inverse of the information matrix of estimators is given. We present new method of construction of E-optimal designs, that extends the class of E-optimal design given in literature. It is based on the incidence matrices of the partially balanced incomplete block designs.
Optimal Two-Level Main-Effect Plans and Biased Weighing Designs

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We consider optimal main-effect plans under the usual orthogonal parametrization and a nonorthogonal baseline parametrization. In the former case, the model matrices have 1, -1 entries, and the designs are equivalent to biased chemical balance weighing designs. In the latter case, the model matrices have 0, 1 entries, and the designs are equivalent to biased spring balance weighing designs. Optimal designs in one setting can be obtained from those in the other via a simple transformation. We obtain exact $\Phi_p$ optimal designs for the cases $N \equiv 0, 1, 2 \pmod{4}$, where $N$ is the run size.
Permutation-based Methods to Design and Analyze Experiments for Ranking of Multivariate Populations

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The purpose of this work is to present some novel permutation-based methods aimed at designing and analyzing experiments for the problem of ranking several multivariate populations (Arboretti et al., 2010). Permutation tests are essentially of an exact nonparametric nature in a conditional context, where conditioning is on the pooled observed data as a set of sufficient statistics in the null hypothesis (Pesarin and Salmaso, 2010a). In the context of ranking of multivariate populations, in many real applications it may happen that the number of observed variables is much larger than that of units. It can be proved that, for a given fixed number of units, when the number of variables increases and the noncentrality parameter of the underlying population distribution increases with respect to each added variable, then power of the multivariate combination-based permutation tests is monotonically increasing. This new property of multivariate permutation and combination-based tests, known as finite-sample consistency (Pesarin and Salmaso, 2010b), proves to be very useful in the context of ranking of multivariate populations. This multivariate problem is formalized through the definition of a so-called ranking-parameter (Gupta and Panchapakesan, 2002) and depending on the assumptions made about the random errors, the distribution of ranking parameter estimators can be derived in a parametric or in a nonparametric way. However, the parametric approach presents a number of drawbacks and limitations; conversely, thanks to its robustness and flexibility, the permutation approach appears to be more reliable and powerful.

Keywords: finite-sample consistency, nonparametric combination, permutation tests.

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Exact D-optimal designs (Computational approaches)

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Some approaches to D-optimal designs construction are discussed on a base of the new methods of delta square distribution modeling.
A typical model for geostatistical data when the observations are counts is the spatial generalised linear mixed model. We present a criterion for optimal sampling design under this framework which aims to minimise the error in the prediction of the underlying spatial random effects. Our criterion is derived by performing an asymptotic expansion to the prediction variance. We perform a computational study to investigate the effect of the parameters of the model in deriving the optimal design and find that, contrary to the widely-used space-filling designs, the mean of the spatial process has a significant effect. Our results are applied to the Norway precipitation data and the rhizoctonia disease data.

**Keywords:** Generalised linear mixed models; Geostatistics; Predictive inference; Sampling design
Correlated/mutually depended endpoints are observed in almost any clinical trial. Typically one of them is claimed as a primary end point and the design (dose allocation and sample size) is driven by a single response model. I try to address the design problem with multiple end points which potentially may be of different nature. For instance, the efficacy end point may be continuous while the toxicity end point may be discrete. I emphasize the difference between the response and utility functions. The response functions are what we can observe while the utility functions are what should be reported or used in the decision making process. The recommended criteria of optimality are related to the latter.
Experimental design for models involving differential equations

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In practice the behavior of many stochastic processes or particular systems is usually modeled by using non-linear models involving differential equations. The models studied here are related to vestibular disorders, benign positional vertigo, to be precise. This is the most common cause of vertigo.

D-optimal designs for non-linear models with two unknown parameters have been analytically calculated although the differential equations appearing are in a simple form. This analytical derivation to find D-optimal designs is not always feasible in practice. In these cases, we must resort to numerical algorithms.
On D-optimality of complete block designs under a mixed interference model

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An interference model with neighbor effects is a model of experiments in which the response to a treatment can be affected by neighboring treatments. Recently some results on universal optimality of circular neighbor balanced designs (CNBDs) have been published (see e.g. Druilhet 1999, Filipiak and Markiewicz 2003, Filipiak and Markiewicz 2007).

It is known, however, that CNBDs cannot exist for each combination of design parameters. For example, in the class of complete block designs, CNBD may exist if the number of blocks is equal to $t-1$ with $t$ - number of treatments. For smaller number of blocks optimality with respect to specified criteria is studied. The aim of this paper is to extend D-optimality results for fixed interference model presented by Filipiak et al. (2011) into the model with random neighbor effects over the class of complete block designs with $b=t-2$.

**Keywords:** Mixed interference model, D-optimal design, information matrix, tridiagonal matrix with corners.

**References:**


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On Optimal Design for Variance Components

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Optimal design for maximum likelihood estimation of variance components in mixed linear models faces the problem that there is no explicit form available for the covariance matrix of the estimators. Hence the usual approach is to use the inverse of the Fisher information as a surrogate, as it is proportional to the asymptotic covariance matrix under certain regularity conditions.

Based on this substitute very unbalanced designs seem to become locally optimal in the one-way random effects model as reported in the literature, if the inter-individual variance is small.

More careful investigations show, however, that balanced designs remain optimal, if an optimal number of observations per individual is chosen, which depends on the variance components. For a fixed total number of observations this leads to a trade-off between the number of individuals and the number of observations per individual to be optimized. Similar results can be obtained under more general cost constraints, when recruitment costs are introduced for the individuals, or if the model is extended to a nested mixed model incorporating fixed treatment effects.
Optimum Designs in Statistical Planning and Inference-
Research of Jagdish N. Srivastava

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Professor Jagdish N. Srivastava recognized the importance of Statistical Planning and Inference at the early stage of his research career. He also recognized the importance of Optimum Designs in Planning and Inference at that time. This talk presents the details of Professor Srivastava’s research and leadership in statistics profession.
An Improved Algorithm for Multi-Stratum Response Surface designs

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Several different approaches for constructing response surface split-plot type designs have been proposed in the literature in the last 10 years or so, which has allowed experimenters to make better use of their resources by using more efficient designs than the classical balanced designs. Unfortunately each approach focuses on only one property which may produce designs which are marginally efficient. In this presentation we compare several desired properties of the designs constructed by some of these approaches and try to find patterns in their performances in order to give guidance for choosing the approaches that tend to produce compromise designs in the sense that they perform well on a range of properties. In particular we consider the stratum-by-stratum (Trinca and Gilmour, 2001) and a modification of it; D-optimum (Jones and Goos, 2007, 2009; Macharia and Goos, 2010) and equivalent-estimation design approaches (Vining, Kowalski and Montgomery, 2005; Parker, Kowalski and Vining, 2007).
On A-optimality of spring balance weighing designs

