Definitive Screening as a System for Experimental Design

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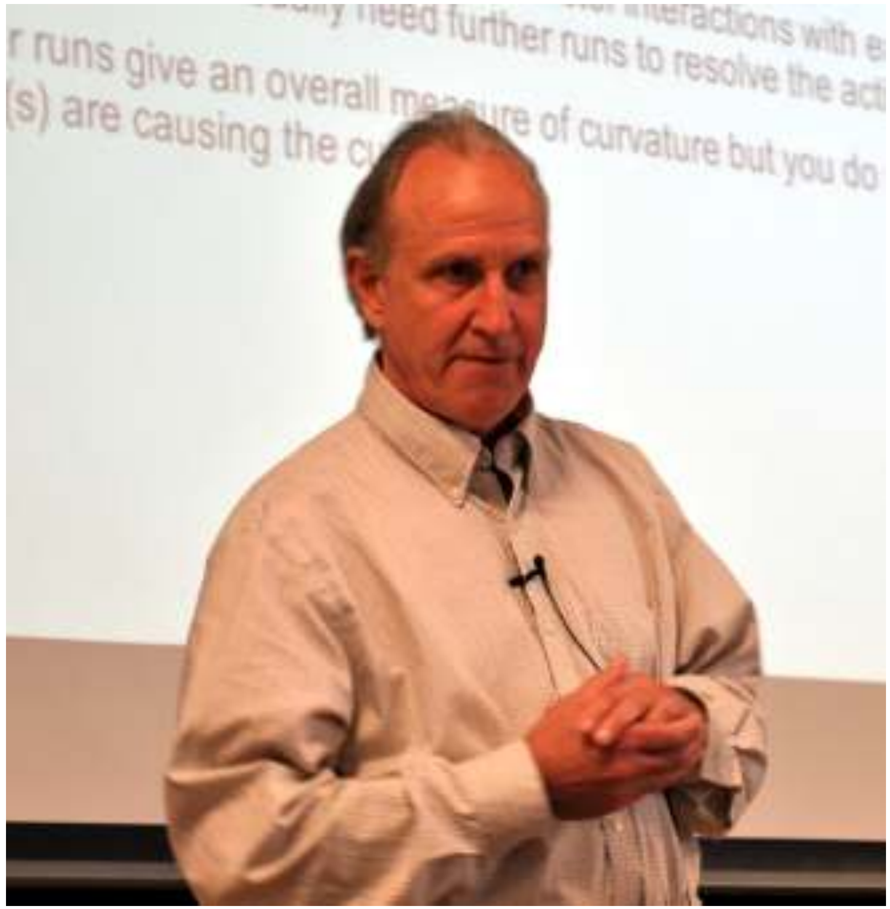
Joint work with Brad Jones, SAS/JMP



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Overview

1. **Some DOE History**
2. **Screening and alias optimality**
3. **What is a definitive screening design (DSD)?**
4. **Conference matrix based DSDs (briefly)**
5. **Adding two-level categorical factors (very briefly)**
6. **Blocking schemes for DSDs (very briefly)**
7. **A new method for model selection**

Where have we been?

- 10th Century: Rhazes
- Hospital director in Baghdad
- First clinical trial---efficacy of bloodletting on meningitis

Where have we been?

- **Avicenna: Eleventh century**
- **Seven rules for medical experimentation, including**
  - **Vary one factor at a time**
  - **Need for controls and replication**
  - **Use of multiple levels of a treatment**
  - **Don't use animals**

Where have we been?

- **James Lind, 1753: "A Treatise on Scurvy"**
- **First (published) one-way layout**

From "A Treatise…"

"On the 20th May, 1747, I took twelve patients in the scurvy on board the Salisbury at sea. Their cases were as similar as I could have them. They all in general had putrid gums, the spots and lassitude, with weakness of their knees.

•Two of these were ordered each a quart of cyder a day…

•Two others took twenty five gutts of elixir vitriol three times a day upon an empty stomach…

•Two others took two spoonfuls of vinegar three times a day upon an empty stomach…

•Two of the worst patients, with the tendons in the ham rigid (a symptom none the rest had) were put under a course of sea water…

•Two others had each two oranges and one lemon given them every day…

•The two remaining patients took the bigness of a nutmeg three times a day…

The consequence was that the most sudden and visible good effects were perceived from the use of the oranges and lemons"

Where have we been?

- **Gergonne: 1815**
- **Designs for polynomial regression, response surface design**

- **S. C. Peirce: 1870s : Randomization**

- **K. Smith, 1918: *Biometrika*, Optimal design for polynomial regression**

R. A. Fisher put it all together

Fisher, 1920s:

- **Randomization as mathematical basis for analysis**
- **Local control and blocking**
- **Replication**
- **Factorial designs**
- **Split plot designs**
- **Confounding**
- **ANOVA**
- **F, t distributions, etc., etc.**

R. A. Fisher put it all together

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To many observers: Father of modern statistics, greatest statistician of the 20th century

R. A. Fisher put it all together

R. A. Fisher:

> **To many observers: Father of modern statistics, greatest statistician of the 20th century**

According to evolutionary biologists Richard Dawkins and W. D. Hamilton, Fisher was:

"The greatest biologist of the 20th Century"

1920s-1950s: Orthogonality is the driving principle

- Fisher, Yates: need for ease of computation, independence of effects
- R. C. Bose, C.R. Rao, and Indian School: Combinatorics, BIBDs, PBIBDs

- Finney, 1945: Fractional replication
- Plackett and Burman, 1946

…culminating in the 2^{k-p} System

Vol. 3, No. 3 TECHNOMETRICS August, 1961

The 2^{k-p} Fractional Factorial Designs*
Part I.

G. E. P. Box and J. S. Hunter

Statistics Department, University of Wisconsin and Mathematics Research Center, University of Wisconsin

1950s: Baby steps away from orthogonality

Journal of the Royal Statistical Society
SERIES B (METHODOLOGICAL)
Vol. XIII, No. 1, 1951

ON THE EXPERIMENTAL ATTAINMENT OF OPTIMUM CONDITIONS

By G. E. P. BOX and K. B. WILSON
Imperial Chemical Industries, Dyestuffs Division Headq...
Blackley, Manchester

A BASIS FOR THE SELECTION OF A RESPONSE SURFACE DESIGN*

G. E. P. BOX
Princeton University
AND
NORMAN R. DRAPER
University of North Carolina and Imperial Chemical Industries

Also Box and Lucas, 1959, Nonlinear Design

Gold Standard in industrial DOE Since 1960

Step 1:

Screen: Resolution III or IV fractional factorial or Plackett-Burman designs

Step 2:

Find interactions: Resolution V fractional factorial designs

Step 3:

Optimize: Central composite response surface designs

Conclusions (by many): DOE is a dead field

- **All of the useful designs have been catalogued**

- **We're now in the age of big data; design of experiments is irrelevant**

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Let's take an example from the Journal of Food Science:

- **Objective is to maximize food solids obtained from the process**
- **6 factors**
- **Budget is 12-16 runs**

1	Water pH level	6.95	8
2	Water temp	20C	60C
3	Extraction time	15	40
4	Water-Peanuts Ratio	5	9
5	Agitation speed	5,000	10,000
6	Presoaking?	0	15

Standard Choice 1: Fractional Factorial Design

- 2^{6-2} fractional factorial design in 16 runs (Resolution IV)

