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(D_t, C) – OPTIMAL RUN ORDERS

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$(\mathcal{D}_t, C)$-Optimal Run Orders

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Cost considerations have rarely been taken into account in optimum design theory. A few authors consider measurement costs, i.e. the costs associated with a particular factor level combination. A second cost approach results from the fact that it is often expensive to change factor levels from one observation to another. We refer to these costs as transition costs. In view of cost minimization, one should minimize the number of factor level changes. However, there is a substantial likelihood that there is some time order dependence in the results. Consequently, when considering both time order dependence and transition costs, an optimal ordering is not easy to find. There is precious little in the literature on how to select good time order sequences for arbitrary design problems and up to now, no thorough analysis of both costs is found in the literature. For arbitrary design problems, our proposed design algorithm incorporates cost considerations in optimum design construction and enables one to compute cost-efficient run orders that are optimally balanced for time trends. The results show that cost considerations in the construction of trend-resistant run orders entail considerable reductions in the total cost of an experiment and imply a large increase in the amount of information per unit cost.

1 Introduction

In optimum design theory designs are constructed that maximize the information on the unknown parameters of the response function. Although such constructed designs have good statistical properties, they may not be fit for use because of economical reasons. Cost considerations have rarely been dealt with in the construction of optimal experimental designs. Generally speaking, two cost approaches are found in the literature.

Firstly, a few authors deal with costs associated with the particular factor level combinations. Henceforth, these costs are referred to as measurement costs. Measurement costs include the equipment cost, the cost of material, the cost of personnel, the cost for spending time during the measurement, etc.

Secondly, it is usually expensive to alter the factor levels from one observation to another. We refer to these costs as transition costs. In order to minimize costs, the number of factor level changes has to be kept low by conducting the runs corresponding to the same treatment combination one after the other.

But performing the observations in a time sequence by allotting them to time points, possibly creates some time order dependence in the results. An experimenter who has knowledge about the nature of the time trend should construct a run order in which the estimates of factorial effects are little disturbed by the presence of the time trend. Often, this time dependence is represented by a polynomial. The objective is to construct a run order such that the estimates of the important factorial effects are orthogonal or nearly orthogonal to the postulated polynomial trend. If the least-squares estimator of a factorial effect is the same as when the time trend of qth order is not present, that effect is said to be q-trend-free or orthogonal to the polynomial time trend.

With the exception of the approach of Atkinson and Donev (1996), there is precious little in the literature on how to select good time order sequences for arbitrary design problems. However, Atkinson and Donev (1996) do not take into account cost considerations. Our concern is about cost-efficient run orders with maximal protection against time order dependence for arbitrary design problems, polynomial time trends of any order and arbitrary cost functions. Up to now, no thorough analysis of both measurement costs and transition costs is found in the literature. It is worth mentioning that the difference between measurement costs and transition costs is not always clear and one has to pay attention for confusion. As a rule of thumb, keep in mind that measurement costs are independent of the sequence in which the observations are taken, as opposed to transition costs.

Section 2 gives a literature review on cost considerations in experimental design and on the construction of trend-robust run orders. Section 3 elaborates our approach to cost considerations in the construction of run orders optimally protected against time trends. Wide applicable cost models are introduced in order to closely reflect real-life industrial design problems. Section 4 describes our proposed algorithm by which $(\mathcal{D}_t, C)$-optimal run orders can be computed, i.e. run orders that maximize the amount of information on the important parameters of the response function per unit cost. The parameters modeling the time dependence are treated as nuisance parameters. Section 5 demonstrates practical utility.

2 Literature review

This section reviews the two cost approaches in optimum design theory. The first approach takes into account measurement costs whereas the second approach deals with transition costs. When minimizing the total transition cost, one needs to preserve protection against time order dependence in the results. The construction of trend-free run orders will constitute the larger part of this section.

2.1 Measurement costs

Many authors assume that the total measurement cost of an experiment only depends on the total number of observations and that this cost is independent of the particular factor level combinations. This means that for fixed design size, the total measurement cost is also fixed. This approach naturally amounts to a too drastic simplification of real-life industrial situations.

In a more realistic approach, measurement costs are assigned to each factor level combination. The problem is then structured as the selection of experimental arrangements by maximizing the experimental efficiency subject to resource constraints, maintaining an integer number of observations for each factor level combination. This integer programming approach refers back to Kiefer (1959) who suggests a complete enumeration of appropriate designs in order to select the optimal design. Unfortunately, the enumeration task becomes unmanageable for moderately sized problems. The partial enumeration algorithm of Lawler and Bell (1966) is especially suited for this purpose. Based on Lawler and Bell (1966), Neuhardt and Bradley (1971) consider constraints on the total number of observations, a constraint on the number of observations for a single factor level combination or a constraint on the cost of the experiment. However, the results obtained by partial enumeration may be far from optimum.

A similar optimization solution comes from Yen (1985) who computes $\mathcal{D}$-optimal designs subject to a budget restriction. The total measurement cost has to be less than the budget available. Yen shows that factorial designs that have a Hadamard information matrix are in fact cost-optimal designs. However, he only considers saturated regression designs.

Based on Neuhardt and Mount-Campbell (1978) and Mount-Campbell and Neuhardt (1982), Pignatiello (1985) provides a procedure for finding fractional factorial designs which permit the estimation of specified main and interaction effects. Given the cost data for the factor level combinations and a rank ordering of the importance of the effects to the experimenters, a sequence of sets of words eligible to appear in defining relations is constructed and cost-optimal fractional factorials are found over these sets.

Rafajlowicz (1989) states the minimum cost problem as follows: the experimenter wishes to attain a given symmetric and positive definite information matrix by using a minimum cost experimental design. He defines a continuous cost function which represents the measurement cost at any design point belonging to the design region. The problem is then to find a minimum cost design where infimum is taken over all designs with the desired information matrix.

Remark that the total measurement cost of an experiment is independent of the sequence in which the observations are taken, as opposed to the costs for changing factor levels discussed in the next section.

2.2 Transition costs and trend-resistant run orders

In practice, it is often expensive to change the levels of one or more factors from one observation to another, such as oven temperature or line set-up. Another problem is that after the factor levels have been changed, it may take a long time for the system to return to steady state. An interesting approach comes from Anbari (1993) and Anbari and Lucas

(1994) who discuss how to run 2^f-factorials when there are hard-to-change and easy-to-change factors. Hard-to-change factors may take more effort, require more time or cost more to change than other factors in the experiment. Anbari (1993) shows how proper blocking on the hard-to-change factors achieves super-efficient designs that have high cost-efficiencies and $\mathcal{G}$-efficiencies larger than 100% compared to completely randomized experiments. The $\mathcal{G}$-optimality criterion minimizes the maximum prediction variance over the experimental region. When hard-to-change factors are present, Ju (1992) points out that running the experiment as a split-plot design can increase precision and save money and time.

In addition, there is a substantial likelihood that there is some time order dependence in the results or that the observations may be affected by uncontrollable variables that are highly correlated with time. As a consequence, the usual estimates of factorial effects become very inefficient. For example, when a batch of material is created at the beginning of an experiment and treatments are to be applied to experimental units formed from the material over time, there could be an unknown effect due to aging of the material which influences the observations obtained. Other examples include poisoning of a catalyst, steady buildup of deposits in a test engine, etc. Variables that often affect observations obtained in some specific order are equipment wear-out, learning, fatigue, etc. The relative cost-effectiveness of any sequence is a function of the cost of changing factor levels and the protection afforded against time order dependence. Minimization of factor level changes is no longer the only design issue of interest. An optimal ordering is not obvious and one needs to strike a balance between designs that have good statistical properties but are quite costly and designs that are very cheap but ineffective.

Cox (1951) was the first to study the construction of designs for the estimation of treatment effects in the presence of polynomial trends. Later on, the problem of constructing trend-robust run orders with respect to additional criteria, i.e. the cost for changing factor levels, was considered.

Draper and Stoneman (1968) explicitly consider the dual problem produced by time order dependence and expensive factor level changes. Based on complete enumeration, they give good run orders for 2^{f-s}-designs with 8 runs when only main effects are of interest, linear drift may be present and all factors are equally expensive to change from low level to high level and vice versa. Dickinson (1974) extends their work to 2^4- and 2^5-factorials.