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Let us consider the experiment in that we determine unknown measurements of \( p \) objects \( n = \sum_{s=1}^{h} (n_s) \) measurement operations taken in different \( h \) conditions or at different installations according to the model \( y = Xw + e \), where \( y \) is the \( n \times 1 \) random vector of the observations, \( X \in \Phi_{n \times p}(0,1) \) where \( \Phi_{n \times p}(0,1) \) denotes the class of \( n \times p \) matrices \( X = (x_{ij}) \) of known elements \( x_{ij} = 1 \) or \( 0 \) according as in the \( i^{th} \) weighing operation the \( j^{th} \) object is placed on the pan or not, \( w \) is the \( p \times 1 \) vector of unknown weights of objects and \( e \) is a \( n \times 1 \) random vector of errors. We assume, that there are no systematic errors, i.e. \( E(e) = 0_n \) and the variances of errors are not equal and the errors are not correlated, i.e. \( \text{Var}(e) = \sigma^2 G \), where \( G \) is the known \( n \times n \) diagonal positive definite matrix.

The problem is to determine spring balance weighing design satisfying the criterion of A-optimality. The lower bound of the trace of information matrix is given and the conditions determining optimal design are presented, also. The incidence matrices of balanced incomplete block designs and group divisible designs with two associate classes are used to constructions of the regular A-optimal spring balance weighing design.
Optimal Design for the Poisson Regression Model with Interactions

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Poisson regression models are commonly used for experiments, where count data are observed. These models are particular cases of generalized linear models, for which the data analysis is well developed. Less is known on design optimality for such models, in particular, if more than one explanatory variable is involved.

For the Poisson regression model locally D-optimal designs have been stated analytically in the literature in the case of additive effects of the explanatory variables, but only some numerical results are available in the presence of interactions.

For the latter case we propose an analytical expression for the locally D-optimal design in the case of a synergy effect and in the case of zero interaction. In the case of an antagonistic effect we show that design optimization is only feasible, if the design region is sufficiently narrow.
Relative projection aberration for mixed level orthogonal arrays

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Traditionally, a few orthogonal arrays have been proposed and studied intensely, e.g. the L12, L18 or L36; additionally, the regular fractional factorial designs and screening designs by Plackett and Burman (1946) have been frequently used. However, researchers often have research needs that go beyond those simple designs. If a more general request is formulated, it is often accommodated using a non-orthogonal design obtained using a specified model and some optimality criterion (e.g. D-optimality), or it is forced into an existing orthogonal scheme by omitting some factors or factor levels.

In statistical theory, general mixed level orthogonal arrays have been systematically studied for some time, starting with the seminal paper by Xu and Wu (2001), who introduced generalized minimum aberration. Xu, Phoa and Wong (2009) gave an excellent overview over this branch of research. In recent years, there are also substantial efforts of enumeration of non-isomorphic orthogonal arrays, for example by Schoen (2009). For many experimental situations, there are a large number of competing arrays. Choice between them (for example, they cannot all be included into any software because of storage space constraints) or choice of a subset of columns from an individual array requires criteria for assessing the quality of the resulting designs.

Orthogonality is an attractive criterion because it comes with model robustness. For example, if all main effects are orthogonal to all two-factor interactions, main effects can be estimated without bias, even if an active two-factor interaction has been omitted from the statistical model. In this sense, the degree of orthogonality a design achieves is a measure of model robustness it guarantees. This talk is concerned with criteria for measuring the degree of orthogonality for mixed level orthogonal arrays, aiming for maximized model robustness (cf. Grömping 2011). The main purpose for developing these criteria is selection of orthogonal arrays for inclusion into software and automatic allocation of experimental factors to selected columns of larger orthogonal arrays (cf. e.g. R-package DoE.base, Grömping 2009-2011).

Mixed level orthogonal arrays compete with letter-optimal designs. Recently, Schoen (2010) compared the behavior of orthogonal arrays and D-optimal
designs for various scenarios and arrived at the (not too surprising) conclusion that neither approach is always superior. Jones and Nachtsheim (2011) proposed to optimize the alias structure of a design under constraints on D-optimality. With the criteria proposed here – once fully understood – it should also be possible to take the reverse route: optimize D-efficiency under constraints on model robustness criteria.

The talk is a presentation of work in progress. The conference participants’ expertise in Design of Experiments will hopefully generate useful feedback to be accounted for in further development and software implementation.

References:


This talk presents a suite of packages for industrial design of experiments in R – packages DoE.base, FrF2 and DoE.wrapper cater for experimenters who are willing and able to use command line programming, package RcmdrPlugin.DoE provides much (but not all) of the functionality from the other packages for users who prefer or need a graphical user interface (GUI).

Package DoE.base provides the infrastructure (classes and methods) and handles full factorial designs (function fac.design) and orthogonal arrays (function oa.design). Package FrF2 provides special functionality for fractional factorial 2-level plans, both regular (function FrF2) and non-regular (function pb). Package DoE.wrapper provides a link to functionality from other packages (AlgDesign, lhs, DiceDesign, rsm) for optimal designs, latin hypercube samples and other space filling designs and classical designs for response surface modeling. The purpose of wrapping existing functionality is to simplify users’ lives as far as possible by a common syntax. The talk presents the most important concepts used in the package suite and some of its special features.

It would be desirable to develop synergies with the work of other conference participants.

References


An investigation of response-adaptive multi-armed two-stage designs

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Consider the following two-stage design for comparing multiple treatments against a single control: initially, control and treatments are allocated by response-adaptive randomization during the first stage; after completion of the first stage, some treatments are selected to proceed to the second stage; finally, control and selected treatments are allocated by block randomization during the second stage. In this talk, we discuss the constructions of tests that protect the familywise error rate in the strong sense. One possible approach (Gutjahr et al., 2011) is to view the trial as a data-dependent modification of a simpler design, for which we know the distributions of its test statistics and to account for the data-dependent modification, by the conditional invariance principle (Brannath et al., 2007). We examine the operating characteristics of resulting multiple test procedure, discuss advantages and disadvantages of the procedure, and investigate alternatives.
Optimal prediction designs in finite discrete spectrum linear regression models

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We solve the n-point optimal prediction design problem for finite discrete spectrum linear regression models with one or two random coefficients. We show that in the case of an interval experimental domain, there exists an optimal prediction design supported on at most three distinct points, which can be computed using one-dimensional optimization. We also discuss the problem of a multidimensional experimental domain.
Preservation of Fisher Information Matrices using Trades

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In statistical experiments, a design is used for collecting data. In many settings we assess the performance of a design by a suitably chosen measure on its Fisher information matrix. Different designs may have the same information matrices, and a choice among such designs can be based on other criteria, possibly of a practical nature. Trades and the theory of trade off provide us with powerful mathematical and statistical tools for identifying classes of designs that in terms of their Fisher information matrices are identical, but that may have different properties with respect to other criteria. In this talk we take the audience on a scientific tour of this subject and point out many unsolved MS and PhD level and beyond research problems.
Estimation of the optimal design of a nonlinear parametric regression problem via Monte Carlo experiments

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A Monte Carlo method for estimation of the optimal design of a nonlinear parametric regression problem is presented. The basic idea is to produce via Monte Carlo values of the error of a parametric regression estimate for randomly chosen designs and randomly chosen parameters and to use nonparametric regression to estimate from this data the design for which the maximal error with respect to all possible parameter values is minimal. A theoretical result concerning consistency of this estimate of the optimal design is presented, and the method is used to find an optimal design for an experimental fatigue test.