Alias Matrix

Effect	X1*X2	X1*X3	X1*X4	X1*X5	X1*X6	X2*X3	X2*X4	X2*X5	X2*X6	X3*X4	X3*X5	X3*X6	X4*X5	X4*X6	X5*X6
Intercept	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X1*X2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
X1*X3	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
X1*X4	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0
X1*X5	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
X1*X6	0	0	0	0	1	0	0	1	0	1	0	0	0	0	0
X2*X3	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0
X2*X4	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0

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Intercept	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X1*X2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
X1*X3	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
X1*X4	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0
X1*X5	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
X1*X6	0	0	0	0	1	0	0	1	0	1	0	0	0	0	0
X2*X3	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0
X2*X4	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0

Standard Choice 1: Fractional Factorial Design

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Aliasing of Effects

Effects	Aliases
X1*X2	= X5*X6
X1*X3	= X4*X6
X1*X4	= X3*X6
X1*X5	= X2*X6
X1*X6	= X2*X5 = X3*X4
X2*X3	= X4*X5
X2*X4	= X3*X5

JMP Analysis

Term	Contrast	Lenth t-Ratio	Individual p-Value	Simultaneous p-Value	Aliases
Agitation Speed	-3.00000	-16.00	<.0001*	0.0002*	Water Temp*Ratio*Extraction Time
pH	2.87500	15.33	0.0001*	0.0003*	Agitation Speed*Water Temp*Pre-S
Water Temp	2.75000	14.67	0.0001*	0.0004*	Agitation Speed*Ratio*Extraction T
Ratio	2.12500	11.33	0.0002*	0.0013*	Agitation Speed*Water Temp*Extra
Extraction Time	0.12500	0.67	0.5315	1.0000	Agitation Speed*Water Temp*Ratic
Pre-Soak Time	-0.12500	-0.67	0.5315	1.0000	Agitation Speed*pH*Water Temp, p
Agitation Speed*pH	0.50000	2.67	0.0280*	0.2381	Water Temp*Pre-Soak Time
Agitation Speed*Water Temp	-0.12500	-0.67	0.5315	1.0000	Ratio*Extraction Time, pH*Pre-Soa
pH*Water Temp	2.75000	14.67	0.0001*	0.0004*	Agitation Speed*Pre-Soak Time
Agitation Speed*Ratio	2.25000	12.00	0.0002*	0.0006*	Water Temp*Extraction Time
pH*Ratio	0.62500	3.33	0.0144*	0.1250	Extraction Time*Pre-Soak Time
Water Temp*Ratio	0.00000	0.00	1.0000	1.0000	Agitation Speed*Extraction Time
pH*Extraction Time	0.12500	0.67	0.5315	1.0000	Ratio*Pre-Soak Time
Agitation Speed*pH*Ratio	0.25000	1.33	0.1783	0.9011	pH*Water Temp*Extraction Time, V
pH*Water Temp*Ratio	0.00000	0.00	1.0000	1.0000	Agitation Speed*pH*Extraction Tim

Standard Choice 1: JMP Analysis

	Term	Contrast	Lenth t-Ratio	Individual p-Value	Simultaneous p-Value	Aliases
✔	Agitation Speed	-3.00000	-16.00	<.0001*	0.0002*	Water Temp*Ratio*Extraction Time
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	pH*Water Temp*Ratio	0.00000	0.00	1.0000	1.0000	Agitation Speed*pH*Extraction Tim

All-knowing oracle: The active effects are:

MEs: Agitation Speed, pH, Water Temp, Ratio

2FIs: pH*WaterTemp, Ratio*AgitSpeed

Curvature: pH^2

Standard Choice 2: Plackett-Burman Design

- **Plackett-Burman Design in 12 runs**

Alias Matrix

Effect	X1*X2	X1*X3	X1*X4	X1*X5	X1*X6	X2*X3	X2*X4	X2*X5	X2*X6	X3*X4	X3*X5	X3*X6	X4*X5	X4*X6	X5*X6
Intercept	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
X1	0	0	0	0	0	0.333	-0.33	-0.33	0.333	0.333	0.333	-0.33	0.333	0.333	-0.33
X2	0	0.333	-0.33	-0.33	0.333	0	0	0	0	0.333	-0.33	-0.33	0.333	0.333	0.333
X3	0.333	0	0.333	0.333	-0.33	0	0.333	-0.33	-0.33	0	0	0	0.333	-0.33	0.333
X4	-0.33	0.333	0	0.333	0.333	0.333	0	0.333	0.333	0	0.333	-0.33	0	0	0.333
X5	-0.33	0.333	0.333	0	-0.33	-0.33	0.333	0	0.333	0.333	0	0.333	0	0.333	0
X6	0.333	-0.33	0.333	-0.33	0	-0.33	0.333	0.333	0	-0.33	0.333	0	0.333	0	0

Standard Choice 2: Plackett-Burman Analysis

Term	Contrast	Lenth t-Ratio	Individual p-Value	Sim
Water Temp	4.00000	1.60	0.1157	
pH	3.83333	1.53	0.1275	
Agitation Speed	-3.33333	-1.33	0.1754	
Pre-Soak Time	1.66667	0.67	0.5002	
Ratio	1.50000	0.60	0.5909	
Extraction Time	1.50000	0.60	0.5909	
Water Temp*pH	2.68328 *	1.07	0.2597	
Water Temp*Agitation Speed	0.21300 *	0.09	0.9384	
pH*Agitation Speed	0.18002 *	0.07	0.9485	
Water Temp*Pre-Soak Time	2.18263 *	0.87	0.3479	
pH*Pre-Soak Time	-0.11785 *	-0.05	0.9661	

Standard Choice 2: Plackett-Burman Analysis

Term	Contrast	Lenth t-Ratio	Individual p-Value	Sim
Water Temp	4.00000	1.60	0.1157	
pH	3.83333	1.53	0.1275	
Agitation Speed	-3.33333	-1.33	0.1754	
Pre-Soak Time	1.66667	0.67	0.5002	
Ratio	1.50000	0.60	0.5909	
Extraction Time	1.50000	0.60	0.5909	
Water Temp*pH	2.68328 *	1.07	0.2597	
Water Temp*Agitation Speed	0.21300 *	0.09	0.9384	
pH*Agitation Speed	0.18002 *	0.07	0.9485	
Water Temp*Pre-Soak Time	2.18263 *	0.87	0.3479	
pH*Pre-Soak Time	-0.11785 *	-0.05	0.9661	

Design Failure!!! Nothing is active

If only there were another design with this alias matrix and no 2FI confounding:

Alias Matrix

Effect	A*B	A*C	A*D	A*E	A*F	B*C	B*D	B*E	B*F	C*D	C*E	C*F	D*E	D*F	E*F
Intercept	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
C	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
D	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Turns out there is: Definitive Screening Design

Six foldover pairs

Run	A	B	C	D	E	F
1	0	1	-1	-1	-1	-1
2	0	-1	1	1	1	1
3	1	0	-1	1	1	-1
4	-1	0	1	-1	-1	1
5	-1	-1	0	1	-1	-1
6	1	1	0	-1	1	1
7	-1	1	1	0	1	-1
8	1	-1	-1	0	-1	1
9	1	-1	1	-1	0	-1
10	-1	1	-1	1	0	1
11	1	1	1	1	-1	0
12	-1	-1	-1	-1	1	0
13	0	0	0	0	0	0

Definitive Screening Design for 6 factors

Center point in each row

Run	A	B	C	D	E	F
1	0	1	-1	-1	-1	-1
2	0	-1	1	1	1	1
3	1	0	-1	1	1	-1
4	-1	0	1	-1	-1	1
5	-1	-1	0	1	-1	-1
6	1	1	0	-1	1	1
7	-1	1	1	0	1	-1
8	1	-1	-1	0	-1	1
9	1	-1	1	-1	0	-1
10	-1	1	-1	1	0	1
11	1	1	1	1	-1	0
12	-1	-1	-1	-1	1	0
13	0	0	0	0	0	0

