Strategies for Supersaturated Screening Experiments

Maria Weese

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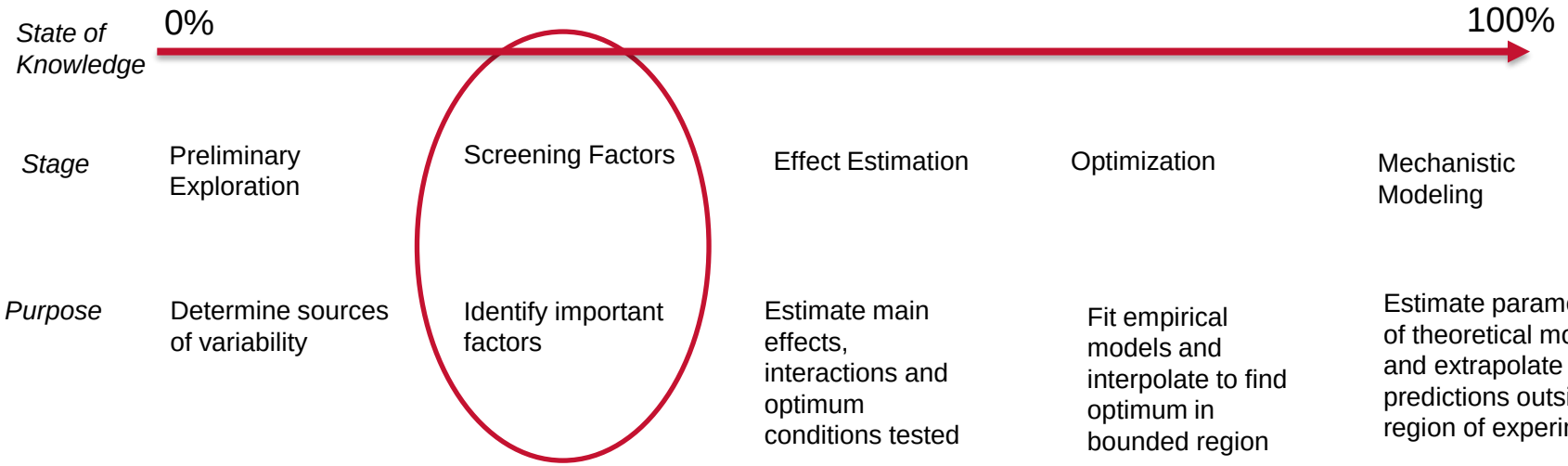
Experimental Design

“Experimental design is a collection of tools that are useful for increasing the state of knowledge about a particular phenomenon.”

Lawson, J. (2014). *Design and Analysis of Experiments with R*. CRC press.

Experimental is Sequential!



Lawson, J. (2014). *Design and Analysis of Experiments with R*. CRC press.

Goal of Screening

The goal of a screening experiment is not to make precise estimates, but to identify the important factors.

For example, suppose I have five factors and first three are truly active with $\beta_1 = \beta_2 = \beta_3 = 5$. And the last two are truly inactive with $\beta_4 = \beta_5 = 0$.

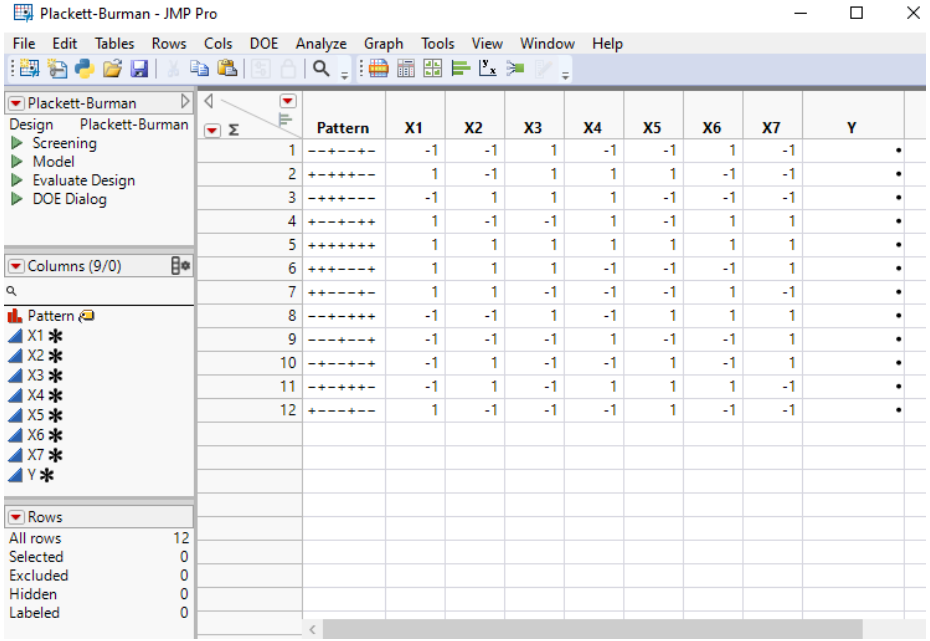
In an analysis, I might estimate $\widehat{\beta_j} = 1$ for j=1,2,3 and $\widehat{\beta_j} = 0$ for j=4,5.