Joiner and Campbell (1976) offer the basis for a simple alternative and look at a random subset of orderings and then use the best ordering out of the set. Furthermore, they no longer assume that the factors are equally expensive to change. The random orderings are generated based on weighting coefficients attached to each factor. Each coefficient represents a probability for changing the corresponding factor level from one run to the next. The basic idea is to change more expensive factors less frequently and very cheap factors more frequently. Therefore, high probabilities are chosen for cheap factors and low probabilities are chosen for expensive factors.

Cheng (1985) and Coster and Cheng (1988) formulate the Generalized Foldover Scheme

(GFS) for generating a run order of an r^{f-s}-fractional factorial plan based on $f-s$ independent treatment combinations, referred to as independent generators. They show that the main effect of a given factor is q-trend-free if this factor appears at least $q+1$ times in the generator sequence. They also show that the GFS can be used to produce systematic run orders which minimize, or nearly minimize, the cost equal to the number of factor level changes and for which all main effects are orthogonal to a polynomial time trend. Coster (1993) presents generator sequences that may be used with the GFS to produce such run orders. An extensive review of constructing trend-free run orders can be found in Cheng (1990) and Jacroux (1990).

Another method for constructing trend-free run orders of factorial designs was originally due to Daniel and Wilcoxon (1966). Extending their results, Cheng and Jacroux (1988) show that in the standard order of a complete 2^f-factorial design, any w-factor interaction is orthogonal to a $(w-1)$-degree polynomial trend. The $(w-1)$-trend-resistance of any factor is obtained by redesignating this factor to the w-factor interaction in the standard order. With this in mind, a method is given for constructing a run order of a complete 2^f-design that yields main effects that are p_1-trend-free and 2-factor interactions that are p_2-trend-free. However, the problem of finding such run orders is usually a nontrivial problem when considered for arbitrary values of p_1 and p_2. Cheng et al. (1998) extend these findings to the construction of run orders of two-level factorial designs with extreme (minimum and maximum) numbers of level changes. Maximizing the number of factor level changes may be important if the main concern of the experimenter is possible positive correlation between adjacent runs.

John (1990) uses the principle of foldover designs for 2^f- and 3^f-factorials and shows how to arrange the runs in a factorial experiment so that the main effects and sometimes the two-factor interactions are uncorrelated with linear or quadratic trends. Trend-free Box-Behnken designs are treated by Hinkelmann and Jo (1998).

Trend-free block designs that completely eliminate the effects of a common trend over plots within blocks are introduced by Bradley and Yeh (1980) and Yeh and Bradley (1983). Yeh et al. (1985) construct nearly trend-free block designs with linear or quadratic trends over plots within blocks. Cheng and Jacroux (1988) also consider the problem of constructing trend-resistant run orders of complete 2^f-designs in 2^s equally sized blocks and of fractional factorial designs. Jacroux et al. (1995) consider efficient block designs in which different blocks can have different linear trends and they emphasize on binary trend-free designs. A design is called binary if each treatment appears at most once in each block. Jacroux (1998) constructs $\mathcal{E}$-optimal block designs with block size 3 in the presence of possibly different linear trends within blocks. In $\mathcal{E}$-optimality, the variance of the least well-estimated contrast $\mathbf{a}'\gamma$ with $\mathbf{a}'\mathbf{a}=1$ is minimized. γ denote the parameters of interest. Lin and Stufken (1999) introduce a new algorithm to convert a binary block design with given treatment-block incidence matrix into a linear trend-free block design.

Another way to model time dependence is to consider correlated errors. Steinberg (1988) represents the trend in an experiment by an ARIMA time series. Cheng and Steinberg

(1991) determine trend-robust run orders of 2^f-factorials under an AR(1) process and other more complex time series models for the trend effects. Run orders with a maximum number of level changes are found to be nearly optimal for the AR(1) process.

The references found assume that the time points are equally spaced, that all factors have the same number of levels, that higher order interactions are negligible, etc. Besides, none of the authors incorporate both costs in the construction of optimum designs. The next section will clarify our approach to the construction of cost-efficient and trend-resistant run orders for arbitrary design problems.

3 Trend-robust and cost-efficient run orders

This section deals with the incorporation of measurement costs and transition costs in the construction of designs that yield maximal protection against time order dependence. Attention will be drawn to arbitrary design problems, arbitrary cost functions, whether time points are equally spaced or not and with polynomial time trends of any order. The aim is the construction of the best run order in terms of information about the unknown parameters of the response function and corresponding costs.

In the sequel of this paper the design problem at hand assumes n observations and d treatment combinations. The allocation of n observations to d distinct design points can be done in

$$E_{n,d} = \binom{n+d-1}{n} = \frac{(n+d-1)!}{n!(d-1)!} \tag{1}$$

different ways. Each allocation $e \in \{1, \ldots, E_{n,d}\}$ represents an experiment described by the set $\{n_i^e\}_{i=1}^d$, where n_i^e denotes the number of replicates at design point i in experiment e. The time sequence in which the observations are performed is obtained by allotting the observations to n out of h time points, with $h \geq n$. For experiment e and h distinct time points there are

$$r_{e,n,d,h} = \frac{n!}{n_1^e! \cdots n_d^e!} \times \binom{h}{n} = \frac{h!}{(h-n)!\, n_1^e! \cdots n_d^e!} \tag{2}$$

distinct run orders. Based on (1) and (2), the total number of distinct run orders associated with an experiment with n observations, d design points and h time points equals

$$R_{n,d,h} = \sum_{e=1}^{E_{n,d}} r_{e,n,d,h} = \frac{h!}{(h-n)!} \sum_{e=1}^{\frac{(n+d-1)!}{n!(d-1)!}} \frac{1}{n_1^e! \cdots n_d^e!}. \tag{3}$$

Table 1 gives examples for $h = n$ and reveals that even for small design sizes, the total number of run orders is extremely large. Consequently, construction algorithms based on complete enumeration rapidly become unmanageable.

n	d 4	5	6	7
4	256	625	1,296	2,401
5	1,024	3,125	7,776	16,807
6	4,096	15,625	46,656	117,649
7	16,384	78,125	279,936	823,543
8	65,536	390,625	1,679,616	5,764,801
9	262,144	1,953,124	10,077,691	40,353,602
10	1,048,576	9,765,621	60,466,144	282,475,208
11	4,194,300	48,828,111	362,796,952	1,977,326,582

Table 1: Total Number of Run Orders $R_{n,d,n}$ (3)

3.1 Cost considerations in experimental design

Before passing on to the construction of optimal run orders, our cost approach will be elaborated. We define the measurement cost $c^m(\mathbf{x}_i)$ at design point $\mathbf{x}_i$ as

$$c^m(\mathbf{x}_i) = \mathbf{m}'(\mathbf{x}_i)\varsigma,$$

where $\mathbf{m}(\mathbf{x}_i)$ is a column vector with p_m elements, representing the polynomial expansion of the design point for the measurement cost and ς is a $(p_m \times 1)$ vector of coefficients. The total measurement cost C^m of an experiment equals

$$\begin{aligned} C^m &= \textstyle\sum_{i=1}^d n_i c^m(\mathbf{x}_i), \\ &= \textstyle\sum_{i=1}^d n_i \; \mathbf{m}'(\mathbf{x}_i) \; \varsigma, \\ &= \textstyle\sum_{i=1}^d n_i \; \mathbf{1}_i' \; \mathbf{M} \; \varsigma, \\ &= \mathbf{1}' \, \mathbf{N} \, \mathbf{M} \; \varsigma, \end{aligned} \tag{4}$$

where n_i denotes the number of replicates at design point i and $\mathbf{N}$ equals diag$(n_1, \ldots, n_d)$. Note that $\mathbf{1}_i$ is a $(d \times 1)$ vector with element 1 at position i and 0 elsewhere. $\mathbf{1}$ is a $(d \times 1)$ vector with elements 1. The $(d \times p_m)$ matrix $\mathbf{M}$ equals

$$\mathbf{M} = \begin{bmatrix} \mathbf{m}'(\mathbf{x}_1) \\ \vdots \\ \mathbf{m}'(\mathbf{x}_d) \end{bmatrix}.$$

In practice, it frequently happens that the factor levels at which cost information is available do not coincide with the factor levels of the allowable design points or that cost information is available at only a subset of all treatment combinations. To deal with this problem, the calculation of costs at any design point is based on an interpolation technique.