**Keywords:** Optimal design, nonparametric regression, consistency.
Exact D-optimal Designs for Linear Log Contrast Models with Mixture Experiments

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In this work, exact D-optimal designs for linear log contrast models with mixture experiments are investigated. In the mixture experiment considered, it is assumed the measured response depends only on the proportions of the ingredients present in the mixture. Aitchison and Bacon-Shone (1984) suggested the log contrast models for mixture experiments and the design space was restricted further by Chan (1992).

With a given sample size, it is conjectured that there is an exact D-optimal design supported as evenly as possible at the supports of approximate D-optimal designs.

The cases for \(k=3, 4\) are verified with a balancing structure on the support points through arithmetic-geometric inequality for matrices as well as some determinant inequalities. The cases for \(k=5, 6\) will also be discussed.

\textbf{Keywords}: Minimal supports; arithmetic-geometric inequality for matrices.
Increasing number of cars and the growth in soil pollution have left scientists to diminish the reasons for that. The Applied Research Centre for Environmental Problems in Eskisehir has focused on soil pollution with two potential reasons (car, tramway) which might be the factors of pollution of soil. Regarding to this, three heavy metals (Cd, Zn, Pb) were recorded as pollutants and a $3^2$ factorial design is considered on soil data. In our investigation, the number of experiments is 45 with 5 times replications and 9 treatment combinations. Significant effect and interactions are obtained, results are given, and response surface plots of each pollutant were interpreted.

**Keywords:** $3^2$ Factorial experiments, Response surface, Heavy metals.
Design of mixture experiments with uniform restrictions on the ingredients

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Mixture experiments are experiments in which the experimental conditions are the relative proportions of ingredients of a whole. Given a second-degree polynomial regression model, Draper and Pukelsheim (1999) and Draper, Heiligers, and Pukelsheim (2000) have identified the class of so-called weighted centroid designs to be essentially complete with respect to a broad family of design criteria. However, weighted centroid designs are concentrated on extreme points of the design space and might thus be unfeasible in many applications. This raises the question whether an essentially complete class of designs can be found when upper or lower bounds on the proportions of the ingredients are imposed. In order to preserve symmetry we consider bounds which are uniform for all ingredients, and we focus on the case of experiments containing at most four factors. We identify essentially complete classes of designs which are described as convex hulls of finitely many designs. Furthermore, we show how these results greatly simplify design optimality problems.

References:


Multiplicity issues when planning confirmatory clinical trials

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Confirmatory clinical trials have to fulfill strict criteria to be taken as basis for approving a new drug. From a statistical point of view strict control of the multiple type I error rate is mandatory for confirmatory clinical trials as far as statistical hypothesis testing is concerned [1, 2]. There are several sources which can lead to a substantial inflation of the type I error rate such as repeated significance testing at interim analyses, adaptation of design features based on information coming from an ongoing trial or multiple hypotheses testing with respect to primary and secondary endpoints and/or multiple treatment-control comparisons. We will discuss how to address these issues adequately in the planning phase. For example it is common for a number of potentially effective treatments to be available for clinical evaluation. How many and which treatment(s) shall be selected for further investigation in a phase III trial? To evaluate the optimal choice of the number of treatments Stallard et al. 2009 [3] propose a Bayesian decision-theoretic approach, which leads to minimization of the total sample size of the trial subject to controlling the familywise type I error rate performing standard frequentist tests in the final analysis. Especially adaptive designs have attracted a lot of attention in the recent years. Such designs use accumulating data of an ongoing trial to decide how to modify design aspects always strictly control the type I error rate [4]. Adaptive designs thus allow for a number of possible adaptations at midterm: Early stopping either for futility or success, sample size reassessment, change of population, etc. We will focus on a particularly appealing application which is the use of adaptive designs in combined phase II/III studies with treatment selection at interim [5, 6].

Keywords: Confirmatory Clinical Trials, Multiple Testing, Adaptive Designs, Closed Testing Principle.

References:


   * The first 2 authors (in alphabetic order) have made equal contributions to this paper. Statistics In Medicine 2009 Apr 15;28(8):1181-217.

Row designs with three treatments under dependence

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Discrete optimal row designs or designs for one-way elimination of heterogeneity under dependence are considered. The \( n \) units are arranged in a row and one out of three treatments is allocated to every unit. The aim is to estimate the treatment effects or their comparison with a control variable effect. The concept of matrix majorization is utilized to prove the universal optimality of the competing designs, if a universally optimal design does not exist, then the vector majorization is applied to reduce the competing designs. Finally the D-A-MV-E-optimal designs are presented. First homogeneous populations are considered and optimal designs are established when the units are either uncorrelated or are dependent under a first order autoregressive model. A filtering technique is applied to reduce the number of competing designs and tables are presented for A-D-E-MV- optimal designs when \( n \) less or equal to 10.
On designing data-sampling for Rasch model calibrating an achievement test