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Definitive Screening Design for 6 factors

Run	A	B	C	D	E	F
1	0	1	-1	-1	-1	-1
2	0	-1	1	1	1	1
3	1	0	-1	1	1	-1
4	-1	0	1	-1	-1	1
5	-1	-1	0	1	-1	-1
6	1	1	0	-1	1	1
7	-1	1	1	0	1	-1
8	1	-1	-1	0	-1	1
9	1	-1	1	-1	0	-1
10	-1	1	-1	1	0	1
11	1	1	1	1	-1	0
12	-1	-1	-1	-1	1	0
13	0	0	0	0	0	0

One overall center point

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How did we find this design?*

We used constrained optimal design:

- **Minimize the average magnitude of the alias matrix entries…**
- **Subject to a constraint on the statistical efficiency of the design for estimating main effects (e.g., efficiency > 90%)**

***Jones, Nachtsheim, *Technometrics*, 2011**

Now generalize this structure for m factors

Table 1: General design structure for m factors

Foldover Pair	Run (i)	Factor Levels $x_{i,1}$	$x_{i,2}$	$x_{i,3}$	$\cdots$	$x_{i,m}$
1	1	0	±1	±1	$\cdots$	±1
	2	0	∓1	∓1	$\cdots$	∓1
2	3	±1	0	±1	$\cdots$	±1
	4	∓1	0	∓1	$\cdots$	∓1
3	5	±1	±1	0	$\cdots$	±1
	6	∓1	∓1	0	$\cdots$	∓1
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$	$\vdots$
m	$2m-1$	±1	±1	±1	$\cdots$	0
	$2m$	∓1	∓1	∓1	$\cdots$	0
Centerpoint	$m+1$	0	0	0	$\cdots$	0

Can we find great designs for any number of factors?

A Class of Three-Level Designs for Definitive Screening in the Presence of Second-Order Effects

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Screening designs are attractive for assessing the relative impact of a large number of factors on a response of interest. Experimenters often prefer quantitative factors with three levels over two-level factors because having three levels allows for some assessment of curvature in the factor–response relationship. Yet, the most familiar screening designs limit each factor to only two levels. We propose a new class of designs that have three levels, provide estimates of main effects that are unbiased by any second-order effect, require only one more than twice as many runs as there are factors, and avoid confounding of any pair of second-order effects. Moreover, for designs having six factors or more, our designs allow for the efficient estimation of the full quadratic model in any three factors. In this respect, our designs may render follow-up experiments unnecessary in many situations, thereby increasing the efficiency of the entire experimentation process. We also provide an algorithm for design construction.

Key Words: Alias; Confounding; Coordinate Exchange Algorithm; D-Efficiency; Response Surface Designs; Robust Designs; Screening Designs.

JOURNAL OF QUALITY TECHNOLOGY , VOL. 43, NO. 1, QICID: 33051, January 2011, pp. 1-15

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It turns out there is a "Conference Matrix" solution

An *mxm* square matrix C with 0 diagonal and +1 or -1 off diagonal elements such that:

$$\mathbf{C}^{\mathrm{T}}\mathbf{C} = (m-1)\mathbf{I}_{m\times m}$$

Conference Matrix of Order 6

$$C = \begin{pmatrix} 0 & +1 & +1 & +1 & +1 & +1 \\ +1 & 0 & +1 & -1 & -1 & +1 \\ +1 & +1 & 0 & +1 & -1 & -1 \\ +1 & -1 & +1 & 0 & +1 & -1 \\ +1 & -1 & -1 & +1 & 0 & +1 \\ +1 & +1 & -1 & -1 & +1 & 0 \end{pmatrix}$$

Here is the amazing result:

Form the augmented matrix:

$$D = \begin{bmatrix} +C \\ -C \\ 0 \end{bmatrix}$$

…and you get an orthogonal (for main effects) definitive screening design!

Conference matrix-based DSDs do not exist for n odd

- **Feasible design sizes (n) are:**

m	n
6	13
8	17
10	21
12	25
14	29
16	33
18	37
20	41
NA	NA
24	49
26	53
28	57
30	61

- **Like Plackett-Burman, the designs are available in steps of four, with the exception of m = 22.**

Our View: What to do if m is odd

- DSDs exist for m odd, but not orthogonal for main effects
- For m odd:
  1. Add one fake factor so that m’ = m + 1 is even
  2. Construct the DSD for m + 1 factors
  3. Now drop the fake factor
  4. Result is an orthogonal m-factor DSD with n = 2(m + 1) + 1
- You obtained an orthogonal design: price is 2 extra runs

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Design Properties

1. **The number of required runs is only one more than twice the number of factors.**

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Design Properties

1. **The number of required runs is only one more than twice the number of factors.**
2. **Unlike resolution III designs, main effects are completely independent of two-factor interactions.**

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Design Properties

1. The number of required runs is only one more than twice the number of factors.
2. Unlike resolution III designs, main effects are completely independent of two-factor interactions.
3. Unlike resolution IV designs, two-factor interactions are not completely confounded with other two-factor interactions, although they may be correlated

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Design Properties

1. The number of required runs is only one more than twice the number of factors.
2. Unlike resolution III designs, main effects are completely independent of two-factor interactions.
3. Unlike resolution IV designs, two-factor interactions are not completely confounded with other two-factor interactions, although they may be correlated
4. **Unlike resolution III, IV and V designs with added center points, all quadratic effects are estimable in models comprised of any number of linear and quadratic main effects terms.**

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Design Properties (continued)

5. **Quadratic effects are orthogonal to main effects and not completely confounded (though correlated) with interaction effects.**

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Design Properties (continued)

5. Quadratic effects are orthogonal to main effects and not completely confounded (though correlated) with interaction effects.

6. With six through (at least) 12 factors, the designs are capable of estimating all possible full quadratic models involving three or fewer factors with very high levels of statistical efficiency.

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Design Properties (continued)

5. **Quadratic effects are orthogonal to main effects and not completely confounded (though correlated) with interaction effects.**

6. **With six through (at least) 12 factors, the designs are capable of estimating all possible full quadratic models involving three or fewer factors with very high levels of statistical efficiency.**

7. **It turns out that DSDs are superior to two level designs for sequential experimentation, design augmentation**

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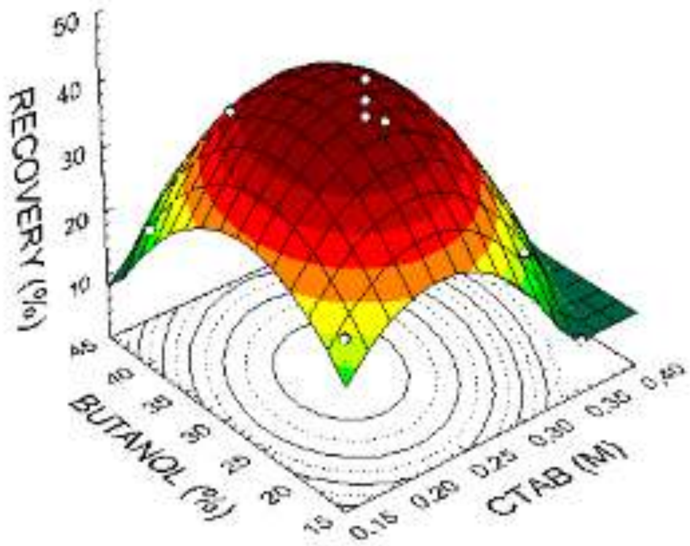
Screening at Three Levels has Distinct Advantages

1. The world is not linear!
2. We can include current settings in experiments where we are assessing the impact of increases and decreases to the current "best" settings.
3. We may be able to screen and optimize in one fell swoop.