In this case the screening results would be perfect, but the estimators would be poor.

Typical Screening Designs

Typical screening designs are fractional factorial design and Placket-Burman designs.

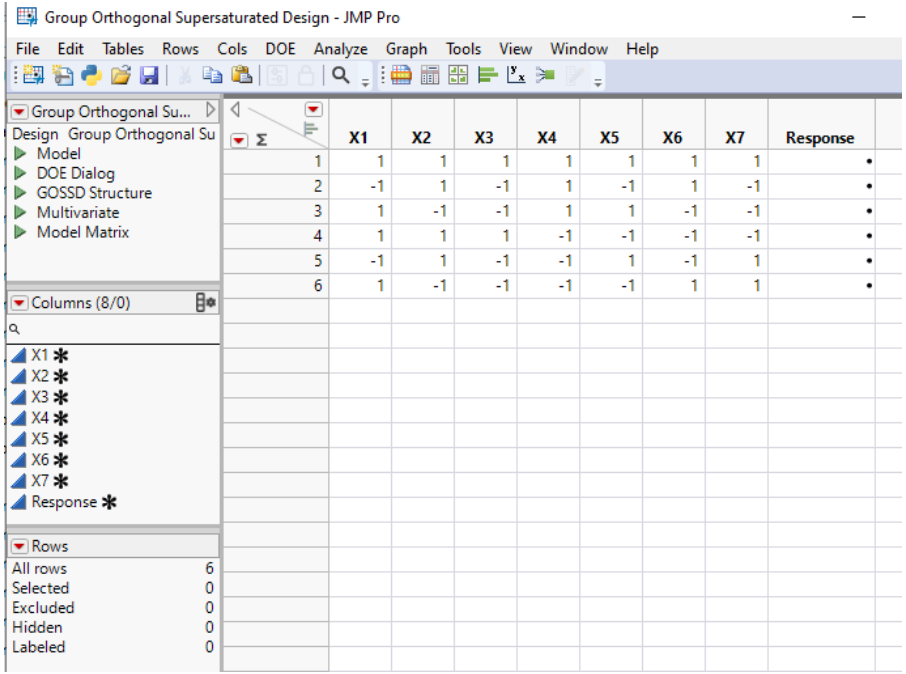
This is a $n = 12$ and $k = 7$ Placket-Burman design.



Supersaturated Screening

Two-level supersaturated designs (SSDs) use fewer runs to examine the k factors.

This is a $n = 6$ and $k = 7$ Group Orthogonal Supersaturated design.



Screening Model

In this talk we will assume we are only interested in estimating the linear main effects:

$$y = \beta_0 + X\beta + e \quad e \sim^{iid} N(0, \sigma^2)$$

Risks:

- there could be important interactions you are missing.
- we are implicitly assuming all active interactions will have strong effect heredity.

Why consider an SSD for screening?

1. Temporal or monetary constraints.
2. A follow up experiment can always be performed.
3. Experimental principles prioritize main effect estimation

Outline

- Examples of SSDs in the published literature.
- Survey of practitioners about their use or non-use of SSDs.
- What does the research say to do?
- Two examples of SSDs and their analysis.
- Recommendations for using SSDs as a screening experiment.

Examples of SSDs

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Application of strategic sample composition to the screening of anti-inflammatory drugs in water samples using solid-phase microextraction

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Abstract

The usefulness of the strategically designed sample composition (SSC) methodology for the screening of four anti-inflammatory drugs (ibuprofen, naproxen, tolfenamic acid and diclofenac) in water samples is demonstrated. Assuming that in screening campaigns only a limited number of the samples are contaminated with the analytes, the proposed approach allows the reliable identification of the contaminated specimens and the approximate estimation of their concentrations, with a 50% reduction in the total number of processed samples. To achieve this, a limited number of composite samples are built from the individual specimens. Automatic preparation of composite samples avoids human mistakes during this time-consuming and tedious operation, increasing the reliability of the predictions. In this work, a low-cost automatic device able to mix the individual specimens in the proportions indicated in the composition matrix is used. Moreover, the efficiency of evolutionary algorithms to predict the concentrations of the anti-inflammatory drugs in ultrapure and river water samples, artificially polluted in the laboratory and their robustness against large errors during the analysis of the composite samples, are evaluated.