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In correspondence with pertinent statistical tests, it is of practical importance to design data-sampling when the Rasch model is used for calibrating an achievement test. That is, determining the sample size according to a given type-I- and type-II-risk, and according to a certain effect of model misfit which is of practical relevance is of interest. However, pertinent Rasch model tests use chi-squared distributed test-statistics, whose degrees of freedom do not depend on the sample size or the number of testees, but only on the number of estimated parameters. We therefore suggest a new approach using an F-distributed statistic as applied within analysis of variance, where the sample size directly affects the degrees of freedom. The Rasch model’s quality of specific objective measurement is in accordance with no interaction effect in a specific analysis of variance design. In analogy to Andersen’s approach in his Likelihood-Ratio-test, the testees must be divided into at least two groups according to some criterion suspected of causing differential item functioning (DIF). Then a three-way analysis of variance design \((A \times B) \times C\) with mixed classification is the result: There is a (fixed) group factor A, a (random) factor B of testees within A, and a (fixed) factor C of items cross-classified with \(A \times B\); obviously the factor B is nested within A. Yet the data are dichotomous (a testee either solves an item or fails to solve it) and only one observation per cell exists. The latter is not assumed to do harm, though the design is a mixed classification. But the former suggests the need to perform a simulation study in order to test whether the type-I-risk holds for the \(A \times C\) interaction F-test – this interaction effect corresponds to Rasch model’s specific objectivity. If so, the critical number of testees is of interest for fulfilling the pertinent precision parameters. The simulation study (100 000 runs for each of several special cases) proved that the nominal type-I-risk holds as long as there is no significant group effect. Analysing a certain DIF, this F-test has fair power, consistently higher than Andersen’s test. Hence,
we advise researchers to apply our approach as long as there is no significant group effect, and only to use other Rasch model tests if it is significant. Keep in mind that this is true only for some special cases and needs to be generalized in further research. Then a formula is to provide which will allow explicit calculation of the number of testees, given a type-I-, a type-II-risk, and a relevant effect as concerns Rasch model misfit.
This paper makes an attempt to provide a general class of ratio type estimators for estimation of the population ratio through double sampling for stratification using multi-auxiliary information. The information collected from initial sample is used only for constructing the strata and estimating the strata weights. Ige and Tripathi (1987) proposed alternative sampling strategies based on DSS, utilizing the information on a single auxiliary variable x both at the designing as well as the estimation stage for improving the precision of estimation. H.P.Singh and V.P.Singh (1995) proposed a class of unbiased dual to ratio estimator in stratified sampling. Unbiased estimators are preferred as compared to biased one, proposed alternatives to formulate unbiased estimators.

i. the case, for bias to be zero, the correlation coefficient of $\bar{y}_t$ and $\bar{x}_t$ must be zero. But this may lead to higher variance which is not feasible.

ii. the sample can be drawn in the form of n independent interpenetrating subsamples.

From a finite population the estimator is calculated using probability proportional to size sampling with/without replacement (ppswr/wor) and optimum estimator is found to be more efficient. Efficiency is compared with comparable estimation sample selection methods.

**Keywords:** Double Sampling Stratification (DSS), Probability proportional to size sampling with/without replacement (ppswr/wor), Bias (B), Mean square error (M), Variance (V), Covariance (C).
There is an ongoing discussion on how an experiment should be run if there is the danger of a time trend in the data. There are two lines of thought on how to deal with a time trend. One option is to use a trend-resistant design, i.e. a design with a run order which reduces the effect on the time trend on the estimates as much as possible. The other option would be to use a randomized run order, which would make the time trend a part of the error. Generally, the trend resistant design will have higher efficiency, if the trend behaves exactly as anticipated. The randomized run order will be less efficient, but it will be robust against the structure of the trend.

In this talk we consider the special instance when the experimental design is an unreplicated fractional factorial design and the analysis is done with the half normal plot. A trend free design then will use only a subset of the columns (see e.g. Cheng and Jacroux, 1988) and thus give away some degrees of freedom. This reduces the power of the analysis. A compromise is the run orders considered by de Leon et al (2005), which do reduce the bias due to the trend but use all columns.

This talk continues the work of Adekeye and Kunert (2006) and compares the performance of the various approaches in the presence of a time trend.

References:


Defining the generalized dimension in the analysis of complex systems

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Fractals have practically entered every domain of interest of the human knowledge, becoming, from a simple subject of reflection, an interest theme for the uninitiated and for experts alike. From the analysis of the climatic phenomenon and to the modeling of the cancerous phenomenon, from the description of the images captured by the Hubble Space Telescope to the use of special effects in movies, fractals proved to be an inexhaustible source of ideas, solutions, tries, algorithms, on ways and directions either classical or surprisingly nonconventional.

The fractal approach on the study of cancerous tissues proved to be one of the successful themes of the systemic modeling. Thus, the medical diagnosis gained a new valence in the informational interpreting of images of the malign tissues, proportionally reducing the need to make a biopsy to take a tissue sample.

A series of fractal characteristics were used by Heymans and his collaborators (O. Heymans, S. Blacher, F. Rouers, G.E. Pierard. The fractal dimension quantifies here the random level of the vascular distribution also, a characteristic not easy to point out through the vascular density.

An analysis of the fractal dimension from a graphic image is useful, because the fractal dimension is a key element in studying the morpho-functional characteristics and the systemic behavior of the cancerous tissues. Searching for new methods of defining the generalized dimension for complex graphic systems leads to an inter-systemic view at the level of the perception of physical properties of the studied entities through the mathematical representation models.

There is a large number of methods that can be used in defining and calculating the fractal dimension of a new graphic object, which we’ll call from now on form.
No matter what the definition of the *dimension of a fractal form*, all ideas are derived from the Haussdorff-Besicovich dimension (HB). This dimension is a real number that can be used in characterizing the geometrical complexity of a limited subset from $\mathbb{R}^n$.

The HB dimension has a more subtle meaning that fractal dimension. One of the reasons as to why this notion is so important is that it allows comparing various “values” of sets for which the fractal dimension is the same.

We notice that the Haussdorff dimension has a more general character than the Euclidean dimension, being able to obtain fractional values, unlike the other one. Due to this fact, we can consider it to be at the base of a special class, called the *class of generalized dimensions*. We mention that the Haussdorff dimension like it was defined before is not the only example that belongs to this class. Any other example of fractal dimension also belongs to this class.

The technique used to define the Haussdroff dimension is the one used to cover the domain $A$ with a set of subdomains $A_i, i \in \mathbb{N}$. This technique allows us to make a deducing reasoning of the fractal dimension of self-similar forms (geometrical objects). For this, let’s consider a form with the linear magnitude (after all the directions of the Euclidean space) equal with one, whose magnitude is reduced to $q < 1$ after every special direction. This way, if the initial form is self-similar, we get coverage of the form with $N(q)$ self-similar forms.

Lewis Fry Richardson is the first one to put the question of a relation between the length of the national borders and the measurement scale. He noticed that this is a *log-log* type of relation (it can be represented in a graphic where the scale logarithm is on the abscissa and on the ordinate the logarithm of the length of the contour as a scale function).

For the coast of Great Britain, Richardson found: $1 - D = -0.24$, so $D = 1.24$, meaning a fractional value. The coast line in South Africa proved to be more leveled, almost a circular arc. The estimated inclination for the Mandelbrot-Richardson diagram is very close to zero, so that we have: $D \approx 1$. Thus it is proven that this contour has the characteristics of a Euclidean geometrical form, just like it was expected to have.
We will continue by making a qualitative analysis of the interpretation of a new type of geometrical dimension, different from the Euclidean topological one. We will call it generalized dimension, its properties being studied subsequently. In order to identify some correlations between the generalized dimension and the fractal dimension, the question of studying the existent relations between the two notions arises.