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Upshot – Definitive Screening Designs

1. My view: engineers, scientists prefer three levels.
2. Can estimate curvatures
3. Can disentangle interactions
4. I see little or no reason to continue the practice of using 2^{k-p} designs or Plackett-Burman designs for four or more continuous factors.

Obtaining the Designs

- SAS/JMP
- Minitab
- Design Ease
- R

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Adding Two-Level Categorical Factors

Many design problems involve categorical factors

Examples:

- **Two operators**
- **Two production lines**
- **Drug and placebo**
- **Two catalysts**
- **Two machines**
- **Etc.,**

DSDs, as originally developed, cannot handle these

Two construction methods*

1. DSD-augment

2. ORTH-augment

*Jones and Nachtsheim, 2013, JQT

Two construction methods*

1. **DSD-augment**

2. **ORTH-augment**

***Jones and Nachtsheim, 2013, JQT**

***Nachtsheim, Shen, Lin, 2017, JQT expand this class of designs**

Blocking Schemes for DSDs*

- Foldover structure of DSDs makes them incredibly easy construct orthogonal incomplete blocks…
- Such that the block effects are orthogonal to the main effects
- Number of incomplete blocks can range from 2 to m (number of factors) in varying block sizes
- Each block contains at least one foldover pair and a center point

*Jones and Nachtsheim (2015), Technometrics

Example: Cases for m = 5 or 6

m	n	B	Blocksizes…							
6 or (5)	14 (13)	2	7 (6)	7						
6 or (5)	15 (14)	3	5 (4)	5	5					
6 or (5)	16 (15)	4	5 (4)	5	3	3				
6 or (5)	17 (16)	5	5 (4)	3	3	3	3			
6 or (5)	18 (17)	6	3 (2)	3	3	3	3	3		
8 or (7)	18 (17)	2	9 (8)	9						
8 or (7)	19 (18)	3	7 (6)	7	5					
8 or (7)	20 (19)	4	5 (4)	5	5	5				
8 or (7)	21 (20)	5	5 (4)	5	5	3	3			
8 or (7)	22 (21)	6	5 (4)	5	3	3	3	3		
8 or (7)	23 (22)	7	5 (4)	3	3	3	3	3	3	
8 or (7)	24 (23)	8	3 (2)	3	3	3	3	3	3	3

Final topic: Analyzing DSDs

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Some background

- Until recently we didn't have any particular method for analysis
- These are supersaturated designs for the full quadratic model
- Need a method for n << p
- Recommendation has been Stepwise/AICc or even better, Dantzig or Lasso (Errore, et al, JQT, in press)
- We now have a better recommendation

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Effective, design-based model selection for DSDs*

- **Design structure allows us to decompose the response vector into two orthogonal components, Y_1 and Y_2**
  - **Y_1 contains all of the information about main effects**
  - **Y_2 contains contains all information about second-order effects and the intercept**
- **In first stage, identify active main effects using Y_1 with no variance inflation from potential second-order terms**
- **In second stage, identify second-order effects Y_2 independent of first-order terms**

*** Jones and Nachtsheim, Technometrics, in press.**

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But first, background on "fake factors"

- **We recommend use of two "fake factors" in the design:**

Run	X1	X2	X3	X4	X5	X6	FF1	FF2
1	0	1	1	1	1	1	1	1
2	0	-1	-1	-1	-1	-1	-1	-1
3	1	0	1	1	-1	1	-1	-1
4	-1	0	-1	-1	1	-1	1	1
5	1	-1	0	1	1	-1	1	-1
6	-1	1	0	-1	-1	1	-1	1
7	1	-1	-1	0	1	1	-1	1
8	-1	1	1	0	-1	-1	1	-1
9	1	1	-1	-1	0	1	1	-1
10	-1	-1	1	1	0	-1	-1	1
11	1	-1	1	-1	-1	0	1	1
12	-1	1	-1	1	1	0	-1	-1
13	1	1	-1	1	-1	-1	0	1
14	-1	-1	1	-1	1	1	0	-1
15	1	1	1	-1	1	-1	-1	0
16	-1	-1	-1	1	-1	1	1	0
17	0	0	0	0	0	0	0	0

Cost = 4 additional runs

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How do fake factors help (besides power)?

- **Model:**

$$y_i = \beta_0 + \sum_{j=1}^{m} \beta_j x_{ij} + \sum_{j=1}^{m-1} \sum_{k=j+1}^{m} \beta_{jk} x_{ij} x_{ik} + \sum_{j=1}^{m} \beta_{jj} x_{ij}^2 + \varepsilon_i \quad i = 1, \ldots, n$$

- **In matrix form:**

$$\mathbf{Y} = \mu \mathbf{1} + \mathbf{D}\boldsymbol{\beta}_D + \mathbf{F}\boldsymbol{\beta}_F + \mathbf{X}_2\boldsymbol{\beta}_2 + \boldsymbol{\varepsilon},$$

- **So:**

$$\mathbf{Y}'\mathbf{Y} = \mathbf{Y}'\mathbf{P}_1\mathbf{Y} + \mathbf{Y}'\mathbf{P}_D\mathbf{Y} + \mathbf{Y}'\mathbf{P}_F\mathbf{Y} + \mathbf{Y}'\mathbf{P}_{X_2}\mathbf{Y}$$

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Now apply Cochran's Theorem

- **Since the projection operators sum to the identity, are mutually orthogonal, and $\beta_f = 0$,**

$$\frac{\mathbf{Y}'\mathbf{P}_\mathbf{F}\mathbf{Y}}{\sigma^2} \sim \chi^2_{m_f} \quad \textbf{and so} \quad s_F^2 = \frac{\mathbf{Y}'\mathbf{P}_\mathbf{F}\mathbf{Y}}{m_f}$$

is an unbiased estimator of σ^2.

- **If we have repeat center points, we can pool their df:**

$$s_p^2 = \frac{(n_c - 1)s_c^2 + m_f s_F^2}{n_c + m_f - 1}$$

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The odd and even regression terms

Miller and Sitter (2005,"Using Folded-Over Non-orthogonal Designs," Technometrics) had a key insight:

- **With foldover designs, structure allows you to conduct separate analyses of the "odd function terms" and "even function terms"**
  - **g is an odd function if $g(-x) = -g(x)$ for all x**
  - **g is an even function if $g(-x) = g(x)$ for all x**
- **Odd function terms: Main effects, third-order effects etc.**
- **Even function terms: Intercept, second-order terms, fourth-order terms, sixth-order terms, etc.**

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The odd and even spaces

Odd Space: space spanned by the odd function terms

Even Space: space spanned by the even function terms

- The response vector for analysis of odd (even) function terms is obtained by projecting Y onto the Odd (Even) Space

Odd Space Y: $\mathbf{y}_{ME} = \mathbf{X}_{DF}(\mathbf{X}'_{DF}\mathbf{X}_{DF})^{-1}\mathbf{X}'_{DF}\mathbf{y}$

Even Space Y: $\mathbf{y}_{2nd} = [\mathbf{I} - \mathbf{X}_{DF}(\mathbf{X}'_{DF}\mathbf{X}_{DF})^{-1}\mathbf{X}'_{DF}]\mathbf{y}$

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Model Selection (Big Picture)

1. **Identify active main effects using Y_{ME} and the unbiased estimate of σ^2.**
2. **If assuming strong heredity, form all possible second-order terms that involve the active main effects terms. If not, form all possible second-order terms.**
3. **Use Y_{2nd} and a "best subsets" procedure to identify up to $(m + m_f)/2$ active second-order terms**
4. **Exception: if there are only three or fewer active main effects, there is no limit to the number of active second-order effects**

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Why is the decomposition effective?