In contrast with the measurement costs, the total transition cost of an experiment depends on the sequence in which the observations are taken. The transition cost $c^t(\mathbf{x}_i, \mathbf{x}_j)$ from design point $\mathbf{x}_i$ to design point $\mathbf{x}_j$ is the cost for changing the factor levels of design point $\mathbf{x}_i$ in the previous run to the factor levels of design point $\mathbf{x}_j$ in the next run. This transition cost is defined as

$$c^t(\mathbf{x}_i, \mathbf{x}_j) = \mathbf{t}'(\mathbf{x}_i, \mathbf{x}_j)\boldsymbol{\tau},$$

where $\mathbf{t}'(\mathbf{x}_i, \mathbf{x}_j)$ is a $(p_t \times 1)$ vector representing the polynomial expansion of design points $\mathbf{x}_i$ and $\mathbf{x}_j$ for the transition cost and $\boldsymbol{\tau}$ is a column vector with p_t coefficients. The total transition cost C^t of a run order equals

$$\begin{aligned} C^t &= \textstyle\sum_{i=1,j=1}^{d} n_{i,j} c^t(\mathbf{x}_i, \mathbf{x}_j), \\ &= \textstyle\sum_{i=1,j=1}^{d} n_{i,j} \mathbf{t}'(\mathbf{x}_i, \mathbf{x}_j)\boldsymbol{\tau}, \\ &= \textstyle\sum_{i=1,j=1}^{d} n_{i,j}\ \mathbf{1}'_{(i-1)d+j}\ \mathbf{T}\ \boldsymbol{\tau}, \\ &= \mathbf{1}'\ \mathbf{L}\ \mathbf{T}\ \boldsymbol{\tau}, \end{aligned} \tag{5}$$

where $n_{i,j}$ denotes the number of transitions from design point $\mathbf{x}_i$ to design point $\mathbf{x}_j$ in the considered run order. $\mathbf{1}_{(i-1)d+j}$ is a $(d^2 \times 1)$ vector with element 1 at position $(i-1)d+j$ and 0 elsewhere. The column vector $\mathbf{1}$ contains d^2 1-elements. $\mathbf{L}$ is the $(d^2 \times d^2)$ matrix $\text{diag}(n_{1,1}, \ldots, n_{1,d}, \ldots, n_{d,1}, \ldots, n_{d,d})$ and the $(d^2 \times p_t)$-matrix $\mathbf{T}$ is written as

$$\mathbf{T} = \begin{bmatrix} \mathbf{t}'_{1,1} \\ \vdots \\ \mathbf{t}'_{1,d} \\ \vdots \\ \mathbf{t}'_{d,1} \\ \vdots \\ \mathbf{t}'_{d,d} \end{bmatrix}.$$

Based on the available cost information, a two-dimensional interpolation technique is used to calculate the transition costs. The first dimension refers to the factor levels of the previous run whereas the second dimension refers to the factor levels of the next run.

The total cost C of a run order is defined as the sum of the total measurement cost (4) and the total transition cost (5), or

$$\begin{aligned} C &= C^m + C^t, \\ &= \mathbf{1}'\ \mathbf{N}\ \mathbf{M}\ \boldsymbol{\varsigma} + \mathbf{1}'\ \mathbf{L}\ \mathbf{T}\ \boldsymbol{\tau}. \end{aligned} \tag{6}$$

Note that in (6), $\mathbf{N}$ and $\mathbf{L}$ are design dependent matrices. The cost information is reflected by $\mathbf{M}$, $\mathbf{T}$, $\boldsymbol{\varsigma}$ and $\boldsymbol{\tau}$.

3.2 Cost-efficient run orders optimally balanced for time trends

Henceforth y denotes the response of interest and $\mathbf{x}' = (x_1 \ \cdots \ x_f)$ is the vector of f control variables presumed to influence the response. Denote by $\mathbf{f}(\mathbf{x})$ the $(p \times 1)$ vector representing the polynomial expansion of $\mathbf{x}$ for the response model and by $\mathbf{g}(t)$ the $(q \times 1)$

vector representing the polynomial expansion for the time trend, expressed as a function of time t. With $\boldsymbol{\alpha}$ the $(p \times 1)$ vector of important parameters and $\boldsymbol{\beta}$ the $(q \times 1)$ vector of parameters of the polynomial time trend, let the model for the response be of the form

$$y = \mathbf{f}'(\mathbf{x})\boldsymbol{\alpha} + \mathbf{g}'(t)\boldsymbol{\beta} + \varepsilon = \mathbf{z}'(\mathbf{x}, t)\boldsymbol{\gamma} + \varepsilon. \tag{7}$$

The independent error terms ε are assumed to have expectation zero and constant variance σ^2. It is convenient to write (7) as

$$\mathbf{Y} = \mathbf{F}\boldsymbol{\alpha} + \mathbf{G}\boldsymbol{\beta} + \boldsymbol{\varepsilon} = \mathbf{Z}\boldsymbol{\gamma} + \boldsymbol{\varepsilon},$$

where $\mathbf{Y}$ is an $(n \times 1)$ vector of responses and $\mathbf{F}$ and $\mathbf{G}$ represent the $(n \times p)$ and the $(n \times q)$ extended design matrices respectively.

In the absence of trend effects, the $\mathcal{D}$-optimal design $\delta_{\mathcal{D}}$ is found by minimizing the generalized variance or, equivalently, by maximizing the determinant of the information matrix $\mathbf{F}'\mathbf{F}$. The $\mathcal{D}$-criterion value equals $\mathcal{D} = |\mathbf{F}'\mathbf{F}|$. Now we consider three additional optimality criteria.

Firstly, we define a run order to be $(\mathcal{D}, C)$-optimal if it maximizes the amount of information per unit cost. The corresponding design $\delta_{(\mathcal{D},C)}$ is also called $(\mathcal{D}, C)$-optimal. Computing $(\mathcal{D}, C)$-optimal run orders is based on maximization of

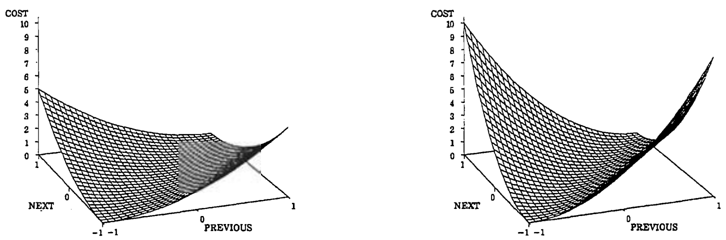
$$(\mathcal{D}, C) = \frac{|\mathbf{F}'\mathbf{F}|}{C}.$$

The efficiency of the $(\mathcal{D}, C)$-optimal design $\delta_{(\mathcal{D},C)}$ compared with the $\mathcal{D}$-optimal design $\delta_{\mathcal{D}}$ in terms of the amount of information per unit cost equals

$$\left(\frac{\mathcal{D}(\delta_{(\mathcal{D},C)})}{\mathcal{D}(\delta_{\mathcal{D}})}\right)^{\frac{1}{p}} \frac{C(\delta_{\mathcal{D}})}{C(\delta_{(\mathcal{D},C)})}. \tag{8}$$

Raising the determinants to the power $\frac{1}{p}$ results into an efficiency measure which is nearly proportional to design size. For instance, two replicates of a design double the $\mathcal{D}$-efficiency and the total measurement cost of that design. However, the total transition cost of the run order is not necessarily doubled but the average transition cost of all run orders belonging to that design certainly does (Appendix 1). Consequently, the interpretation of linearity is only precise when considering the average transition cost instead of the total transition cost.

The benefit of incorporating cost information in the construction of optimal designs is demonstrated by the following example. An imaginery experiment is set-up to study the influence of two factors x_1 and x_2 on a response of interest. The assumed model is described by $\mathbf{f}'(\mathbf{x}) = (1\ x_1\ x_2\ x_1x_2)$. The number of parameters p then equals 4 and the number of observations n equals 15. The design points constitute the full 2^2-factorial. The measurement costs are described by $c^m(\mathbf{x}) = 15 - 2.5x_1 + 2.5x_2$ and the transition costs are shown in Figure 1. According to (1) with $n = 15$ and $d = 4$, there are 816 designs. For each design, the amount of information $|\mathbf{F}'\mathbf{F}|$ and the total cost $C^m + C^t_{\min}$ is calculated. $C^t_{\min}$ denotes the total transition cost of the cheapest run order of that design. The results are shown in Figure 2 with labeled $\mathcal{D}$- and $(\mathcal{D}, C)$-optimal designs. One observes that the less informative designs have the largest variation in the total cost. The designs indicated by the points just above and beneath the $\mathcal{D}$-optimal design are a little less informative than the $\mathcal{D}$-optimal one but this is not perceptible in Figure 2. Of course, no design is more informative than the $\mathcal{D}$-optimal one, but many experiments are much cheaper. However, the decrease in cost goes at the expense of the amount of information obtained. The $(\mathcal{D}, C)$-optimality criterion seeks a trade-off between the amount of information obtained and the total cost of the experiment by maximizing the amount of information per unit cost. The decrease in information of the $(\mathcal{D}, C)$-optimal design is negligible and the decrease in the total cost amounts to 2%. Compared with the conventional $\mathcal{D}$-optimal design, the increase in the amount of information per unit cost amounts to 2%.