Keywords: Strategic sample composition; Screening analysis; Anti-inflammatory drugs

FOOD AND BIOPRODUCTS PROCESSING 94 (2015) 525–535

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Screening of factors influencing the extraction of gelatin from the skin of cuttlefish using supersaturated design

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ABSTRACT

Supersaturated design (SSD) was used for screening the key parameters influencing gelatin extraction yield from cuttlefish (*Sepia officinalis*) skin. Results indicated that among a list of 17 factors only five parameters, namely, alkali (NaOH) concentration, acid reagent (acetic acid), enzyme, thermal treatment temperature and centrifugation time, were factors influencing gelatin yield. The optimal conditions for gelatin extraction were found to be: pretreatment with NaOH 0.03 M for 1 h; treatment with pepsin for 24 h at 4 °C in acetic acid 100 mM; extraction for 14 h at 40 °C. The yield of gelatin extraction was 54.6%. Cuttlefish skin gelatin (CSG) contained protein as the major compound (90.95%) and low fat (0.3%) and ash (0.05%) contents. The physico-chemical properties of the CSG were characterized and compared with those of bovine gelatin (BG). The result of textural properties showed that hardness, elasticity and cohesiveness of CSG were lower than those of BG. Further, the gel strength of CSG (192.01 g) was lower than that of BG (259.65 g), possibly due to lower imino-acid content. The functional properties, including emulsion activity index and foam stability were similar to those of BG. The CSG showed stronger ability of apple juice clarification, than BG without affecting its nutritional values.

Keywords: Supersaturated design; Gelatin extraction process; Cuttlefish skin; Textural properties; Functional properties; Application

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Supersaturated design for screening factors influencing the preparation of sulfated amides of olive pomace oil fatty acids

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Olive pomace oil

ABSTRACT

In a previous paper, we showed that the preparation of sulfated diethanolamide of fatty acids is easy to carry out without organic solvents when using olive pomace oil as starting material; the reaction yield was, however, highly variable as a function of factor levels. The purpose of this research is to look for the optimal experimental conditions. We started by applying a supersaturated experimental design to screen for important factors among a list of 31 potentially influential factors in 18 experiments. Thus, we constructed a two-level supersaturated design as a half fraction of a 36-experiment Hadamard matrix and used it for this screening purpose. Multiple regression methods namely stepwise selection procedure, ridge regression and all-subset regressions were used to analyze the supersaturated design results according to a four step procedure. Results indicated that six factors, namely, molar ratio SO_3/ester, amidation time, amide addition rate, alkali reagent, alkali concentration, and amidation temperature, were very influential factors. Three other factors were moderately influential: neutralization temperature, sodium methanoate amount, and methanol amount. In future research, these factors will be further studied in order to perform robustness tests of the process.

Informal Survey

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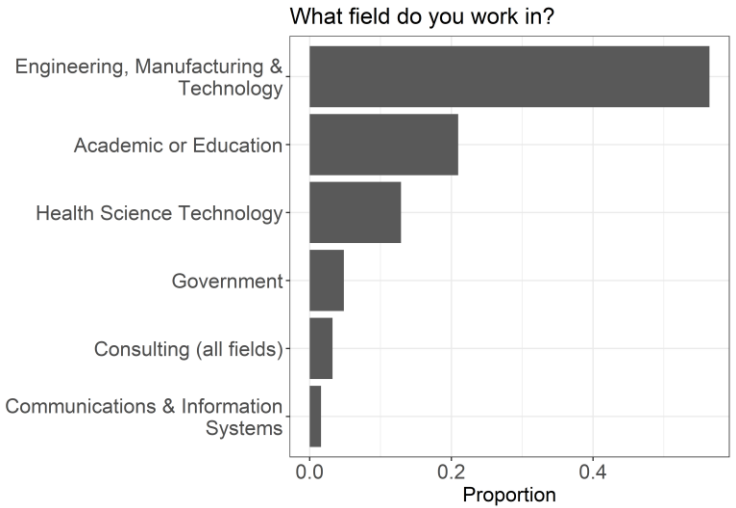
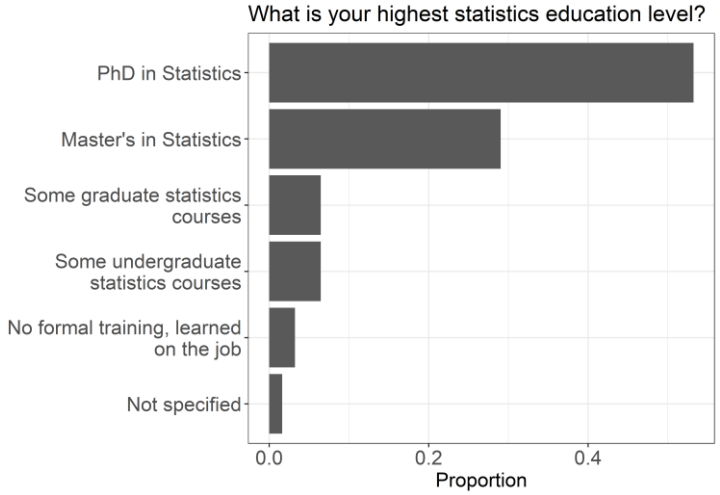
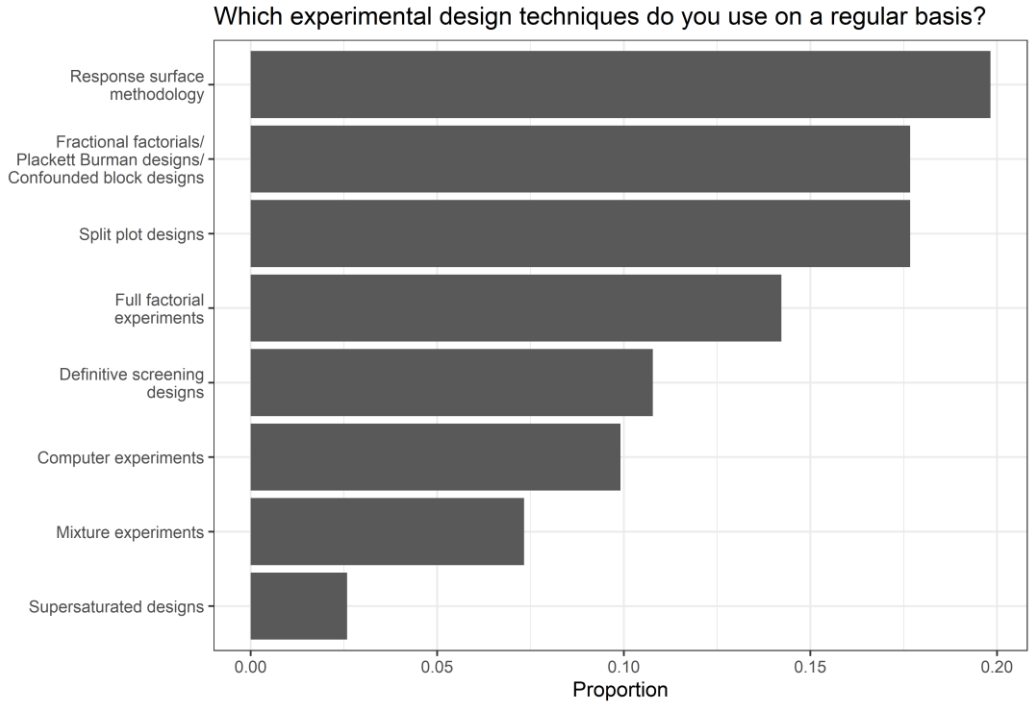
Who did we survey?