Simple example: Y is generated from a model containing four main effects and six second-order terms

The next page shows the decomposition of Y into Y_{ME} and Y_{2nd}.

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	A	B	C	D	E	F	Fake1	Fake2	Y	Y_ME	Y_2nd
1	0	1	1	1	1	1	1	1	94.51	-6.53	101.04
2	0	-1	-1	-1	-1	-1	-1	-1	107....	6.53	101.04
3	1	0	1	1	-1	1	-1	-1	94.36	-6.815	101.175
4	-1	0	-1	-1	1	-1	1	1	107....	6.815	101.175
5	1	-1	0	1	1	-1	1	-1	91.80	1.275	90.525
6	-1	1	0	-1	-1	1	-1	1	89.25	-1.275	90.525
7	1	-1	-1	0	1	1	-1	1	93.70	-0.785	94.485
8	-1	1	1	0	-1	-1	1	-1	95.27	0.785	94.485
9	1	1	-1	-1	0	1	1	-1	89.55	0.84	88.71
10	-1	-1	1	1	0	-1	-1	1	87.87	-0.84	88.71
11	1	-1	1	-1	-1	0	1	1	94.58	-0.655	95.235
12	-1	1	-1	1	1	0	-1	-1	95.89	0.655	95.235
13	1	1	-1	1	-1	-1	0	1	93.23	3.65	89.58
14	-1	-1	1	-1	1	1	0	-1	85.93	-3.65	89.58
15	1	1	1	-1	1	-1	-1	0	98.11	2.295	95.815
16	-1	-1	-1	1	-1	1	1	0	93.52	-2.295	95.815
17	0	0	0	0	0	0	0	0	99.75	0	99.75

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Y_ME
-6.53
6.53
-6.815
6.815
1.275
-1.275
-0.785
0.785
0.84
-0.84
-0.655
0.655
3.65
-3.65
2.295
-2.295
0

Examining the ME response vector

- **Note responses for each foldover pair sum to zero.**
- **The response for the center run is zero.**
- **There are 17 rows but only 8 independent values**
- **There are 6 real factors but 8 df, so there are 8 – 6 = 2 df for estimating σ^2**

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Examining the 2nd Order Effects Response

Y_2nd
101.04
101.04
101.175
101.175
90.525
90.525
94.485
94.485
88.71
88.71
95.235
95.235
89.58
89.58
95.815
95.815
99.75

- **Note responses for each foldover pair are the same.**
- **The response for the center run is nonzero.**
- **There are 17 rows but only 9 independent values (df)**
- **Once you estimate the intercept, there are 8 df left to estimate 2nd order effects.**
- **Use the estimate of σ^2 from the analysis of the main effects to guide subsets selection from the 2nd order effects.**

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Using Y leads to an inflated estimate of the variance

- **Regress Y on main effects (nothing active):**

s = 5.42

Parameter Estimates

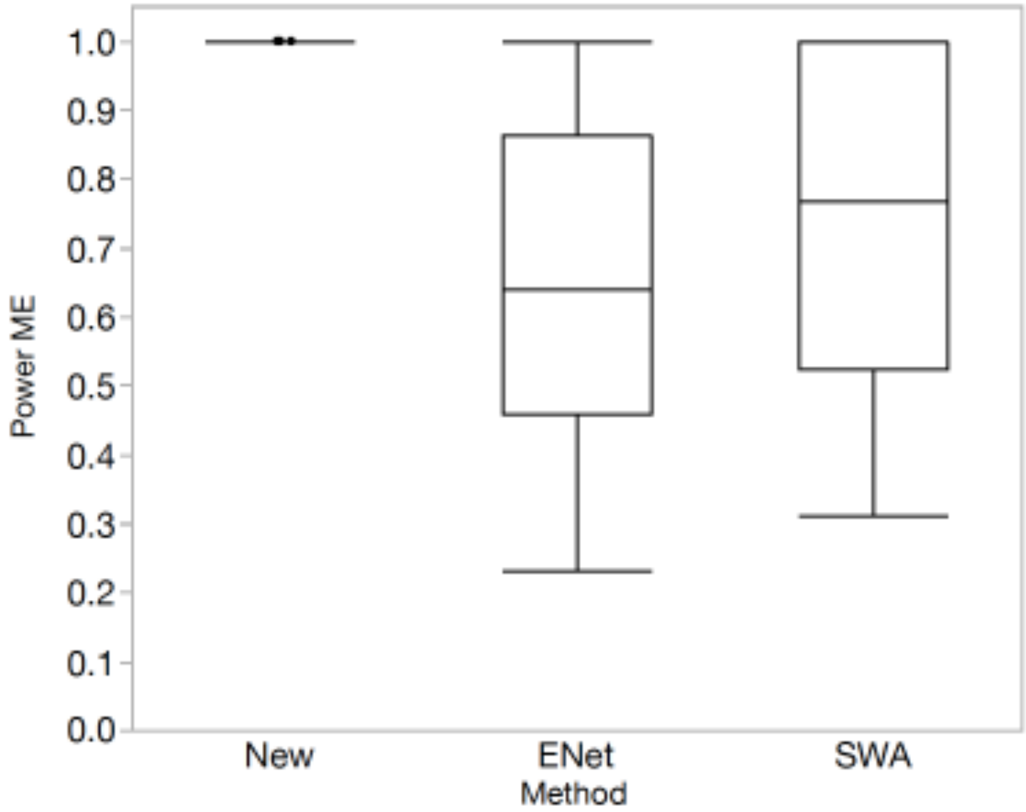
Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	94.875294	1.437893	65.98	<.0001*
A	-0.027857	1.584481	-0.02	0.9863
B	0.06	1.584481	0.04	0.9705
C	-2.201429	1.584481	-1.39	0.1949
D	-1.557143	1.584481	-0.98	0.3489
E	0.0107143	1.584481	0.01	0.9947
F	-2.93	1.584481	-1.85	0.0942

- **Regress Y_{ME} on main effects (3 or 4 terms active):**

s = 0.07

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	0	0.018317	0.00	1.0000
A	-0.027857	0.020184	-1.38	0.1976
B	0.06	0.020184	2.97	0.0140*
C	-2.201429	0.020184	-109.07	<.0001*
D	-1.557143	0.020184	-77.15	<.0001*
E	0.0107143	0.020184	0.53	0.6071
F	-2.93	0.020184	-145.16	<.0001*