(a) factor x_1 (b) factor x_2

Figure 1: Transition Costs

Secondly, in the presence of time trends and when no costs are calculated for, designs are constructed that maximize the information on the important parameters $\boldsymbol{\alpha}$, whereas the q parameters modeling the time dependence are treated as nuisance parameters. The corresponding $\mathcal{D}_t$-optimal design $\delta_{\mathcal{D}_t}$ is found by maximizing

$$\mathcal{D}_t = \frac{|\mathbf{Z}'\mathbf{Z}|}{|\mathbf{G}'\mathbf{G}|},$$

where

$$|\mathbf{Z}'\mathbf{Z}| = \begin{vmatrix} \mathbf{F}'\mathbf{F} & \mathbf{F}'\mathbf{G} \\ \mathbf{G}'\mathbf{F} & \mathbf{G}'\mathbf{G} \end{vmatrix} = |\mathbf{G}'\mathbf{G}||\mathbf{F}'\mathbf{F} - \mathbf{F}'\mathbf{G}(\mathbf{G}'\mathbf{G})^{-1}\mathbf{G}'\mathbf{F}|.$$

A run order is called trend-free if the least-squares estimates of the factorial effects of interest are free of bias that might be introduced from the unknown trend effects in $\boldsymbol{\beta}$.

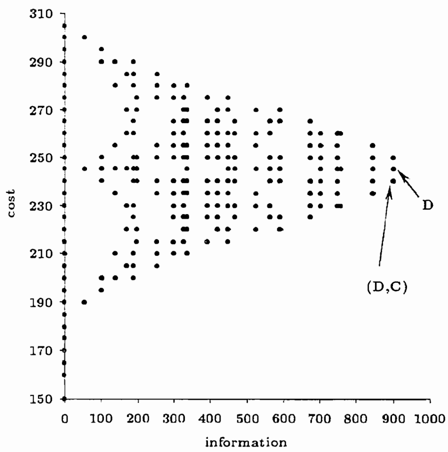


Figure 2: Cost and Information

Otherwise stated, trend-robustness is ascertained when the columns of $\mathbf{F}$ are orthogonal to the columns of $\mathbf{G}$ or, equivalently, when

$$|\mathbf{Z}'\mathbf{Z}| = \begin{vmatrix} \mathbf{F}'\mathbf{F} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}'\mathbf{G} \end{vmatrix} = |\mathbf{F}'\mathbf{F}||\mathbf{G}'\mathbf{G}|.$$

To compare the $\mathcal{D}$- and $\mathcal{D}_t$-optimal design for information about the important parameters $\boldsymbol{\alpha}$, the generalized variance of $\boldsymbol{\alpha}$ is compared through

$$\left(\frac{\mathcal{D}_t(\delta_{\mathcal{D}_t})}{\mathcal{D}(\delta_{\mathcal{D}})}\right)^{\frac{1}{p}}, \tag{9}$$

denoting the trend-resistance of the $\mathcal{D}_t$-optimal design or, equivalently, the protection of the $\mathcal{D}_t$-optimal design $\delta_{\mathcal{D}_t}$ against time order dependence.

Finally, in the presence of trend effects and when both measurement costs and transition costs are taken into account, the $(\mathcal{D}_t, C)$-optimal run order maximizes

$$(\mathcal{D}_t, C) = \frac{|\mathbf{Z}'\mathbf{Z}|}{|\mathbf{G}'\mathbf{G}|C}.$$

Analogous to the trend-resistance of the $\mathcal{D}_t$-optimal run order (9), the trend-resistance of the $(\mathcal{D}_t, C)$-optimal run order is defined as

$$\left(\frac{\mathcal{D}_t(\delta_{(\mathcal{D}_t,C)})}{\mathcal{D}(\delta_{\mathcal{D}})}\right)^{\frac{1}{p}} \tag{10}$$

and the efficiencies of the $(\mathcal{D}_t, C)$-optimal design compared with the $\mathcal{D}$-optimal design and the $\mathcal{D}_t$-optimal design in terms of the amount of information about the important parameters $\boldsymbol{\alpha}$ per unit cost equal

$$\left(\frac{\mathcal{D}_t(\delta_{(\mathcal{D}_t,C)})}{\mathcal{D}(\delta_{\mathcal{D}})}\right)^{\frac{1}{p}} \frac{C(\delta_{\mathcal{D}})}{C(\delta_{(\mathcal{D}_t,C)})}$$

and

$$\left(\frac{\mathcal{D}_t(\delta_{(\mathcal{D}_t,C)})}{\mathcal{D}(\delta_{\mathcal{D}_t})}\right)^{\frac{1}{p}} \frac{C(\delta_{\mathcal{D}_t})}{C(\delta_{(\mathcal{D}_t,C)})}$$

respectively. In the next section, we propose an algorithm for the construction of $(\mathcal{D}, C)$-, $\mathcal{D}_t$- and $(\mathcal{D}_t, C)$-optimal run orders.

4 The design construction algorithm

Many algorithms have been proposed to construct optimal designs. Welch (1982) applies branch and bound to compute $\mathcal{D}$-optimal designs. Approaches based on simulated annealing can be found in Haines (1987) and Meyer and Nachtsheim (1988). Exchange algorithms sequentially add and delete design points in order to improve the objective function. Some examples include Wynn's algorithm (Wynn (1972)), the DETMAX algorithm of Mitchell (1974), Fedorov's algorithm (Fedorov (1972)), the modified Fedorov algorithm of Cook and Nachtsheim (1980), the k-exchange algorithm of Johnson and Nachtsheim (1983), the kl-exchange algorithm of Atkinson and Donev (1989), the BLKL algorithm of Atkinson and Donev (1992) and the coordinate-exchange algorithm of Meyer and Nachtsheim (1995). The aim of our proposed exchange algorithm is the construction of optimal run orders by allocating n observations selected from a candidate list of d design points to n out of h available time points in such a way as to maximize the value of the optimality criterion used.

4.1 Description of the algorithm

In the first phase of the algorithm, the experimenter can include n_1 treatment combinations with corresponding time points. Then the problem converts to design augmentation. This frequently occurs when additional observations are needed after a screening experiment or when an initial experiment has failed. None of the observations specified by the experimenter can be removed from the run order during the optimization procedure. Next, a starting run order is constructed by allotting n_2 randomly chosen treatment combinations from the candidate list to n_2 randomly chosen time points from the list of allowable time points. This starting run order is then augmented to n trials in the second phase, by sequentially adding $n - n_1 - n_2$ treatment combinations at time points still available so that these additions lead to the largest improvement of the optimality criterion. Finally, the trials are subject to iterative improvement in the third phase. This improvement of the run order consists of alternate exchange and interchange of design points. The effect of the deletion of a design point $\mathbf{x}_i$ at time point t_k and the addition of a new design point $\mathbf{x}_j$ from the list of candidate points at a time point t_l still available is investigated. The interchange of design points $\mathbf{x}_i$ and $\mathbf{x}_j$ from $(\mathbf{x}_i, t_k)$ and $(\mathbf{x}_j, t_l)$ to $(\mathbf{x}_i, t_l)$ and $(\mathbf{x}_j, t_k)$ is also investigated. The process continues as long as an exchange or interchange increases the value of the optimality criterion used. In order to avoid being stuck at a local optimum, the probability of finding the global optimum can be increased by repeating the search several times from different starting designs or 'tries'. The input to the algorithm consists of the number of tries v, the number of factors f, the order and the number of parameters p of the response model, the polynomial expansion for the response model $\mathbf{f}(\mathbf{x})$, the order and the number of parameters q of the time trend, the polynomial expansion for the time trend $\mathbf{g}(t)$, the number of observations n, cost information $\mathbf{m}$, $\mathbf{t}$, ς and $\boldsymbol{\tau}$, the list of n_1 treatment combinations and n_1 corresponding time points to be included in the starting run order, the list of h allowable time points and the list of d candidate points. The list of d candidate design points can be either user specified or computed as shown in Atkinson and Donev (1992). Our algorithm is outlined in Appendix 2.