We used our informal networks and social media to reach out to the greater design of experiment community. The following analysis is based on 63 survey responses.

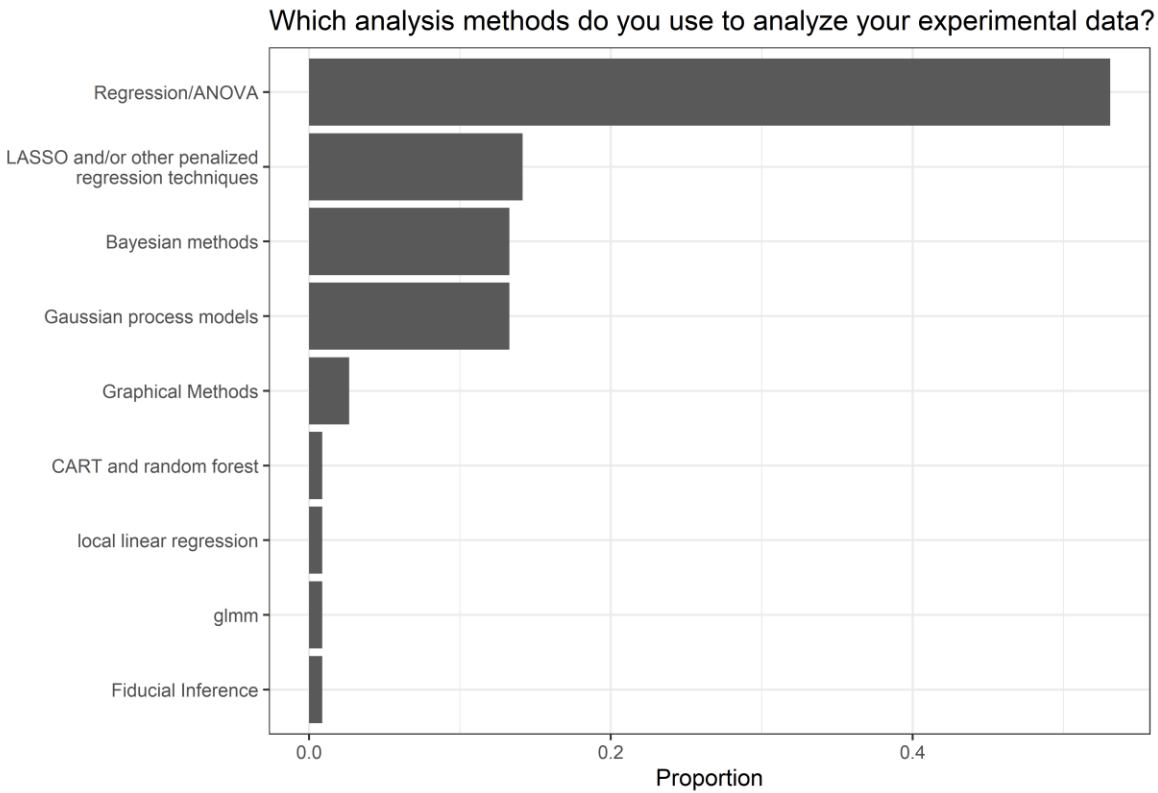




Commonly used Designs and Analysis Methods



Commonly used Analysis Methods



User Experience with SSDs

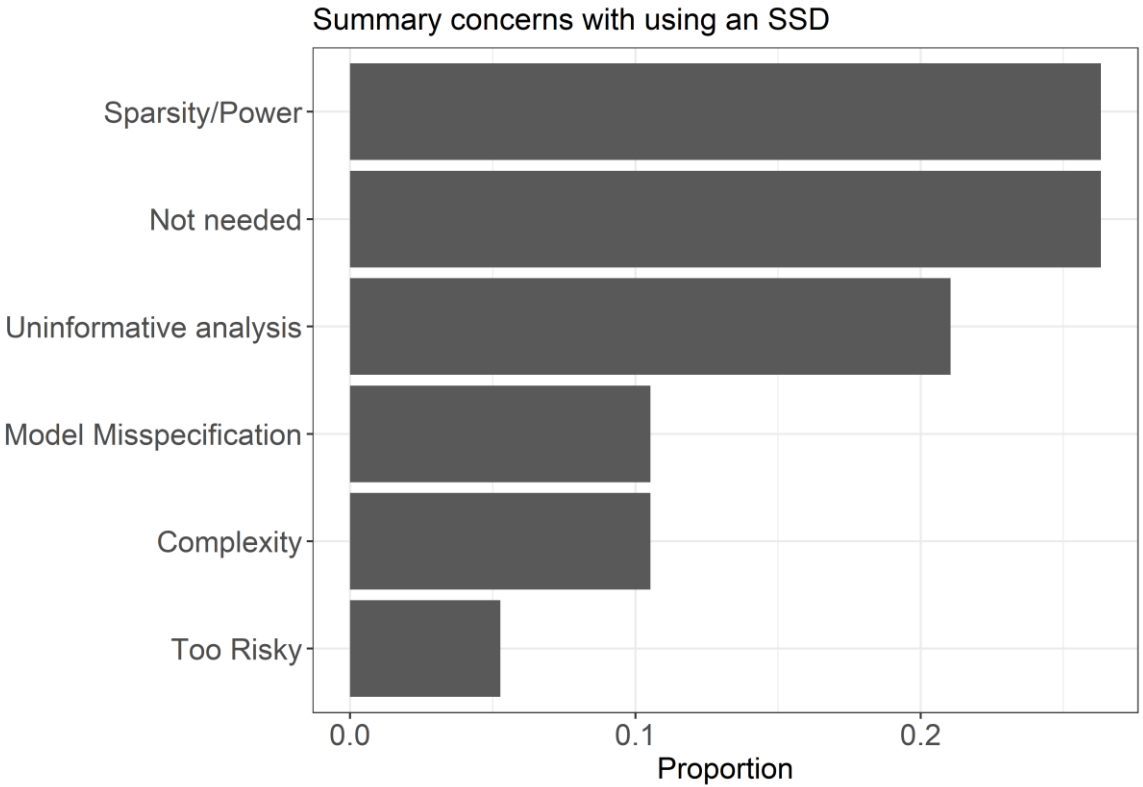
"*100+ factors 64 runs; failed experiment*"

"*Bayesian D-optimal design with many terms that weren't able to be estimated by the design, but were able to be estimated after unimportant factors were removed*"

"*Analytical Method Robustness testing. Successful*"

"*Testing to characterize drill bit effectiveness as a function of many input parameters. Experiment was successful due to engineering expertise for interpretation.*"

Concerns with using a SSD



What does the research say?

Contradictions in the Literature