Finding main effects:
New vs Hierarchical Net vs SW/AICc



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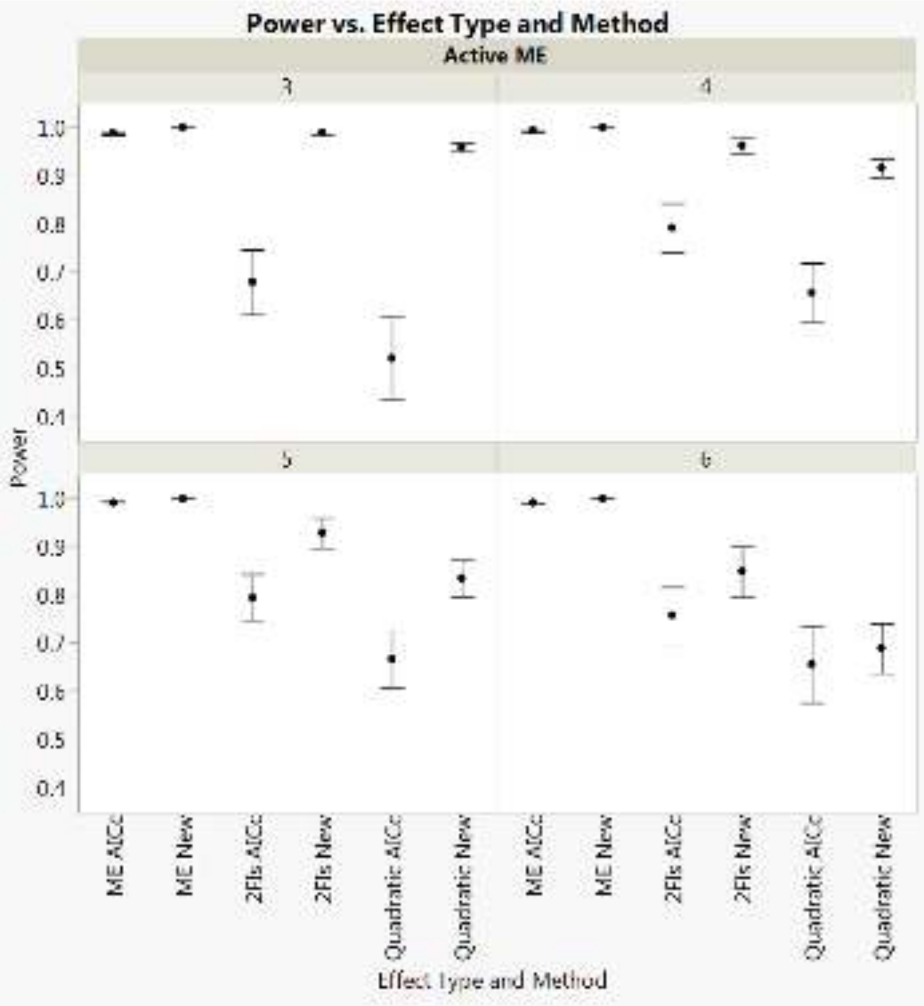
Simulation Comparisons New Method vs. Stepwise



Comparison for DSD with 6 factors and 17 runs (i.e. 2 fake factors)

Power for detecting 2FIs and Quadratic effects is much higher for the new method especially when fewer MEs are active

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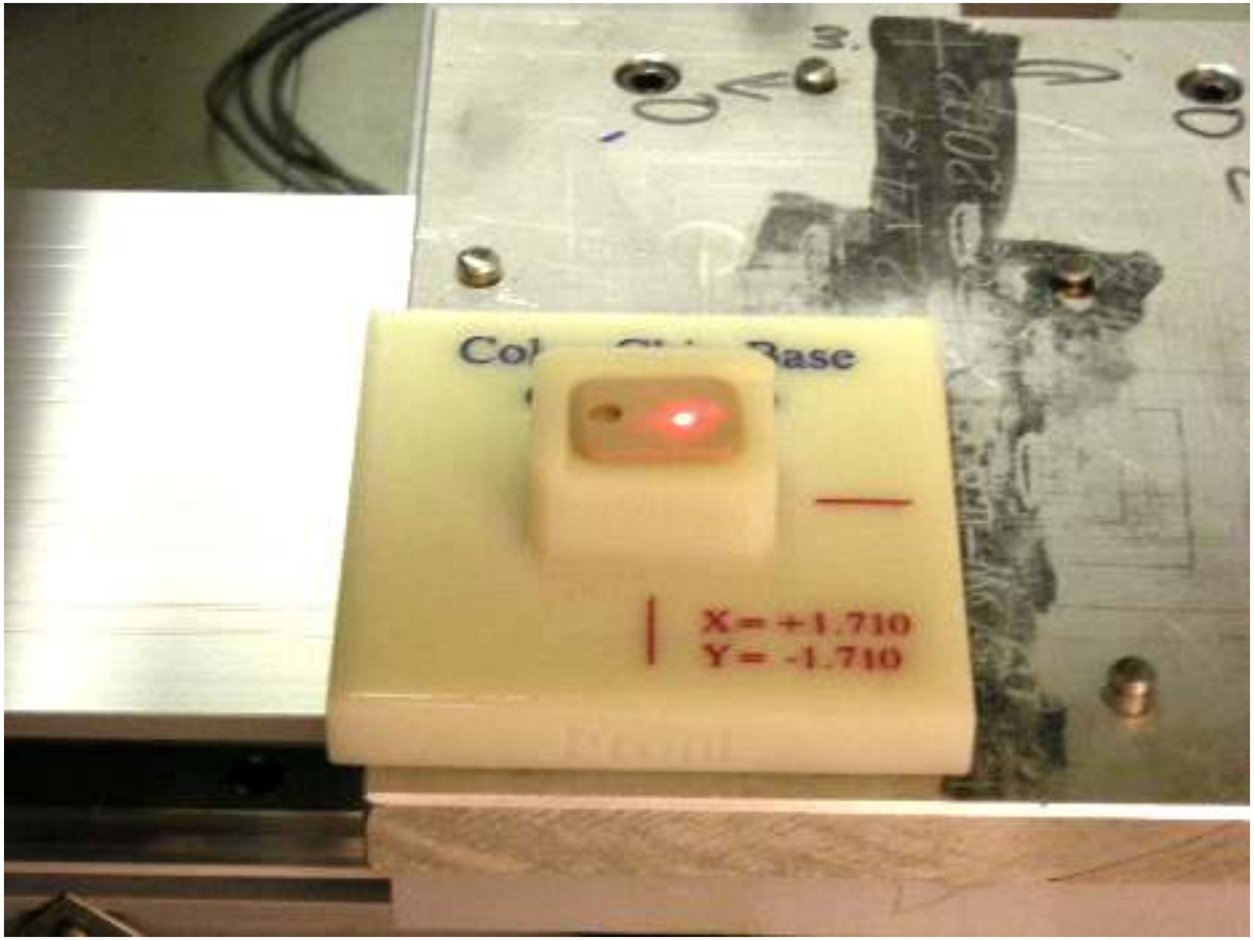
A Recent Experiment at In'Tech Industries