4.2 Update formulae

Reduction of computation time is obtained by using powerful update formulae in order to evaluate the effect of a newly added design point or of an exchange and interchange.

As an example, addition of a new design point $\mathbf{x}_i$ at time point t_k leads to a new total cost of the experiment equal to

$$C_{\text{new}} = C_{\text{old}} + \mathbf{m}'(\mathbf{x}_i)\varsigma + (\mathbf{t}'(\mathbf{x}_{b_i}, \mathbf{x}_i) + \mathbf{t}'(\mathbf{x}_i, \mathbf{x}_{a_i}) - \mathbf{t}'(\mathbf{x}_{b_i}, \mathbf{x}_{a_i}))\boldsymbol{\tau},$$

where $\mathbf{x}_{b_i}$ and $\mathbf{x}_{a_i}$ are the respective design points just before and after $\mathbf{x}_i$ in the new run order. The newly obtained $(\mathcal{D}_t, C)$-value equals

$$(\mathcal{D}_t, C)_{\text{new}} = (\mathcal{D}_t, C)_{\text{old}} \cdot \frac{1 + \mathbf{z}'(\mathbf{x}_i, t_k)(\mathbf{Z}'\mathbf{Z})^{-1}\mathbf{z}(\mathbf{x}_i, t_k)}{1 + \mathbf{g}'(t_k)(\mathbf{G}'\mathbf{G})^{-1}\mathbf{g}(t_k)} \frac{C_{\text{old}}}{C_{\text{new}}}. \tag{11}$$

After addition of a new design point, the updated matrices $(\mathbf{Z}'\mathbf{Z})^{-1}$ and $(\mathbf{G}'\mathbf{G})^{-1}$ are

$$\{\mathbf{Z}'\mathbf{Z} + \mathbf{z}(\mathbf{x}_i, t_k)\mathbf{z}'(\mathbf{x}_i, t_k)\}^{-1} = (\mathbf{Z}'\mathbf{Z})^{-1} - \frac{(\mathbf{Z}'\mathbf{Z})^{-1}\mathbf{z}(\mathbf{x}_i, t_k)\mathbf{z}'(\mathbf{x}_i, t_k)(\mathbf{Z}'\mathbf{Z})^{-1}}{1 + \mathbf{z}'(\mathbf{x}_i, t_k)(\mathbf{Z}'\mathbf{Z})^{-1}\mathbf{z}(\mathbf{x}_i, t_k)} \tag{12}$$

and

$$\{\mathbf{G}'\mathbf{G} + \mathbf{g}(t_k)\mathbf{g}'(t_k)\}^{-1} = (\mathbf{G}'\mathbf{G})^{-1} - \frac{(\mathbf{G}'\mathbf{G})^{-1}\mathbf{g}(t_k)\mathbf{g}'(t_k)(\mathbf{G}'\mathbf{G})^{-1}}{1 + \mathbf{g}'(t_k)(\mathbf{G}'\mathbf{G})^{-1}\mathbf{g}(t_k)}. \tag{13}$$

Since all components in the right hand side of (11), (12) and (13) are known, the effect of the design change is readily calculated without computationally intensive matrix inversions and determinant operations. Similar update formulae can be established for the considered exchanges and interchanges.

5 Applications

This section illustrates the benefits of incorporating cost information in the construction of optimal designs. In the first application the effect of incorporating cost considerations on the trend-resistance of the optimal run orders is investigated. Afterwards, two case studies clarify practical utility in industrial environments.

5.1 Trend effects in experimental design

The aim of this example is to investigate the influence of incorporating cost information on the protection against time order dependence. A 2-factor experiment is conducted and a full second-order response function is assumed. The support points constitute the full 3^2-factorial. The number of observations equals 30 and as many time points are available. The observations are expected to be distorted by a linear time trend. The measurement costs are described by $c^m(\mathbf{x}) = 10 + 100x_1^2 + 100x_2^2$. This means that measurements at moderate factor levels can be performed at low costs, whereas low and high factor levels involve large costs. The transition costs are shown in Figure 3. For instance, altering factors x_1 or x_2 from the low level to the high level or vice versa amounts to a cost of 100.

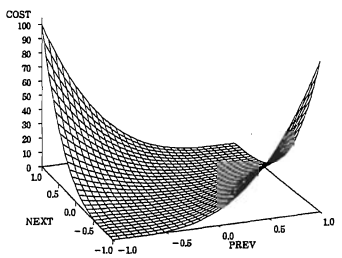
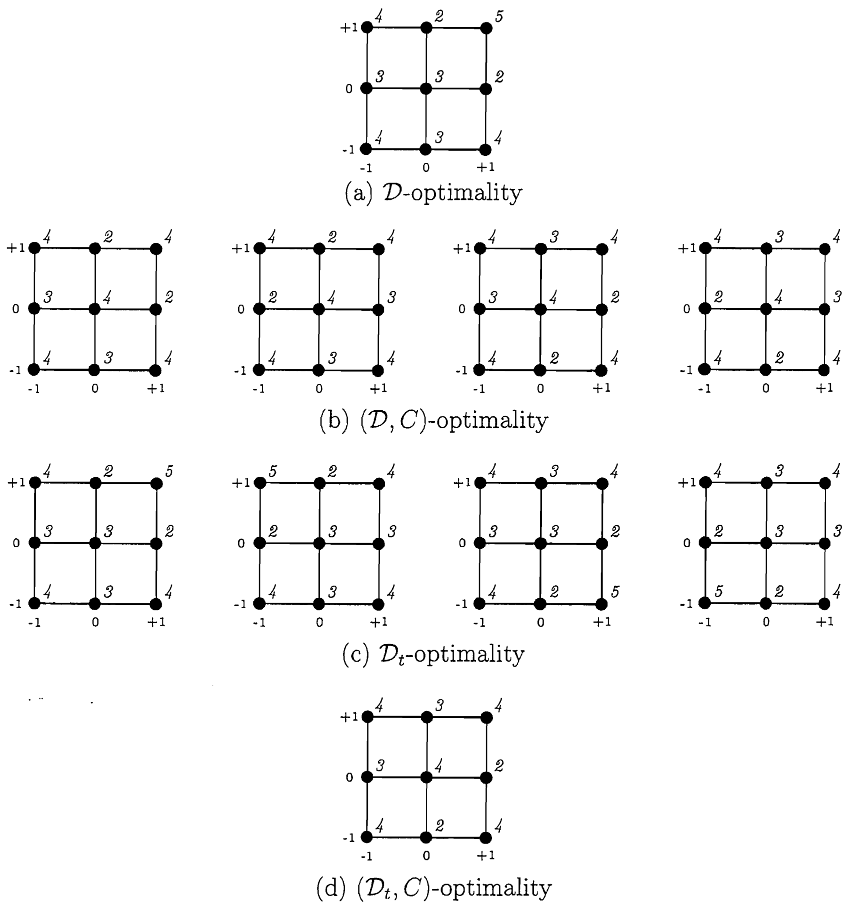


Figure 3: Transition Costs for Factors x_1 and x_2

Figure 4 displays the computed optimal designs for various optimality criteria and the results are intuitively appealing. Comparison of the $\mathcal{D}$-optimal design and the $(\mathcal{D}, C)$-optimal designs reveals a little shift in the number of replicates from design point (1,1) to design point (0,0). This shift can be explained from the fact that average factor level settings are cheapest. When the experiment is designed to be protected against a linear time trend, four $\mathcal{D}_t$-optimal designs are obtained, from which one corresponds with the $\mathcal{D}$-optimal design. Taking into account both a linear time trend and cost considerations, the $(\mathcal{D}_t, C)$-optimal design especially differs from the $\mathcal{D}$-optimal design in that the expensive design point (1,1) and the cheap design point (0,0) are replicated once less and once more respectively.