"*I think it is perfectly natural and wise to do some supersaturated experiments*"-John Tukey, 1959

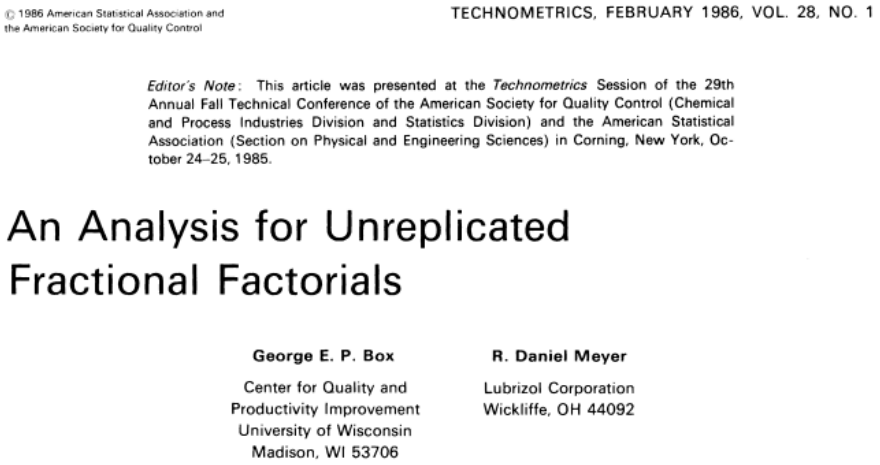
"*We have no experience of practical problems where such designs are likely to be useful; the conditions that interactions should be unimportant and that there should be a few dominant effects seems very severe*."-Kathleen Booth and David. R. Cox 1962

"*…we can say that one should be very cautions when using any method for constructing, analyzing or generally using SSDs*."—Stelios Georgiou 2014

"*For situations where there really is no prior knowledge of the effects of factors, but a strong belief in factor sparsity, and where the aim is to find out if there are any dominant factors and to identify them, experimenters should seriously consider using supersaturated designs*."—Steven Gilmour 2006

Core Principles

The success of screening experiments depends heavily on the assumptions of effect sparsity and effect hierarchy.