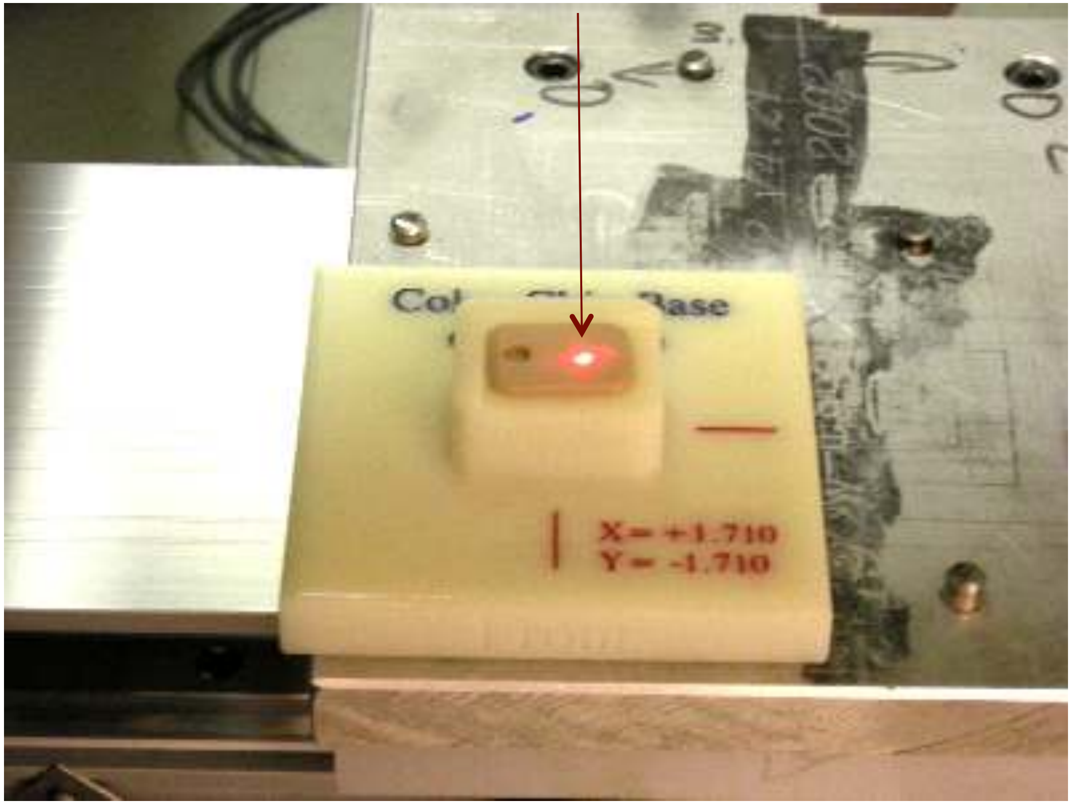
Problem: Need to laser etch labels on small plastic parts in an "optimal" fashion

Laser etching in progress….

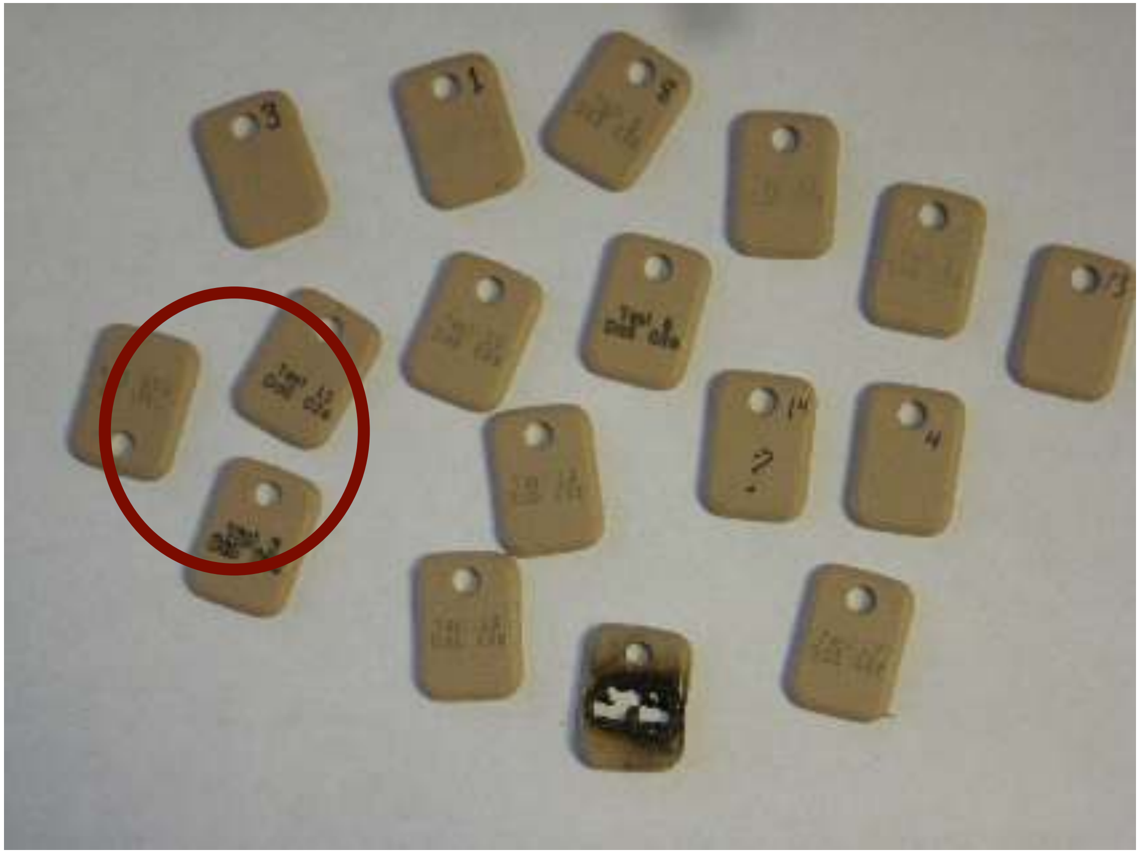


Laser etching in progress….