(a) $\mathcal{D}$-optimality

(b) $(\mathcal{D}, C)$-optimality

(c) $\mathcal{D}_t$-optimality

(d) $(\mathcal{D}_t, C)$-optimality

Figure 4: Optimal Designs for Different Optimality Criteria

Other polynomial time trends of the form $\mathbf{g}'(t) = (t^q)$ are also investigated. According to (9) and (10), the protection against time trends of the $\mathcal{D}_t$- and $(\mathcal{D}_t, C)$-optimal run orders $\delta_{\mathcal{D}_t}$ and $\delta_{(\mathcal{D}_t,C)}$ are given in Table 2. The results show that incorporating cost information goes at the expense of the protection against time order dependence. However, this loss in protection against time order dependence is rather negligible. The results can be generalized to other cost functions.

	trend-resistance (%)	
q	$\delta_{\mathcal{D}_t}$	$\delta_{(\mathcal{D}_t,C)}$
1	99.99	99.64
2	87.33	86.98
3	100	99.62
4	92.78	92.45
5	100	99.64

Table 2: Trend-Resistance for Several Polynomial Time Trends

5.2 Case 1: The platen and wafer frequency experiment

This example is based on an experiment reported by Freeny and Lai (1997). Advanced photolithography in very large scale integration (VLSI) increasingly demands global planarity across a chip-sized printing field for fine resolution. Chemical mechanical polishing (CMP) is a simple technique to achieve this.

In a designed experiment a polisher which does oxide planarization by CMP is evaluated for possible use in the wafer fabrication manufacturing process. The goal is to find the maximum rate of oxide removal which could be used without degrading the uniformity of the removal over the surface of the wafer. Consequently, the important responses are the polisher removal rate and the uniformity across the wafer. We confine ourselves to the polishing rate. In CMP, a wafer is held by a rotating carrier and is polished by pressing the wafer face down onto a polishing pad on a rotating platen. The rotating padded platen is impregnated with a slurry of extremely fine abrasive. The important parameters for the polishing process are platen and wafer rotation frequencies, x_1 and x_2 respectively, whereas the polishing pressure was held constant at a single optimum value based on previous work. All combinations of three platen and five wafer rotation frequencies were used. These are 11, 15 and 19 rpm and 12, 22, 32, 42 and 52 rpm respectively. The 15 polishing conditions combining every platen frequency with every wafer frequency form a full factorial experiment. A tendency of the polisher removal rate to drift lower through time had previously been noticed. This drift results in imperfect process reproducibility even with automation. For that reason, we introduce a linear trend described by g(t) = (t). An important design issue was to choose the order of the fifteen combinations to estimate the effects of the design parameters independent of the linear drift. In the experiment mentioned by Freeny and Lai (1997), the run sequence of polishing conditions is chosen to confound the effect of the linear drift with interaction component $x_1^2x_2^3$ (Table 3).

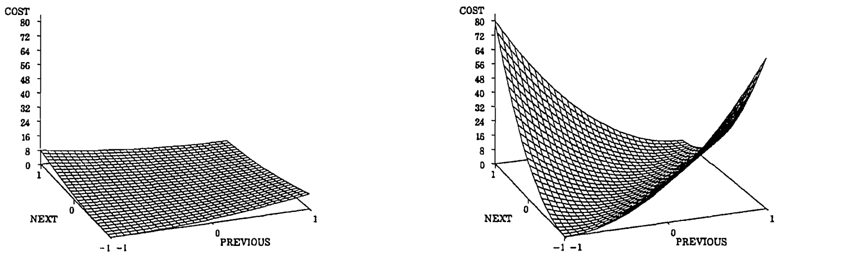
							Freeny and Lai								
run	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
x_1	15	19	11	15	11	19	11	15	19	11	19	15	19	11	15
x_2	22	42	42	52	12	12	32	32	22	52	52	12	32	22	42
								$\delta_{\mathcal{D}_t}$							
run	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
x_1	15	11	15	11	19	19	11	15	19	11	11	19	15	15	19
x_2	42	22	12	52	22	52	32	32	32	12	42	12	52	22	42

Table 3: Run Orders

The assumed response function is given by

$$\mathbf{f}'(\mathbf{x}) = (1\ x_1\ x_2\ x_1^2\ x_1x_2\ x_2^2\ x_1^2x_2\ x_1x_2^2\ x_2^3\ x_1^2x_2^2\ x_1x_2^3\ x_2^4\ x_1x_2^4\ x_1^2x_2^4).$$

Previous work indicated that the polisher may not reach equilibrium immediately after a change in the parameter settings. We turn this knowledge into a transition cost c^t and assume an increasing cost function of factor level changes. Moreover, $c^t = c_1^t + c_2^t$ where c_i^t refers to the transition cost associated with changing the levels of factor i. We computed the $\mathcal{D}_t$- and $(\mathcal{D}_t, C)$-optimal run orders $\delta_{\mathcal{D}_t}$ and $\delta_{(\mathcal{D}_t,C)}$ for several ratios $\frac{c_1^t}{c_2^t}$. For instance, $\frac{c_1^t}{c_2^t} = 0.1$ means that factor x_1 is ten times cheaper to change than factor x_2. The transition costs for $\frac{c_1^t}{c_2^t} = 0.1$ are shown in Figure 5. The optimal run orders are compared with the run order of Freeny and Lai in Table 4. The results presented relate to the quadratic cost functions of Figure 5 but also hold for other increasing cost functions.



(a) c_1^t for Platen Rotation Frequency (x_1) (b) c_2^t for Wafer Rotation Frequency (x_2)

Figure 5: Transition Costs in Platen and Wafer Frequency Experiment for $\frac{c_1^t}{c_2^t} = 0.1$

One observes from Table 4 that the $\mathcal{D}_t$-optimal run order $\delta_{\mathcal{D}_t}$ is a little more trend-resistant than the run order proposed in Freeny and Lai (1997). This $\mathcal{D}_t$-optimal run order is shown

$\frac{c_1^t}{c_2^t}$	trend-resistance (%) Freeny and Lai	$\delta_{\mathcal{D}_t}$	$\delta_{(\mathcal{D}_t,C)}$	cost per unit information Freeny and Lai	$\delta_{\mathcal{D}_t}$	$\delta_{(\mathcal{D}_t,C)}$
1000	98.67	99.14	95.22	22865	22180	4720
100	98.67	99.14	95.22	2296	2227	490
10	98.67	99.14	95.22	239	231	67
1	98.67	99.14	98.43	34	32	21
0.1	98.67	99.14	95.80	130	118	71
0.01	98.67	99.14	93.99	1094	983	527
0.001	98.67	99.14	93.99	10736	9630	4967

Table 4: Comparison of Run Orders

in Table 3. A small decrease in trend-robustness is observed when transition costs are calculated for. Both the $\mathcal{D}_t$- and $(\mathcal{D}_t, C)$-optimal run orders outperform the run order of Freeny and Lai in terms of cost per unit information. This especially comes true for the $(\mathcal{D}_t, C)$-optimal run orders. In conclusion, the $\mathcal{D}_t$- and $(\mathcal{D}_t, C)$-optimal run orders offer an outperforming alternative for the run order mentioned in Freeny and Lai (1997).

5.3 Case 2: The flame spectroscopy experiment

This case refers to an application mentioned by Joiner and Campbell (1976). An experiment is executed in order to evaluate the sensitivity of a spectrophotometer. Five factors are included to be examined: lamp position, burner position, burner height, type of flame and flow rate. The measurements are believed to drift linearly with time due to carbon build-up. For this reason, it is necessary to interrupt the measurements and remove all of the built up carbon after every 20 observations. The number of levels per factor and the times needed to change the factor levels are given in Table 5.

	factor	number of levels	time to change (sec)
x_1	lamp position	2	1
x_2	burner position	2	60
x_3	burner height	3	1
x_4	type of flame	3	60
x_5	flow rate	3	120

Table 5: Description of the Flame Spectroscopy Experiment

We assume that each observation has a fixed measurement cost and that the transition cost equals the time needed to change the factor levels. As a consequence, the $(\mathcal{D}_t, C)$-optimality criterion can be seen as the criterion with which run orders that maximize the amount of information per unit time are preferred.