It is obvious that the maximum number of grid points that can be found on the grid is $N^2$, where $N$ the number of reticles is after each axis. Not all these points, though, will have this property in practice, making this number equal to $n \cdot N$, where $n$ is the average of nods on each axis of the grid and simultaneously on the graphic. We will define the nods with this property as active nods, whereas the nods without this property will be called passive nods. The points of intersection with the graphic which are not found on the cover matrix are ignored (they are eliminated from the algorithm that determines the generalized dimension). We have in the example above three passive nods and just one active nod.

We will consider that the weight of $n$’s value in reference to $N$ can vary between 0 and 1, these limits realizing, formally speaking, the all or nothing function. In other words, $n$ can take values between 0 and $N$. If by modifying $N$’s value, this characteristic remains unchanged, then this is a specificity of the considered curve. Thus, we can proceed to determine the generalized dimension as a specificity index. We notice that the $\frac{n}{N}$ ratio indicates a space factor (or an overlap factor) with active nods (nods situated on the graphic). Due to this fact, the method used to define the generalized dimension will be called the cover matrix method (CMM).
Adaptive Choice of Resampling Tests for Scale in Flexible Two Stage Designs

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The two sample scale problem is addressed within the rank framework which does not require to specify the underlying distribution. However, since the power of a rank test depends on the underlying distribution, it would be very useful for the researcher to have some information on it in order to use the possibly most suitable test. A two stage adaptive design is used with adaptive tests where the data from the first stage are used to compute a selector statistic to select the test statistic for stage two. More precisely an adaptive scale test due to Hall and Padmanabhan and its components are considered in one stage and several adaptive and non adaptive two stage procedures. A simulation study shows that the two stage test with the adaptive choice in the second stage and with Liptak combination when it is not more powerful than the corresponding one stage test shows however a quite similar power behavior. The tests procedures are illustrated using an ecological application.

Keywords: Resampling Tests, Scale, Flexible Two Stage Designs.
A multidimensional approach for ability estimation in educational assessment

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In the field of student assessment, latent variable models are used intensively in order to infer individuals’ abilities, which are typically not observable. In operational testing, unidimensional models of the Rasch family are often preferred, despite the research is oriented toward the implementation of models for multiple abilities or with a complex structure. In this work, a comparison between different multidimensional models for ability estimation is conducted, taking into account the distinction between general and specific latent traits. Results are discussed with respect to data on Italian student performances given by the National Assessment System.
A construction method of incomplete split-plot designs supplemented by control treatments

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We give a construction method of incomplete split-plot designs supplemented by control treatments, using a modified Kronecker product of two resolvable designs. We use a resolvable design and a square lattice design for test treatments of whole-plots and subplots, respectively. We give the stratum efficiency factors for such incomplete split-plot designs, which have the general balance property.

AMS Subject Classification : 62K15; 62K10; 05B05

Keywords: Incomplete split-plot designs; Test treatments; Control treatments; General balance property; Stratum efficiency factors.
On the functional approach to Bayesian efficient designs

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The present talk is devoted to an extension of the functional approach elaborated in the book (Melas, 2006) for studying optimal designs in linear and nonlinear regression models. Here we consider Bayesian efficient designs for nonlinear models. We assume that the observation errors obey standard assumptions. Sufficient conditions of uniqueness of locally optimal and Bayesian efficient designs for common optimality criterions are given. L-efficient Bayesian designs are constructed and investigated for a peculiar nonlinear regression model of a rational form as an illustration of main results. The model is both interesting in practical and theoretical sense.

In particular, our research showed that for the considered model the locally optimal designs are rather close to Bayesian L-efficient designs in there properties if the relative error in approximate values for parameters is less then 50 %.

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Block design with AR(1)-correlated errors for the comparison of treatments with a control

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This talk deals with the simple block model with autocorrelated errors and determines A-optimal designs for the comparison of treatments with a control. The method of proof is based on the paper "A-optimal block designs for the comparison with a control for correlated errors and analysis with the weighted least squares estimate" by Kunert, Martin and Eccleston (Journal of Statistical Planning and Inference, 2010). These authors determined optimal approximate designs when the block size k is restricted to be less or equal than 4.

This talk presents a generalization of these results for arbitrary k. In particular, it shows that all blocks of an optimal approximate designs will consist of two sequence classes only, where each treatment appears at most once while the control appears i times in the first and i+1 times in the second class. If, for fixed k and fixed autorcorrelation coefficient lambda, the number of treatments increases, then i decreases. It becomes 0 for sufficiently large t.
Approximation of the Fisher Information and Design in Nonlinear Mixed Effects Models

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The missing closed form representation of the probability density of the observations is one main problem in the analysis of Nonlinear Mixed Effects Models. Often local approximations based on linearizations of the model are used to approximately describe the properties of estimators. The Fisher Information is of special interest for designing experiments, as its inverse yields a lower bound of the variance of any unbiased estimator. Different linearization approaches for the model yield different approximations of the true underlying stochastical model and the Fisher Information (Mielke and Schwabe (2010)). Target of the presentation are alternative motivations of Fisher-Information approximations, based on conditional moments. For an individual design $\xi_i$, known inter-individual variance $\sigma^2_D$ and intra-individual variance $\sigma^2$, the Fisher Information for estimating the population location parameter vector $\beta = E(\beta_i)$ results in

$$I_\beta(\xi) = \frac{1}{\sigma^2} D^{-1} \text{Var}(E_{Y_i}(\beta_i)) D^{-1} \frac{1}{\sigma^2}$$

$$= \frac{1}{\sigma^2} D^{-1} - \frac{1}{\sigma^2} D^{-1} E(\text{Var}_{Y_i}(\beta_i)) D^{-1} \frac{1}{\sigma^2},$$

such that approximations of the expectation of the conditional variance and the variance of the conditional expectation yield approximations of the Fisher Information, which are less based on distribution assumptions. Tierney et. al. (1986) described fully exponential Laplace approximations as an accurate method for approximating posterior moments and densities in Bayesian models. We present approximations of the Fisher Information, obtained by approximations of conditional moments with a similar heuristic and compare the impact of different Fisher Information approximations on the optimal design for estimating the population location parameters in pharmacokinetic studies.
Taguchi method in physical deposition systems

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Growth from the vapor of a specific material often requires a challenging effort due to the many parameters that can affect the deposition of the required phase. In spite of this, multivariate analysis like the Taguchi method is rarely employed in the field. Here, we present as an example of the Taguchi methodology the deposition by sputtering of Europium monoxide, a highly reactive oxide that is unstable in ambient conditions and readily forms higher oxides. The Taguchi method significantly reduces the number of experiments required to optimize a fabrication process. The selected input parameters controlling the success of the growth process are: substrate temperature, deposition rate, oxygen pressure, vacuum base pressure and substrate type. It is observed that while all parameters influence the formation of the oxide, the most relevant appears to be the deposition rate.
A comparison between D-optimality for Poisson regression with random intercept and Poisson regression with random Slope