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An Analysis for Unreplicated Fractional Factorials

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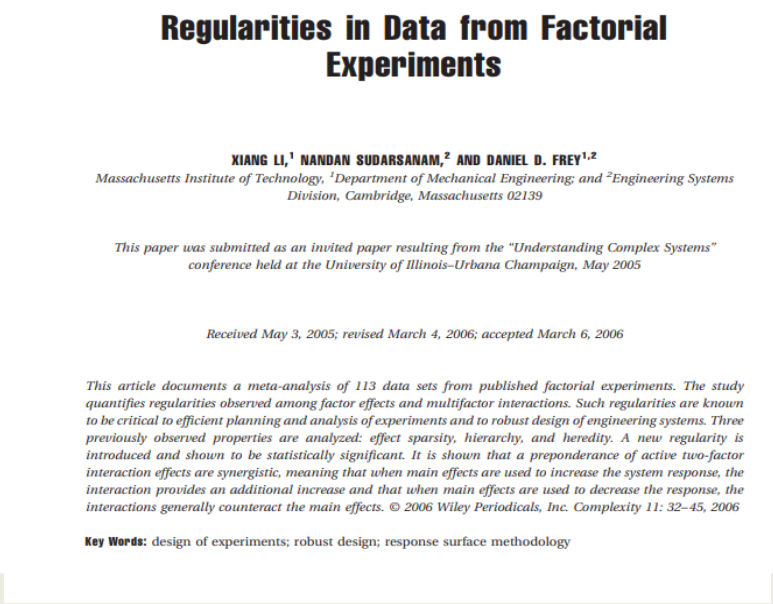
Core Principles

Effect sparsity and effect hierarchy have been empirically verified and quantified.



Regularities in Data from Factorial Experiments

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This paper was submitted as an invited paper resulting from the "Understanding Complex Systems" conference held at the University of Illinois–Urbana Champaign, May 2005

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This article documents a meta-analysis of 113 data sets from published factorial experiments. The study quantifies regularities observed among factor effects and multifactor interactions. Such regularities are known to be critical to efficient planning and analysis of experiments and to robust design of engineering systems. Three previously observed properties are analyzed: effect sparsity, hierarchy, and heredity. A new regularity is introduced and shown to be statistically significant. It is shown that a preponderance of active two-factor interaction effects are synergistic, meaning that when main effects are used to increase the system response, the interaction provides an additional increase and that when main effects are used to decrease the response, the interactions generally counteract the main effects. © 2006 Wiley Periodicals, Inc. Complexity 11: 32–45, 2006

Key Words: design of experiments; robust design; response surface methodology

Two SSDs Analysis+ Methods

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Traditional Screening Designs and Analysis

- Traditional screening designs are constructed with good Least Squares estimation properties, such as a small covariance matrix.
- “Small” covariance is achieved in classical screening by ensuring the columns in the design matrix are orthogonal.
- Is that the best strategy for an SSD where $n < k$?
- Recall, the goal of screening is not to make precise estimates, but to identify important factors.

Successful Screening Defined

To identify the truly important factors the SSD + analysis combination must have high power to detect those truly active factors.

In many cases we might consider a screening experiment successful, even if high power came at a cost of increased type 1 error.

SSDs should be constructed to enhance factor identification, not estimation.

SSDs Constructed for Screening

Technometrics

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Construction, Properties, and Analysis of Group-Orthogonal Supersaturated Designs

Bradley Jones, Ryan Lekivetz, Dibyen Majumdar, Christopher J. Nachtsheim & Jonathan W. Stallrich

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A Criterion for Constructing Powerful Supersaturated Designs When Effect Directions Are Known

Maria L. Weese, David J. Edwards & Byran J. Smucker

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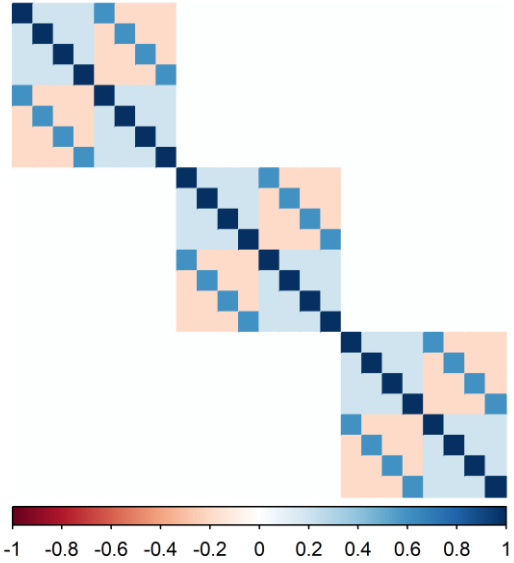
Group Orthogonal SSDs (GO-SSDs)