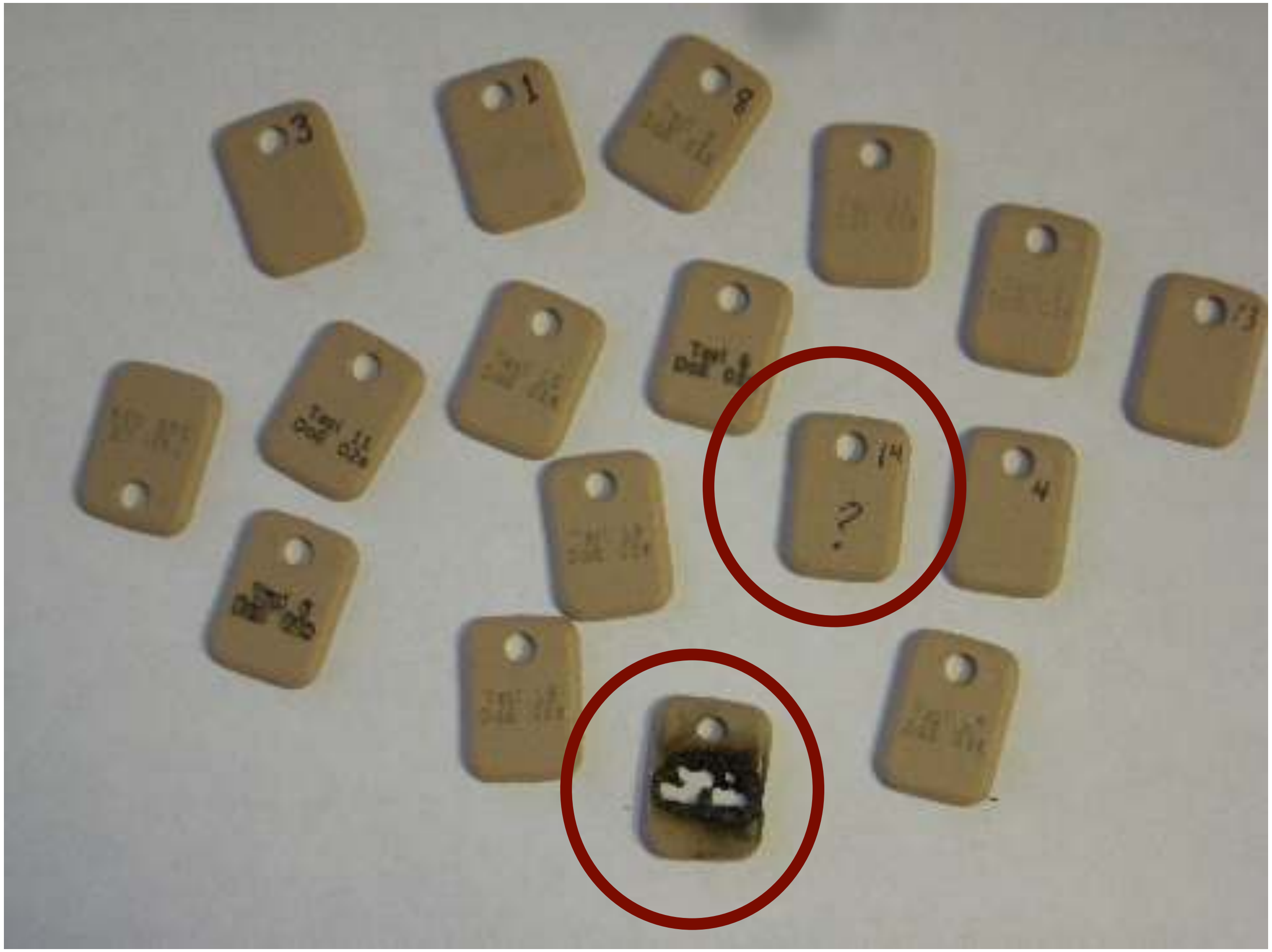
Laser



Initial experience: From easy to read,



Initial results: ……………. to not so easy to read



Factors and ranges….

Factors	Factor ranges Low level	 High level
Mark Speed	8	15
Frequency	1	5
Percent Power	15	55
Repetitions	1	5
Humidity	5%	15%

Blocking factor is operator

Analysis of the data

- **Stage 1**
- **Stage 2**
- **Full model**

Stage 1 - Main Effect Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Speed	0.987	0.2432	4.0589	0.0270*
Frequency	1.539	0.2432	6.3289	0.0080*
Power	-1.912	0.2432	-7.863	0.0043*

Statistic	Value
RMSE	0.769
DF	3

Stage 2 - Even Order Effect Estimates

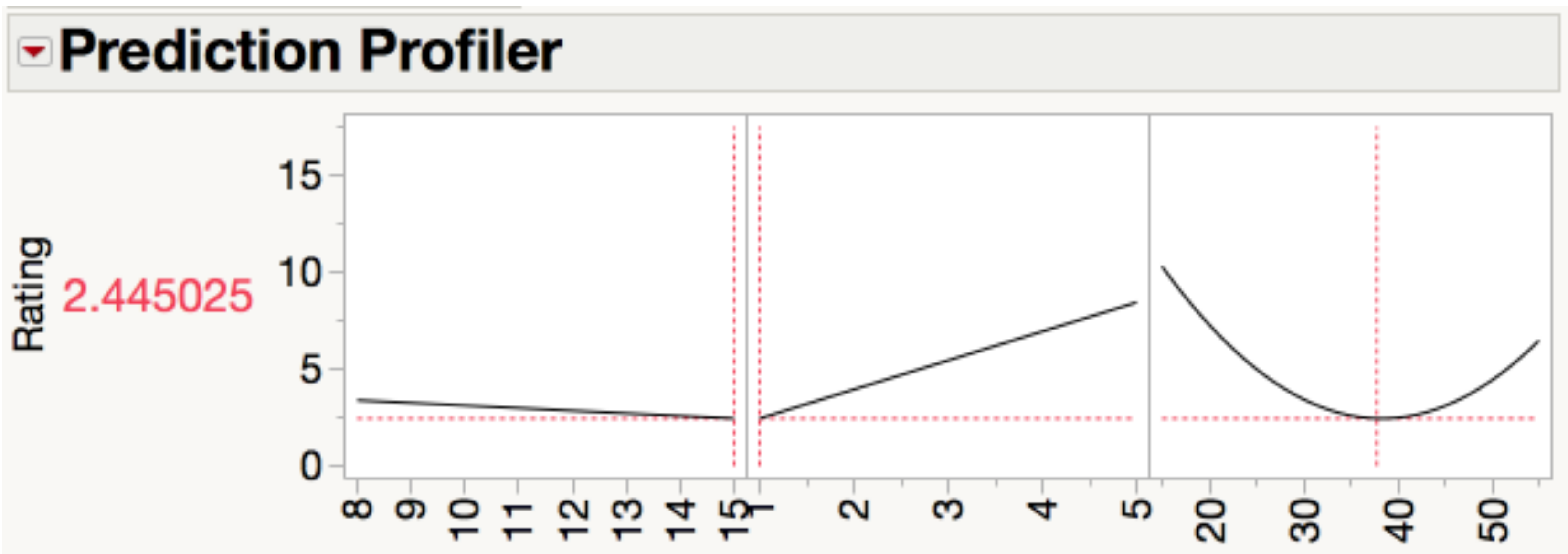
Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	4.6079	0.4351	10.591	0.0004*
Speed*Frequency	1.4568	0.2734	5.3294	0.0060*
Power*Power	5.7828	0.509	11.362	0.0003*

Statistic	Value
RMSE	0.6843
DF	4

Combined Model Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	4.6079	0.4589	10.04	<.0001*
Speed	0.987	0.2283	4.3241	0.0035*
Frequency	1.539	0.2283	6.7425	0.0003*
Power	-1.912	0.2283	-8.377	<.0001*
Speed*Frequency	1.4568	0.2883	5.0525	0.0015*
Power*Power	5.7828	0.5369	10.772	<.0001*

Optimal Laser Etch Settings



Speed **Frequency** **Power**

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Optimal Etch

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Conclusions

- **DSDs are general purpose, three-level screening designs that provide useful second-order information**
- **My bias: they are superior to classical screening designs such as PBDs, Resolution III and IV FF designs**
- **We can now:**
  - **Add categorical factors**
  - **Block flexibly**
  - **Augment (see Nachtsheim, Jones, Montgomery, Stufken)**
  - **Analyze effectively**

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Impact? First published DSD case study, 2013

Biotechnol Lett
DOI 10.1007/s10529-012-1089-y

ORIGINAL RESEARCH PAPER

Efficient biological process characterization by definitive-screening designs: the formaldehyde treatment of a therapeutic protein as a case study

Axel Erler · Nuria de Mas · Philip Ramsey · Grant Henderson

Impact? From the conclusions:

"*Definitive-screening designs were used to efficiently select a model describing the formulation of a protein under clinical development. The ability of the single definitive screening design to identify and model all the active effects obviated the need for further experimentation, reducing the total number of experimental runs required to 17 from the greater than or equal to 70 runs that would have been necessary using the traditional screening/RSM approach.*"

Doug Montgomery on DSDs

The most important development in DOE since response surface designs*

*2013 Hunter Conference

Summary

- **DSDs are general purpose three-level screening designs that provide useful second-order information**
- **My bias: they are superior to classical screening designs such as PBDs, Resolution III and IV FF designs**
- **We can now:**
  - **Add categorical factors**
  - **Block flexibly**
  - **Augment**
  - **Analyze effectively**

If you're lucky, they can be used to screen and optimize in one step

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Questions?

- **DSDs are general purpose three-level screening designs that provide useful second-order information**
- **My bias: they are superior to classical screening designs such as PBDs, Resolution III and IV FF designs**
- **We can now:**
  - **Add categorical factors**
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  - **Analyze effectively**

If you're lucky, they can be used to screen and optimize in one step

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