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In spite of wide applications of models with random effects, there are few studies have been investigating the optimal designs for these kinds of models. Optimal designs, which can significantly enhance the performance of the models, have received increasing attention recently. In this paper, we use Quasi-likelihood approach to obtain the optimal designs for two particular categories of Poisson regression models:

1. Poisson Regression models with random Intercept;
2. Poisson Regression model with random slope.

Then we empirically study the efficiency of the proposed optimal designs. This work provides a framework to obtain optimal designs when the variance covariance structure of the model is a function of the mean of the observations.
Experimental design for sampling windows has caught the attention of the pharmaceutical industry since it ensures a predefined efficiency and gives the study nurse more flexibility. Starting with Dufull et al. (2001) most approaches have been heuristic. We will give an overview of these approaches and study a new heuristic approach based on Sahm and Schwabe (2001). Further we will present some new results on optimal experimental design for sampling windows.
Strange design points in linear regression

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We discuss two kinds of „strange design points": one in models with uncorrelated observations, one in models with correlated observations.

i. In a quadratic polynomial $p(x)$ without intercept one can show that direct observations at a given point $\bar{x}$ give neither the best design for obtaining the estimator of the value of $p(x)$ at $\bar{x}$ (which follows e.g. from the Elfving theorem), nor can be substituted by observations at several design points very close to $\bar{x}$, but different from $\bar{x}$ (which is related to discontinuity of variances, for computational details of this example cf. p. 63-69 in Pázman, A. (1986). *Foundations of Optimum Experimental Design*, Reidel (Kluwer Group), Dordrecht). These mathematical facts lead to paradoxes from the point of view of the experimenter, and are to be explained statistically in the talk. Moreover, as shown in Pázman A., Pronzato, L. (2006). On the irregular behavior of LS estimators for asymptotically singular designs. *Statistics & Prob. Letters* 76, p. 1089-1096, if we consider in the same model a design for the estimation of the extreme value of the polynomial, then, in this nonlinear problem, the asymptotic normality of the estimator can be broken, and the Kiefer’s concept of a design as a probability measure may loose its justification as well.

ii. In a linear experiment with correlated observations

$$y_x = f^T (x) \theta + \varepsilon_x$$

$$\text{Cov} (\varepsilon_x, \varepsilon_z) = C'(x, z)$$

performed according to a finite exact design without replications, $x_1, ..., x_N$ we may find a design point $\bar{x}$ giving zero information about the parameters $\theta$. In a certain sense this point is „strange“. It is known a longer time that necessary and sufficient for that is

$$f (\bar{x}) = \sum_{x_i \in D} C'(\bar{x}, x_i) a(x_i)$$

for some vectors $a(x_i)$ and some subset $D \subset \{x_1, ..., x_N\}$. This result can be reformulated and extended: Define for each $i = 1, ..., N$

$$a(x_i) = \sum_{j=1}^{N} \left\{ C^{-1} \right\}_{i,j} f(x_j)$$

with $C$ the covariance matrix of observations in the design. Let $\Phi[.]$ denote a concave design criterion having a gradient matrix $\nabla \Phi[.]$. Then the amount of information about $\theta$, which is measured by the criterion $\Phi$, and which is contained in one design point $\bar{x}$, is small if $\|a(\bar{x})\|_\Phi$ is small where
\[ \|a(\tilde{x})\|_{\phi}^2 = a^T(\tilde{x}) \nabla \Phi[M]a(\tilde{x}) \]

and where \( M \) is the information matrix of the design \( x_1, \ldots, x_N \). This is an easy way how to delete non-necessary design points. Interpretations of this result will be discussed. For more mathematical details cf. Pázman, A. (2010). Information contained in design points of experiments with correlated observations. *Kybernetika* 46, 769-781. The full discussion indicated here will be published under the same title as the present talk in Acta Universitatis Palackianae Olomoucensis (Czech Republic).
On dynamic-statistical Model of the Forecast of the tropical Cyclones Intensity and of the Forecast of Tornadoes over the European part of Russia using the Theory of Optimal Design of Experiments

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The model and method of the predicting of the intensity of tropical cyclone with an axially symmetrical hydrodynamic model is submitted. The coefficient of horizontal turbulence is applied as the parameter to be tuned there. Computations are based on the theory of optimal design of experiments. During experiments two regressive equations were obtained, using the rules from (1965, Nalimov V.). Predictions are performed using both regressive equation and the numerical twelve-level model. The results from predicted evolutions of 10 tropical cyclones during their lifetime confirm the method efficiency (1994, Ivanidze T., Agrenich E.).

Advance forecast (to 12-24-36 hours) of storm wind (including tornadoes) stays a very difficult problem for synoptic still nowadays. The existing graphic and calculation methods depend on subjective decisions of operators. These methods usually use the dependence of these phenomena only from two-three parameters, but an appear of these phenomena is connected with great convective cloudiness entailed the hydrodynamic and thermodynamic instability. Nowadays there is no hydrodynamic model for forecast of the storm wind (including tornadoes), hence the main tools of objective forecast are the methods of statistical analysis. For this purpose the statistical model of recognition and prediction of storm wind including tornadoes was developed (1963, Anderson ). Before the construction of the decision rule F(X) the most informative and week dependent parameters were selected without loosing information. Our empirical statistical method of the choosing of the informative vector-predictor for the forecast of squalls and tornadoes is described at (1985, Perekhodtseva E.). As a criterion of informativity were used the Mahalanobis distance $\Delta^2$ and the Vapnik-Chervonenkis criterion of the minimum entropy $H_{min}$ (1974, Vapnik V.). We have investigated the combinations of 12 parameters and in the accordance to the assessments of the recognition of the sets $\{X(A)\}$ and $\{X(A)\}$ on the teaching and example samples we have obtained the vector-predictor including six atmospheric parameters.:

$$(V_{700}, H_0, (T-T'), nT/\partial n_{ea}, T_{ea}, Td).$$
These assessments of the recognition on the independent prognostic samples of presence of the wind velocity V>20m/s and of the absence of these events are P=0,95 and P=0,82 according (1992, Perekhodtseva E.). But it was very difficult to select the maximal wind with V>20m/s from the tornadoes in the forecast. So we hoped to use the theory of Optimal Design Experiments for the finding new main predictor as the parameter to be tuned. It was successful. The assessment of recognition was higher (2002, Perekhodtseva). The examples of the forecast of tornadoes at the European part of Russia are submitted at this report: on 9.06.1984 in Ivanovo, on 20.06.1998 in Moscow, on 02.07.2002 in S.-Petersburg, on 26.06.2005 in Dubna, on 3.06.2009 in Moscow area and other (2008, Perekhodtseva E., Zolin L.).