- GO-SSDs include “fake” factor columns that allow for the estimation of the experimental error.
- The factor columns are partitioned into mutually-orthogonal groups.
- You can construct and analyze them in JMP!



n = 20, k = 24 GO-SSD

Fit GO-SSD Analysis

Stage 1: Group Testing

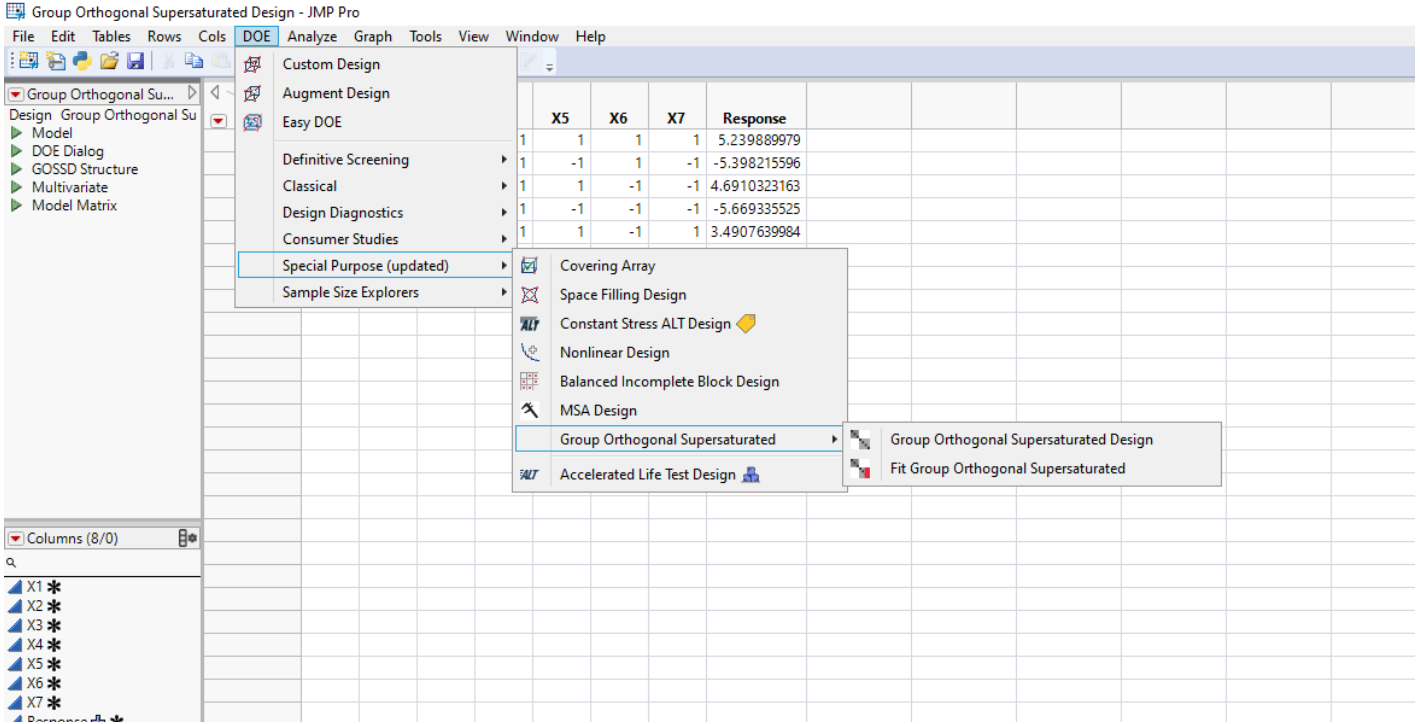
- Obtain an estimate for σ^2 using the fake factor columns.
- Test the significance of each group using the error estimate.
- Pool the degrees of freedom for any non-significant groups.

Fit GO-SSD Analysis

Stage 2: Factor Testing

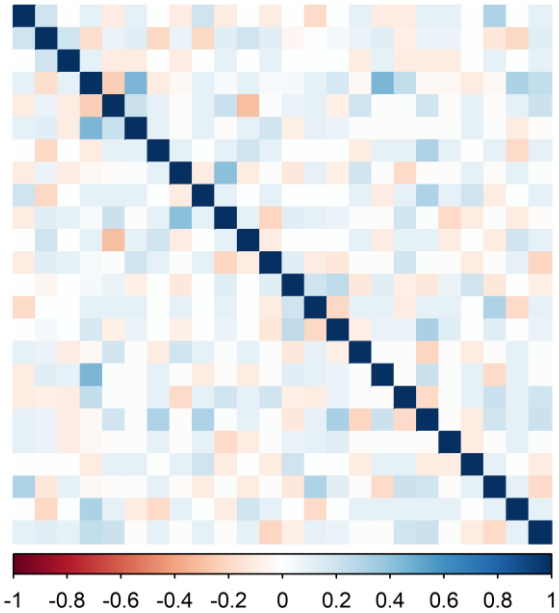
- For the factors in the groups identified as active in stage 1, test all models of size 1, then 2,…etc. Collect all models for a given size with a significant F-test and classify all the factors in these models as potentially active.
- Repeat for models up to a certain size
- If all models up to that size are significant, then we will designate all factors in the group as “potentially active”.