Table 6 compares the computed $\mathcal{D}_t$- and $(\mathcal{D}_t, C)$-optimal run orders for the following response models:

(1) $\mathbf{f}'(\mathbf{x}) = (1\ x_1\ x_2\ x_3\ x_4\ x_5)$
(2) $\mathbf{f}'(\mathbf{x}) = (1\ x_1\ x_2\ x_3\ x_4\ x_5\ x_3^2\ x_4^2\ x_5^2)$
(3) $\mathbf{f}'(\mathbf{x}) = (1\ x_1\ x_2\ x_3\ x_4\ x_5\ x_1x_2\ x_1x_3\ x_1x_4\ x_1x_5\ x_2x_3\ x_2x_4\ x_2x_5\ x_3x_4\ x_3x_5\ x_4x_5)$
(4) $\mathbf{f}'(\mathbf{x}) = (1\ x_1\ x_2\ x_3\ x_4\ x_5\ x_3^2\ x_4^2\ x_5^2\ x_1x_2\ x_1x_3\ x_1x_4\ x_1x_5\ x_2x_3\ x_2x_4\ x_2x_5\ x_3x_4\ x_3x_5\ x_4x_5)$

The reduction in terms of percentage in the total transition cost, trend-resistance and the cost per unit information of the $(\mathcal{D}_t, C)$-optimal run order with respect to the $\mathcal{D}_t$-optimal run order is also mentioned.

	transition cost			trend-resistance (%)			cost per unit information		
$\mathbf{f}'(\mathbf{x})$	$\delta_{\mathcal{D}_t}$	$\delta_{(\mathcal{D}_t,C)}$	red.	$\delta_{\mathcal{D}_t}$	$\delta_{(\mathcal{D}_t,C)}$	red.	$\delta_{\mathcal{D}_t}$	$\delta_{(\mathcal{D}_t,C)}$	red.
(1)	≥ 2669	1107	59	100	99.29	0.7	≥ 133	56	58
(2)	≥ 2537	1177	54	99.99	99.00	1.0	≥ 243	114	53
(3)	4170	3151	24	82.70	82.48	0.3	263	200	24
(4)	3864	3034	21	77.81	73.39	5.7	526	345	34

Table 6: Comparison of Optimal Run Orders for Different Response Models

Remark that for the first two models in Table 6 more than one $\mathcal{D}_t$-optimal run order is found. Consequently different total transition costs are obtained for these $\mathcal{D}_t$-optimal run orders but Table 6 only mentions the lowest transition cost. Table 6 shows that the performance of the $\mathcal{D}_t$- and $(\mathcal{D}_t, C)$-optimal run orders in terms of trend-resistance and cost per unit information decreases when the response model becomes more complicated. It is also shown that when costs are considered, the reduction in the total transition cost ranges from 21% for the fourth model to 59% for the simplest model. Again, taking into account costs in optimum design theory partly goes at the expense of trend-resistance of the optimal run order but the decrease in trend-resistance is negligible for quite simple models. Furthermore, incorporating costs entails a decrease in the cost per unit information that ranges from 24% for the third model to 58% for the first model.

6 Conclusion

Economical reasons often limit the usefulness of experimental designs computed on the basis of alphabetic optimality criteria. However, the incorporation of cost considerations in optimum design theory is a topic about which the literature is suspiciously silent. This paper provides a thorough analysis of cost considerations in the construction of optimum designs. Measurement costs refer to the costs associated with particular factor level combinations and transition costs are involved by changing the factor levels from one observation to another. In view of cost minimization, the experimenter should minimize the total number of factor level changes by performing the runs that correspond with the same treatment combination one after the other. However, run trends may affect the observed response. Minimization of the number of factor level changes is no longer the only design issue. This paper presents an algorithm for the construction of cost-efficient run orders that are optimally protected against time trends. Arbitrary design problems and arbitrary cost models can be treated. The results show that incorporating cost information implies a considerable increase in the amount of information per unit cost and the loss in trend-resistance of the cost-efficient run orders is rather negligible.

Appendix 1. The average transition cost per run order

Theorem

The average transition cost per run order of an experiment $\{n_i\}_{i=1}^{d}$ with $n = \sum_{i=1}^{d} n_i$ observations equals $\frac{1}{n}\mathbf{1}'(\mathbf{N}\otimes\mathbf{N})\mathbf{T}\boldsymbol{\tau}$.

Proof

For all $i \in \{1,\ldots,d\}$, we denote each observation $r \in \{1,\ldots,n_i\}$ of design point $\mathbf{x}_i$ as $\mathbf{x}_{i(r)}$. The experiment now consists of n design points $x_{i(r)}$, with $i \in \{1,\ldots,d\}$ and $r \in \{1,\ldots,n_i\}$. Now, $n-1$ distinct transitions can be associated with each design point $\mathbf{x}_{i(r)}$:

$$(\mathbf{x}_{i(r)},\mathbf{x}_{1(1)}),\ldots,(\mathbf{x}_{i(r)},\mathbf{x}_{1(n_1)}),\ldots,(\mathbf{x}_{i(r)},\mathbf{x}_{i(1)}),\ldots,(\mathbf{x}_{i(r)},\mathbf{x}_{i(r-1)}),$$

$$(\mathbf{x}_{i(r)},\mathbf{x}_{i(r+1)}),\ldots,(\mathbf{x}_{i(r)},\mathbf{x}_{i(n_i)}),\ldots,(\mathbf{x}_{i(r)},\mathbf{x}_{d(1)}),\ldots,(\mathbf{x}_{i(r)},\mathbf{x}_{d(n_d)}).$$

This means that for the n design points $\mathbf{x}_{i(r)}$, the total number of distinct transitions equals $n(n-1)$. Furthermore, n distinct design points yield $n!$ different orderings and each run order involves $n-1$ transitions. As a consequence, the total number of transitions over all run orders equals $n!(n-1)$. It follows that each transition $(\mathbf{x}_{i(r)},\mathbf{x}_{i'(r')})$ occurs $\frac{n!(n-1)}{n(n-1)} = (n-1)!$ times.

Besides, each transition $(\mathbf{x}_i,\mathbf{x}_i)$ belongs to the following set of $n_i(n_i-1)$ distinct transitions:

$$(\mathbf{x}_{i(1)},\mathbf{x}_{i(2)}),\ldots,(\mathbf{x}_{i(1)},\mathbf{x}_{i(n_i)}),\ldots,(\mathbf{x}_{i(r)},\mathbf{x}_{i(1)}),\ldots,(\mathbf{x}_{i(r)},\mathbf{x}_{i(r-1)}),$$

$$(\mathbf{x}_{i(r)},\mathbf{x}_{i(r+1)}),\ldots,(\mathbf{x}_{i(r)},\mathbf{x}_{i(n_i)}),\ldots,(\mathbf{x}_{i(n_i)},\mathbf{x}_{i(1)}),\ldots,(\mathbf{x}_{i(n_i)},\mathbf{x}_{i(n_i-1)}).$$

The total number of transitions $(\mathbf{x}_i,\mathbf{x}_i)$ over all $n!$ run orders now equals $(n-1)!n_i(n_i-1)$. This is a fraction $\frac{(n-1)!n_i(n_i-1)}{n!(n-1)} = \frac{n_i(n_i-1)}{n(n-1)}$ [1] of the $n!(n-1)$ transitions over all run orders.

In a similar way, the transition $(\mathbf{x}_i, \mathbf{x}_j)$ belongs to the following set of $n_i n_j$ distinct transitions:

$$(\mathbf{x}_{i(1)}, \mathbf{x}_{j(1)}), \ldots, (\mathbf{x}_{i(1)}, \mathbf{x}_{j(n_j)}), \ldots, (\mathbf{x}_{i(n_i)}, \mathbf{x}_{j(1)}), \ldots, (\mathbf{x}_{i(n_i)}, \mathbf{x}_{j(n_j)}).$$

These $n_i n_j$ distinct transitions together occur $(n-1)! n_i n_j$ times, namely a fraction $\frac{(n-1)! n_i n_j}{n!(n-1)} = \frac{n_i n_j}{n(n-1)}$ [2] of the $n!(n-1)$ transitions over all run orders.

Generally speaking, an experiment $\{n_i\}_{i=1}^d$ can be run in $\frac{n!}{n_1! \cdots n_d!}$ different ways, resulting into $(n-1)\frac{n!}{n_1! \cdots n_d!}$ transitions. According to [1], the total number of transitions $(\mathbf{x}_i, \mathbf{x}_i)$ over all run orders is a fraction $\frac{n_i(n_i-1)}{n(n-1)}$ of $(n-1)\frac{n!}{n_1! \cdots n_d!}$ transitions or equals $n_i(n_i - 1)\frac{(n-1)!}{n_1! \cdots n_d!}$ [3]. From [2], the total number of transitions $(\mathbf{x}_i, \mathbf{x}_j)$ is a fraction $\frac{n_i n_j}{n(n-1)}$ of $(n-1)\frac{n!}{n_1! \cdots n_d!}$ or equals $n_i n_j \frac{(n-1)!}{n_1! \cdots n_d!}$ [4]. Based on [3], [4] and the expression for the total transition cost of a run order (5), the total transition cost summated over all run orders belonging to experiment $\{n_i\}_{i=1}^d$ equals

$$\frac{(n-1)!}{n_1! \cdots n_d!}\mathbf{1}' \begin{bmatrix} n_1(n_1-1) & 0 & \cdots & 0 & \cdots & 0 & \cdots & 0 & 0 \\ 0 & n_1 n_2 & \cdots & 0 & \cdots & 0 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & & \vdots & & \vdots & \vdots \\ 0 & 0 & \cdots & n_1 n_d & \cdots & 0 & \cdots & 0 & 0 \\ \vdots & \vdots & & \vdots & \ddots & \vdots & & \vdots & \vdots \\ 0 & 0 & \cdots & 0 & \cdots & n_d n_1 & \cdots & 0 & 0 \\ \vdots & \vdots & & \vdots & & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \cdots & 0 & \cdots & 0 & \cdots & n_d n_{d-1} & 0 \\ 0 & 0 & \cdots & 0 & \cdots & 0 & \cdots & 0 & n_d(n_d-1) \end{bmatrix} \mathbf{T}\boldsymbol{\tau}.$$

This total transition cost can be rewritten as

$$\frac{(n-1)!}{n_1! \cdots n_d!}\mathbf{1}'\left(\mathbf{N} \otimes \mathbf{N} - \mathbf{H}(\mathbf{I} \otimes \mathbf{N})\right)\mathbf{T}\boldsymbol{\tau},$$

with $\mathbf{H} = \text{diag}(\mathbf{1}_1\mathbf{1}_1' \cdots \mathbf{1}_d\mathbf{1}_d')$. Because there are $\frac{n!}{n_1! \cdots n_d!}$ run orders, the average transition cost per run order now equals

$$\frac{1}{n}\mathbf{1}'(\mathbf{N} \otimes \mathbf{N})\mathbf{T}\boldsymbol{\tau} - \frac{1}{n}\mathbf{1}'(\mathbf{H}(\mathbf{I} \otimes \mathbf{N}))\mathbf{T}\boldsymbol{\tau} = \frac{1}{n}\mathbf{1}'(\mathbf{N} \otimes \mathbf{N})\mathbf{T}\boldsymbol{\tau} - \frac{1}{n}(n_1\mathbf{t}_{1,1}' + \ldots + n_d\mathbf{t}_{d,d}')\boldsymbol{\tau}.$$

It goes without saying that no costs are associated with transition $(\mathbf{x}_i, \mathbf{x}_i)$, or equivalently, $\mathbf{t}_{i,i}'\boldsymbol{\tau} = 0$ for all $i \in \{1, \ldots, d\}$. The average transition cost per run order then simplifies to

$$\frac{1}{n}\mathbf{1}'(\mathbf{N} \otimes \mathbf{N})\mathbf{T}\boldsymbol{\tau}.$$

□

The design dependence of the average transition cost per run order is reflected by matrix $\mathrm{N} = \mathrm{diag}(n_1 \;\cdots\; n_d)$. Replicating the experiment $\{n_i\}_{i=1}^{d}$ ρ times, results into an average transition cost per run order equal to

$$\frac{1}{\rho n}\mathbf{1}'((\rho\mathrm{N}) \otimes (\rho\mathrm{N}))\mathbf{T}\boldsymbol{\tau} = \rho\,\frac{1}{n}\mathbf{1}'(\mathrm{N} \otimes \mathrm{N})\mathbf{T}\boldsymbol{\tau}.$$

This means that the average transition cost per run order is proportional to the number of replicates of the experiment.

Appendix 2. The construction algorithm

In the outline of the algorithm, we denote the value of the user specified optimality criterion as $\mathcal{Q}$. Possibilities are the $\mathcal{D}$-, $(\mathcal{D}, C)$-, $\mathcal{D}_t$- and $(\mathcal{D}_t, C)$-criterion. The list of d candidate points is denoted as $D = \{1, \ldots, d\}$ and the initial list of available time points is given as $T = \{1, \ldots, h\}$. The addition of design points to the run order diminishes the number of time points available. For that reason, the list of available time points T has to be updated after each addition or deletion of a design point. A design is denoted as a series $\{n_i\}$ and a run order is written as a series $R = \{(\mathbf{x}_i, t_j)\}$. After addition of design points that the experimenter wants to include in the starting design, the list of still available time points. the value of the optimality criterion, the design and the run order are denoted as T_0, $\mathcal{Q}_0$, $\{n_{0i}\}$ and R_0 respectively. Besides, the optimal value of the criterion, the optimal run order and the optimal design will be written as $\mathcal{Q}_{\text{opt}}, R_{\text{opt}}$ and $\{n_i\}_{\text{opt}}$ respectively. After inclusion of the user specified n_1 design points and corresponding time points, the algorithm proceeds as follows:

1. Set $\mathcal{Q}_{\text{opt}} = \mathcal{Q}_0$.
2. Set $\forall i \in D : n_i = 0$, $R = R_0$, $T = T_0$ and $\mathcal{Q} = \mathcal{Q}_0$.
3. Repeat v times:
   (a) Randomly choose n_2 subject to $\max(0, p + q - n_1) \leq n_2 \leq n - n_1$.
   (b) Repeat n_2 times:
      i. Randomly choose $i \in D$.
      ii. $n_i = n_i + 1$.
      iii. Randomly choose $k \in T$.
      iv. $R = R \cup \{(\mathbf{x}_i, t_k)\}$.
      v. $T = T \setminus \{k\}$.
      vi. Update $\mathcal{Q}$.
   (c) Repeat $n - n_1 - n_2$ times:
      i. Determine $i \in D$ and $k \in T$ with largest effect on $\mathcal{Q}$.

ii. $n_i = n_i + 1$.

iii. $R = R \cup \{(\mathbf{x}_i, t_k)\}$.

iv. $T = T \setminus \{k\}$.

v. Update $\mathcal{Q}$.

(d) Consider the exchanges and interchanges.

i. Set $\triangle = 1$.

ii. Find the best exchange:
$\forall j \in D, \forall l \in T_0, \forall (\mathbf{x}_i, t_k) \in R, \mathbf{x}_i \neq \mathbf{x}_j$ or $t_k \neq t_l$:
compute the effect $\triangle^E_{(\mathbf{x}_i,t_k),(\mathbf{x}_j,t_l)}$ on $\mathcal{Q}$ of deleting $(\mathbf{x}_i, t_k)$ and adding $(\mathbf{x}_j, t_l)$.
If $\triangle^E_{(\mathbf{x}_i,t_k),(\mathbf{x}_j,t_l)} > \triangle$ then $\triangle = \triangle^E_{(\mathbf{x}_i,t_k),(\mathbf{x}_j,t_l)}$, $S = 1$ and store i, j, k, l.

iii. Find the best interchange:
$\forall (\mathbf{x}_i, t_k), (\mathbf{x}_j, t_l) \in R, t_k \neq t_l$:
compute the effect $\triangle^I_{(\mathbf{x}_i,t_k),(\mathbf{x}_j,t_l)}$ on $\mathcal{Q}$ of interchanging $(\mathbf{x}_i, t_k)$ and $(\mathbf{x}_j, t_l)$.
If $\triangle^I_{(\mathbf{x}_i,t_k),(\mathbf{x}_j,t_l)} > \triangle$ then $\triangle = \triangle^I_{(\mathbf{x}_i,t_k),(\mathbf{x}_j,t_l)}$, $S = 2$ and store i, j, k, l.

(e) If $\triangle > 1$ then

i. If $S = 1$ then $R = R \setminus \{(\mathbf{x}_i, t_k)\} \cup \{(\mathbf{x}_j, t_l)\}, n_i = n_i - 1, n_j = n_j + 1$ and $T = T \setminus \{k\} \cup \{l\}$.

ii. If $S = 2$ then $R = R \setminus \{(\mathbf{x}_i, t_k), (\mathbf{x}_j, t_l)\} \cup \{(\mathbf{x}_i, t_l), (\mathbf{x}_j, t_k)\}$.

iii. Update $\mathcal{Q}$.

iv. Go to step (d).

(f) If $\mathcal{Q} \geq \mathcal{Q}_{\text{opt}}$, then $\mathcal{Q}_{\text{opt}} = \mathcal{Q}, R_{\text{opt}} = R \cup R_0$ and $\{n_i\}_{\text{opt}} = \{n_{0i}\} \cup \{n_i\}$.

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