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On some stochastic models with a covariance structure depending on the mean, with an application to compartmental models

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We develop locally D-optimal designs for nonlinear models when the covariance of the response is a function of its mean. For a stochastic process defined on the real line, its covariance must satisfy the nontrivial requirement of positive definiteness. We show that there exists a class of functions that, composed with the mean of the process, preserve positive definiteness and can be used for the purposes of the present paper. We offer some examples for an easy construction of such covariances and then study the problem of locally D-optimal design through both simulation studies as well as real data inherent to a radiation retention model in the human body.
Optimal designs for prediction in random coefficient regression models

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Random coefficient regression models attract an increasing popularity in many fields of applications, in particular in biosciences. Besides the estimation of population parameters for the mean behaviour of the individuals a prediction of the response for the specific individuals under investigation may be of prior interest.

For estimating the population parameters some developments in optimal design can be found in literature. Less is known about optimal design for prediction. There are results for given population parameters and approximations, if the number of individuals is large. Here we will develop the theory and some solutions for prediction in the case of small to moderate numbers of individuals. The results will be illustrated by a simple example on linear regression.
Multi-Criteria Optimization of a Gluten-free Product

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The development of new and healthy food products of high quality and the optimization of food technological processes are very complex and require the application of statistical methods of experimental design. By an example of baking industry the application of fractional factorial and mixture designs are shown. The range of gluten-free products for persons, who are suffering from the disease “Zöliakie” is not sufficient. That’s why the baking industry was interested in producing glutenfree products which are enriched by roughage compounds.

Two partial tasks needed to be completed: At first a gluten-free product with specified properties was developed. Therefore a fractional factorial design of type $2^5-1$ was used and three response variables and an overall desirability function were optimized. The levels of the five input variables that produce the most desirable product in terms of its properties could be defined. The results of the analyzed fractional factorial design are illustrated by prediction profiles for the three responses and the response desirability.

In a second step four different roughage compounds were investigated concerning their suitability for a use in gluten-free products. The aim was to find an optimal combination of roughage compounds by applying and analyzing a simplex-centroid mixture design. A maximal volume yield of the product could be found, if the mixture of roughage compounds was including only two components in a ratio of 75% and 25%. Contour, surface and trace plots visualize the conditions for a maximal volume yield. Additional experiments on the recommended levels of factors and compounds have confirmed the results.
Application of Experimental Design for Studying the Stability of Copper(II) Complex

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The bioactive copper (II) complex with oligosaccharide pullulan can use for treatment of copper deficiency in the human organism. Therefore, the aim of this study was to investigate the stability of this potential active substance by the experimental design. In this case was used full factorial design for 3 factors at 3 levels. The value of electrical conductivity was taken as a response, while time of degradation, temperature and pH values as the independent variables. The levels of the independent variables were: 0, 30, 60 min for time; 20, 40, 60 °C for temperature and 1, 7, 13 for pH values. The significant impact on the change of the electrical conductivity of complex has a pH value, while a temperature has slightly lower. The least effect on the stability of complex shows a time of degradation, because the sum of squares (ANOVA test) is the lowest for this factor.

Keyword: stability, copper, complex, experimental, design.
Sequential design for comparing two binary endpoints: how to minimize type II error

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Assume that you wish to test whether the success probabilities of two binary valued random variables differ. We compare two sampling schemes. Under sequential sampling you sample one observation after another, for each sample you are allowed to determine which variable to observe next based on the previously observed outcomes. Under (simultaneous) balanced sampling each variable is sampled equally often, independently of which outcomes are generated. We compare inference under the exact randomized tests that minimize type II error. We find that if the two success probabilities are not too similar under the alternative hypothesis then balanced sampling is just as good as sequential sampling. Standard nonrandomized tests for balanced sampling perform only slightly worse in such situations, that is they perform almost as well as the theoretically best possible sequential sampling tests.
Use of Stein`s 2-step procedure for construction of confidence intervals with specified length to determine sample sizes for t-tests without specification of the standard deviation.

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The sample sizes for tests about means with the t-statistic is determined by the requirement that the power of a level $\alpha$ test should be $1-\beta$, if the deviation of the mean $\mu$ in one sample resp the difference of two sample means $\mu_1-\mu_2$ form the value specified in the null-hypothesis has at least a given amount $\Delta$. As the power of the t-test depends on the non-centrality parameter (i.e. the ratio of the mean to standard deviation), sample size determination requires the specification of the standard deviation in addition to $\alpha$, $1-\beta$ and $\Delta$. This can be avoided, if a $(1-\alpha)$-confidence interval (or range) for $\mu$ resp. $\mu_1-\mu_2$ is constructed with the data of the sample(s) and the null hypothesis is rejected, if the parameter values specified by the null-hypothesis lie outside this interval (or range), and accepted otherwise. The power requirement is equivalent to the requirement of a maximal length of the confidence interval which depends only on $\alpha$, $1-\beta$ and $\Delta$. A procedure to construct a confidence interval with specified length was proposed by STEIN. This proceeds in 2 steps: in the 1. step samples of reduced size (total sample size between 10 and 20) are drawn and an estimate for the variance is performed with the data. If the length of the confidence interval calculated with this estimate is equal or less than the specified length, the test is performed with this confidence interval. If it is greater than the specified length, additional sample values are drawn, so that the length of the confidence interval calculated with the variance estimate of the first sample and the total size of both samples is equal or less than the specified length. The test is performed with the means of both samples and the length based on the variance estimate of the first sample. The method is demonstrated with Monte Carlo simulation for one and two sample tests, where in the case of two samples equal and separate variances are proposed.

References:

Response surface methodology is used in experiments in which the main interests are to determine the relationship between the response and the settings of a group of experimental factors and to find the combination of the factor levels that gives the best expected response. In these cases an appropriate design should be employed in order to explore this underlying relation. When a quadratic relation between the response and the experimental factors must be established a second-order design should be used. We present a methodology for constructing second-order designs in order to explore and optimize response surfaces. The produced designs achieve both properties of rotatability and efficiency for the estimation of a second-order response surface model.
In applications often more than one dependent variable is observed in each experimental unit. In some of these situations the explanatory variables may be adjusted separately for the components in these models. For example, if one is interested in both pharmacokinetics and pharmacodynamics, the time points need not be identical for the measurements of the two quantities within one subject. As the observations will be correlated within one unit, the data may be described by a multivariate model, which has the structure of a seemingly unrelated regression (SUR).

While the data analysis is well developed for SUR models, there seem to be no results available on design optimization in such models. To fill this gap we establish that under certain regularity conditions D-optimal designs for seemingly unrelated regression and related multivariate linear models can be generated as products of the D-optimal designs for the corresponding univariate models of the single components. This construction turns out to yield optimal designs independent of the covariance structure of the components. Thus design optimization for SUR models can be reduced to univariate problems, for which the theory is well developed.