Fit GO-SSD in JMP



Var(s+) SSDs

- The Var(s+) criterion (Weese et. al(2017)) minimizes the variance of the off-diagonal values of the $X'X$ matrix subject to some constraints. Recall we defined the X matrix as our model matrix in the linear model: $y = \beta_0 + X\beta + e$
- This criterion forces the off diagonals to be more positive but with lower variability.



n = 20, k = 24 Var(s+) SSD

Analysis of Var(s+) SSDs

- Weese et al. (2017) showed that Var(s+) designs are superior to other optimal SSDs designs when effect directions were correctly specified in advance and the analysis was performed using a regularization method (Dantzig selector or Lasso).
  - Var(s+) designs have higher power
  - Var(s+) designs do not elevate type 1 error
- Even when the effect directions were mis-specified, the Var(s+) designs fared no worse than other D-optimal SSDs.

Obtaining Var(s+) Designs

There is a catalogue of Var(s+) optimal designs posted with the supplementary materials of this paper:

Weese, M. L., Stallrich, J. W., Smucker, B. J., & Edwards, D. J. (2021). Strategies for supersaturated screening: Group orthogonal and constrained var (s) designs. *Technometrics*, *63*(4), 443-455.

Regularization methods such as the Dantzig selector and Lasso are available in JMP (or R, Python, etc.).

GO-SSD vs. Var(s+) SSD

Var(s+)+Regularization

1. More aggressive screening
2. Algorithmically constructed
3. Flexible design sizes
4. More robust to interactions

GO-SSD+Fit GO-SSD

1. Conservative screening
2. Measure of sparsity
3. Easy construction
4. Limited design sizes
5. Less robust to interactions

Recommendations for Using SSDs for Screening

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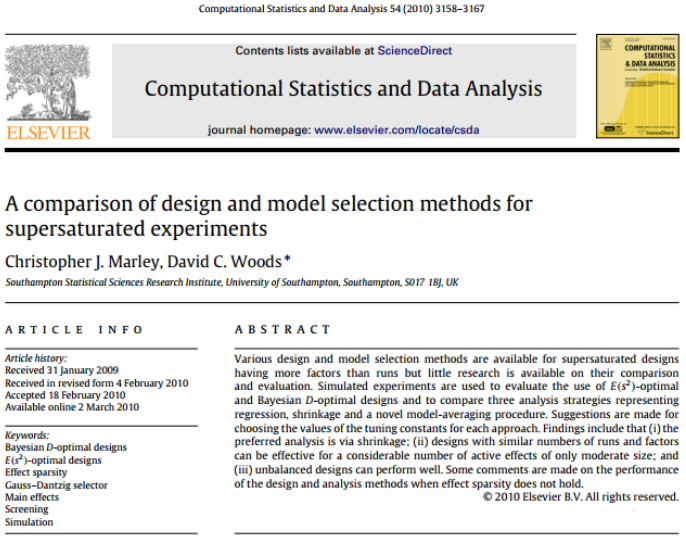
Research Based Recommendations

For a successful experiment using an optimal SSD, like Var(s+), Marley and Woods (2010) state the following rules:

1. The ratio of the run size, n, to the number of truly active factors, a, should be greater than 3.
2. The ratio of the number of factors, k, to n should be no more than 2.

We have replicated these results in separate simulations.



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A comparison of design and model selection methods for supersaturated experiments

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Main effects
Screening
Simulation

ABSTRACT

Various design and model selection methods are available for supersaturated designs having more factors than runs but little research is available on their comparison and evaluation. Simulated experiments are used to evaluate the use of $E(s^2)$-optimal and Bayesian *D*-optimal designs and to compare three analysis strategies representing regression, shrinkage and a novel model-averaging procedure. Suggestions are made for choosing the values of the tuning constants for each approach. Findings include that (i) the preferred analysis is via shrinkage; (ii) designs with similar numbers of runs and factors can be effective for a considerable number of active effects of only moderate size; and (iii) unbalanced designs can perform well. Some comments are made on the performance of the design and analysis methods when effect sparsity does not hold.

Practical Advice for Using a SSD for Screening

1. Keep the ratio of factors to runs less than 2.

2. Plan for the number of active effects to be sparse, specifically less than n/3.

3. Specify effect directions ahead of time (even if you have to guess).

Practical Advice for Using a SSD for Screening

4. For aggressive screening or specific run size and factor combinations, construct the SSD using constrained Var(s)+-optimality and analyze with the Dantzig selector profile plot.

5. For conservative screening, construct a GO-SSD using JMP and analyze with the Fit Group Orthogonal analysis method if you find the factor and run size combinations suitable.

6. You will need to follow up a screening experiment using an SSD. A good option is the method of Gutman et al. (2014) who suggest an approach based on Bayesian D-optimality.

Thank You!

Maria Weese

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