In the special case that the components share the same model structure it might be tempting to simplify the design by letting the experimental settings equal across all components within each unit. Then the observations would result in a MANOVA or multivariate regression model and the analysis would be essentially facilitated. However, an example shows that the efficiency of such MANOVA designs may substantially decrease, if the correlation between the components increases.
Spatial sampling design for random fields having skewed distributions: The case of trans-Gaussian kriging

Gunter Spöck
Alpen Adria Universität Klagenfurt

So far, methodologies for spatial sampling design assume the investigated random field to be Gaussian. Most often the minimization of the kriging variance averaged over the investigated spatial design region is considered as a design criterion. The actual advantage of using this design criterion is that the kriging variance is independent of the actual data values but only dependent on their relative locations. The independence of data values is a result of the Gaussian assumption for the considered random field. If the data follow a skew distribution, like for example data whose Box-Cox transformation is multivariate Gaussian, the assumption of independence of the design criterion from data values can no longer be held. Kriging with Box-Cox transformed data is also known as trans-Gaussian kriging. We consider as design criterion the average of the expected lengths of 95% predictive intervals from trans-Gaussian kriging and show how sampling designs may be calculated efficiently using recent results of Spöck and Pilz (2011). To make the computations of such sampling designs faster NVIDIA CUDA technology is used and the design algorithms are implemented in parallel on fast NVIDIA graphical processing units (GPUs). Moreover, both, design criteria taking covariance function estimation by REML into account and not, are investigated. All theoretical findings are illustrated by a practical example taken from a rainfall monitoring network.

References:
How powerful is my study?

Straif Michael

BI Plus GmbH, Austria

You may want to know statistical power of a test to detect a meaningful effect, given sample size, test size (significance level), and standardized effect size. You may also want to determine the minimum sample size required to get a significant result, given statistical power, test size, and standardized effect size. With IBM® SPSS® Sample Power you can examine the sensitivity of statistical power and sample size to other components, enabling users to efficiently use research resources.
Tools to Identify Optimal Designs for Generalized Linear Models

John Stufken

University of Georgia, Athens, USA

The literature on optimal design for linear models is very well developed. In spite of seminal advances over the past decades, tackling the optimal design problem for non-linear models has proven to be much more difficult. In recent years, new tools that yield very general results have been developed. As a result, searches for optimal designs under many different optimality criteria can be restricted to relatively small classes of fairly simple designs. Many models are covered by this new approach, including generalized linear models for binary and count data, such as logistic, probit, and loglinear models. We discuss the basic idea underlying the new method, present key results obtained by its use, discuss its limitations, and offer some open problems in this area.
Integrated Design of Experiments and Analysis of Results with the offering of JMP® and SAS®

Dr. Gerhard Svolba
SAS Austria

To reveal or model relationships between an input or factor and an output or response, the best approach is to deliberately change the first and see whether the second changes, too: Actively manipulating factors according to a pre-specified design is the best way to gain useful, new understanding. However, whenever there is more than one factor – that is, in almost all realworld situations – a design that changes just one factor at a time is essentially useless. To properly uncover how factors jointly affect the response, design of experiments (DOE) come into play, which is the focus of this conference.

JMP offers a complete library of tried and tested classical DOE designs, but also an innovative custom design capability that tailors your design to answer specific questions without wasting precious resources. Once the data has been collected, JMP and SAS streamline the analysis and model building so you can easily see the pattern of response, identify active factors and optimize responses.

This presentation shows the leading-edge JMP offering for Design of Experiments and data analysis and illustrates how SAS and JMP are integrated. See also http://www.jmp.com/applications/doe/index.shtml
Simultaneous choice of time points and the block design in the growth curve model

Anna Szczepańska

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In the talk the experiment in the block design, where \( v \) treatments are compared, and one characteristic is measured in the time, is studied. Two kinds of designs are analysed: the design of time points which means the set of time points from the given experimental domain and the block design which means the allocation of treatments in the blocks. The growth curve model is used in such experiment. The aim of talk is to consider optimality in the growth curve model and determine of optimal designs with respect to both aspects: time and block design. Moreover some relations between information functions for different designs are showed. The A-, D- and E-optimality is studied.

Keywords: Growth curve model, Information matrix, Information function, Optimal design, A-, D- and E- optimality
Dynamic Programming Approach to Sensor Trajectory Design for Parameter Estimation of Spatiotemporal Systems

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A systematic procedure for planning sensor movements in a specified spatial domain in such a way as to maximize the accuracy of parameter estimation of a given spatiotemporal system is proposed. The global design criterion is a general local design criterion defined on the Fisher information matrix associated with the parameters to be identified. The approach converts the problem to an optimal control one in which the control forces of the sensors are optimized. Its solution is obtained with the use of an iterative dynamic programming algorithm capable of handling various constraints imposed on sensor motions. Some refinements to make the computational procedure more efficient are discussed. A summary of numerical performance of the resulting algorithms is given in the final part of the paper.

**Keywords:** D-optimum design, Moving sensors, Optimal trajectory, Dynamic programming
Size of Experiments in ANOVA models with R

Minghui Wang

ORTEC Finance BV, Rotterdam, The Netherlands

The R program package OPDOE offers capability to calculate the size of experiments in several situations. In this presentation it will be demonstrated how the maximum size (for the least favorable situation) and the minimum size (for the most favorable situation) of an experiment for a three-way ANOVA can be calculated using OPDOE. Because the size of an experiment depends on the type of the classification (cross, nested or mixed) and the model specification, some cases will be selected and presented from the complete list of cases covered by OPDOE. Participants will be given the chance to select a few cases for the demonstration from the following list (bold means random factor, x factors are crossed, \( \succ \) means nested).

<table>
<thead>
<tr>
<th>Case</th>
<th>Model equation</th>
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<tr>
<td>( A \times B \times C )</td>
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Statistical Methodology for Adaptive Patient Enrichment Designs

Gernot Wassmer
ADDPLAN An Aptiv Solutions Company, Köln

Statistical Methodology for Adaptive Patient Enrichment Designs

Adaptive patient enrichment designs enable the data-driven selection of one or more pre-specified subpopulations in an interim analysis, and the confirmatory proof of efficacy in the selected subset at the end of the trial. Strong control of the experimentwise Type I error rate is guaranteed by use of the combination testing principle due to Bauer and Koehne (1994) together with the closed testing argument (see, e.g., Wassmer, 2010). Using these principles, the way of how to perform the subset selection and the sample size recalculation needs not to be pre-specified. This procedure can be extended to the multi-stage case including additional sample size reassessment procedures at the interim analyses. It also applies to nested subsets of patients as described in Wang et al. (2009). In this talk the general methodology and designing issues when planning such a design are described. It is shown how to define overall confidence intervals and p-values. Furthermore, the advantage of using the adaptive approach as compared to the classical approach is assessed by simulation.

References: