U.S. ARMY COMBAT CAPABILITIES DEVELOPMENT COMMAND – CHEMICAL BIOLOGICAL CENTER

Transitioning from conventional experimentation to DOE: The benefits and challenges encountered

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DISCLAIMER

The views and opinions expressed in this presentation are those of the authors and do not necessarily reflect the official policy or position of the U.S. Army, the Department of Defense or the Federal Government.

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- U.S. Army DEVCOM CBC Lab personnel for laboratory execution and analytical analysis

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MY BACKGROUND

Jay Davies- Research Physicist (Applied Experimentalist/Statistician)

- U.S. Army DoD Civilian, DEVCOM CBC, at Aberdeen Proving Grounds, MD
- Research and Technology Directorate
- Chemical and Biological Protection Division
- Decontamination Sciences Branch (13 years)
- Prior- Manufacturing Process Engineer (20 years), Solar cells, Ceramic composites

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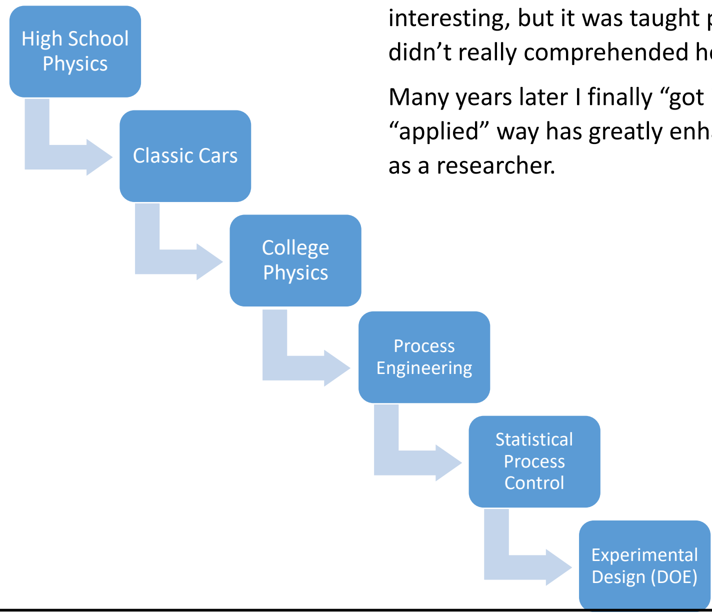
MY PATH

As a process engineer, I took an introductory DOE class in ’95. It was interesting, but it was taught purely from classical perspective, and I just didn’t really comprehend how DOE could be applied to what I did.

Many years later I finally “got it”, and the ability to use DOE methods in a very “applied” way has greatly enhanced my career as a process engineer and now as a researcher.



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OUTLINE

Part #1 Some thoughts and experiences with DOE in general

- Tips for students, non-users, and advanced users
- Selling DOE to potential new users
- Conceptual illustrations of DOE vs “one-factor-at-a-time” (OFAT)
- SME knowledge/insight and participation is essential

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Part 1

CBC OVERVIEW

Who are we?

What do we do?

Overview of the DEVCOM Chemical Biological Center:

“The best thing about being a statistician is that you get to play in everyone's backyard.”
(John Tukey)

“Most chemists and physicists graduate without a knowledge of [practical applied] statistical methods, and are often unaware of the value of such methods in their work. An early reaction when they are introduced to the subject is that statistical methods are in some way an alternative to whatever method they would normally have used---an alternative which is applied by enthusiasts and which is entirely optional.”*

* (*Design and Analysis of Industrial Experiments*, G. Box et al, 1967)

"I wish that I'd known this when I was just starting out!"

(Me and a whole lot of other engineers and researchers after trying applied DOE methods for the first time.)

STATISTICAL DESIGN COMBINED WITH SME KNOWLEDGE / EXPERIENCE IS IDEAL

Statistical design is often perceived as competing with the Subject Matter Expert (SME) for control

> **"Statistical techniques are useless unless combined with appropriate subject matter knowledge and experience." ***

George Box one of the founders of applied experimental design. Statistical design is a complement to and not a replacement for the SME.

However, that being said, without statistical techniques such as DOE….

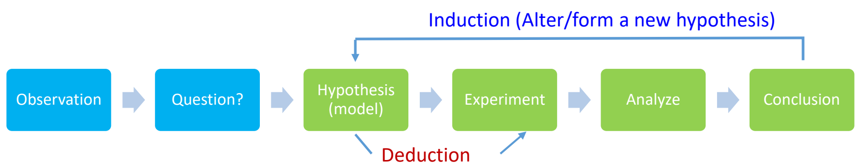
> **"It is easy to conduct an experiment in such a way that no useful inferences can be made."****

> **Statistical Design is a "catalyst" to scientific discovery.***

*G. Box
**W,G. Cochran, G. M. Cox, Experimental Designs, 1950.

Scientific Method- Iterative Learning

Scientific Method

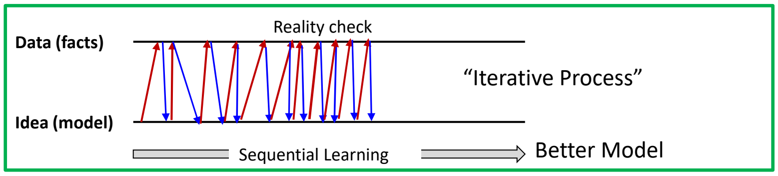


(Figure adapted from fig. 1.1 , "Statistics for Experimenters" Second Edition, Box/Hunter/Hunter)

DOE AND THE SCIENTIFIC METHOD

5 Factors
Materials (2)
Decons (2)
Pressure
Time
Temp

Traditional Intuition based (One hypothesis at a time, "one-shot")



(Figure adapted from fig. 1.1 , "Statistics for Experimenters" Second Edition, Box/Hunter/Hunter)

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CONCEPTUAL VISUALIZATION- OFAT

Our 50 samples gives us high resolution but only at disjointed snap-shots. The majority of the design space remains unexplored.

Design Space

Image taken from Wikipedia, accessed 10-29-20

Sample count= 卌 卌 卌 卌 卌 卌 卌 卌 卌 卌 =50 Total!

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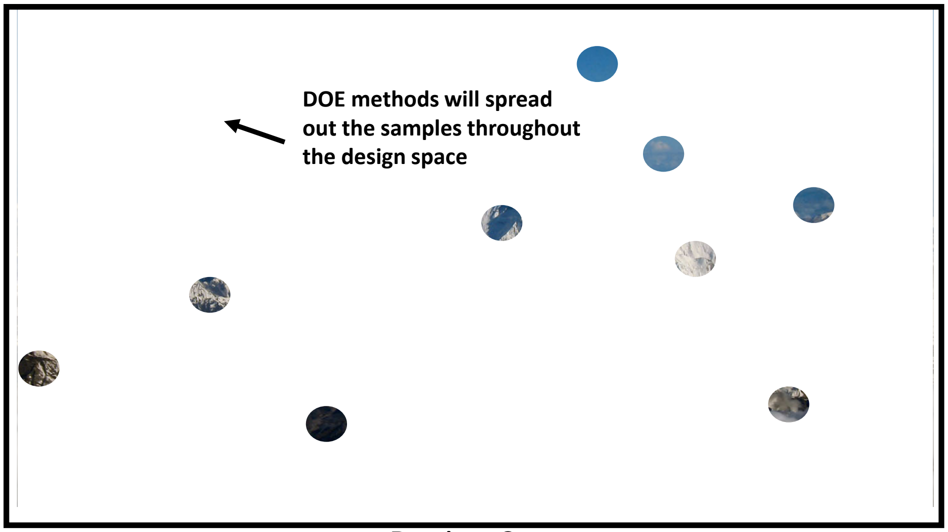
DOE SPREADS THE SAMPLES OUT



Design Space

DOE methodology eliminates exact replication and spreads all 50 samples out over the whole design space.

Image taken from Wikipedia, accessed 10-29-20

Sample count= =50 Total!

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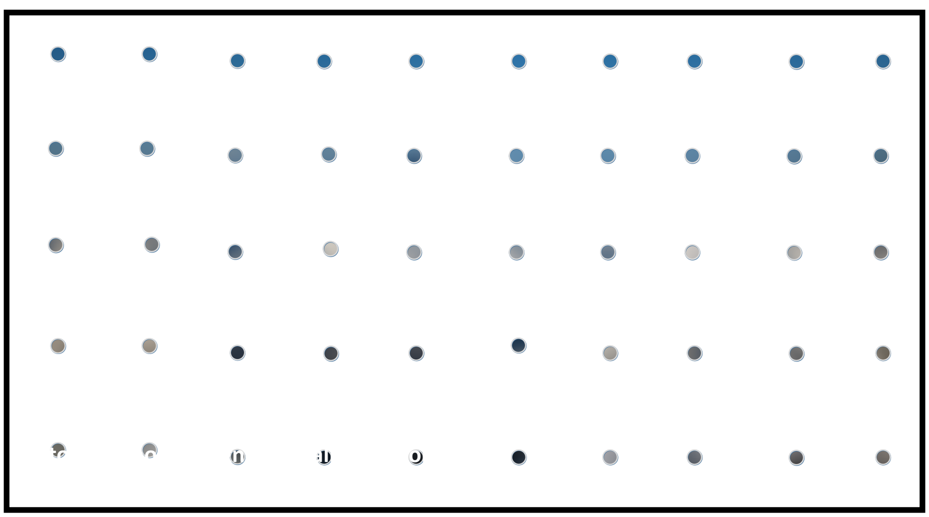
CONCEPTUAL VISUALIZATION- DOE



Design Space

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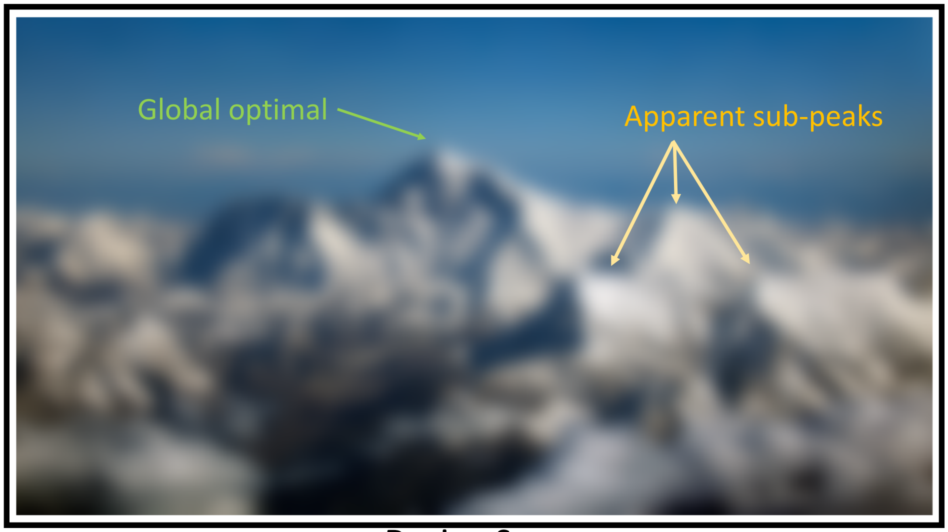
CONCEPTUAL VISUALIZATION- DOE



Design Space

Image taken from Wikipedia, accessed 10-29-20

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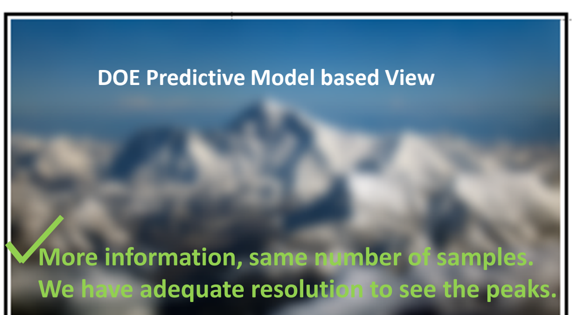
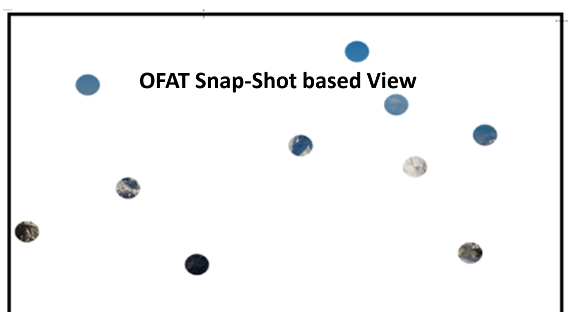
CONCEPTUAL COMPARISON OF DESIGN SPACE CHARACTERIZATION: DOE VS OFAT



Design Space



Design Space

These illustrations contrast the ability of OFAT and DOE to characterize a design space. (Equal sample sizes)

DOE: Lower resolution but with full illumination

OFAT: High-resolution but only at discrete snap-shot locations.

The “wider” view output makes DOE much more efficient than OFAT especially when design spaces are complex.

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EVEN WITH A GOOD DESIGN DETAIL IN EXPERIMENTAL EXECUTION STILL MATTERS.

“When running an experiment the safest assumption is that unless extraordinary precautions are taken it will be run wrong.”

(Box, Hunter, Hunter)

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SOME RECOMMENDATIONS

Students/Early Career

- Be optimistic, diligent, and patient in finding a role that you're passionate about.
- DOE is a great tool to have. It’s a big advantage for anyone that deals with data.
- You don’t need to be a theoretical statistician to use DOE.

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Part 2

IMPACT OF DOE AT CBC

Counting just the major programs within or in collaboration with the Decontamination Sciences Branch, CBC has executed 19 DOEs since 2016.

DOE Type	Number DOEs Executed	Actual Lab days used by the DOEs	Lab days that would have been needed for conventional experimentation
Non-Mixture	5	14	241
Mixture-Process	14	43	1,445

Total lab days used by the DOEs = 57
Total lab days that would have been needed = 1,686

The efficiency of the DOEs has allowed for more factors to be included in the studies which increases the applicability of the results and allows for greater chance of unexpected discoveries.

Formulation optomization time has been reduced from months to days.

$ZR(OH)_4$ SLURRY AS A DECONTAMINANT

Zr(OH)4 currently being used as a filter media.

Decontaminant Slurry Components

Hydration

Kerosene

Zr(OH)4 Slurry on Panel

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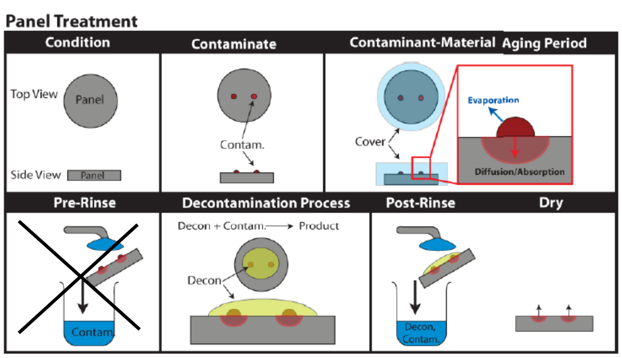
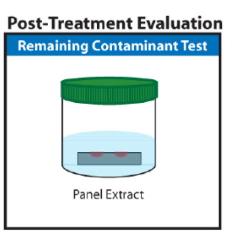
DECONTAMINANT PANEL TESTING: PANEL TREATMENT PROCESS





Panel Testing response is transformed to "log10 reduction", (Stabilizes variance and provides a meaningful response metric.)

Log10 reduction = log10(Contam.(ng)) - log10(Panel Extract (ng))

Log10 reduction of 1 = 90.0% efficacy
Log10 reduction of 2 = 99.0% efficacy
Log10 reduction of 3 = 99.9% efficacy

Source: *Chemical Contaminant and Decontaminant Test Methodology Source Document Second Edition, ECBC-TR-980, APG , MD 21010*

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TERNARY PLOTS OF DESIRABILITY- AGENT SPECIFIC AND COMBINED/WEIGHTED MODEL

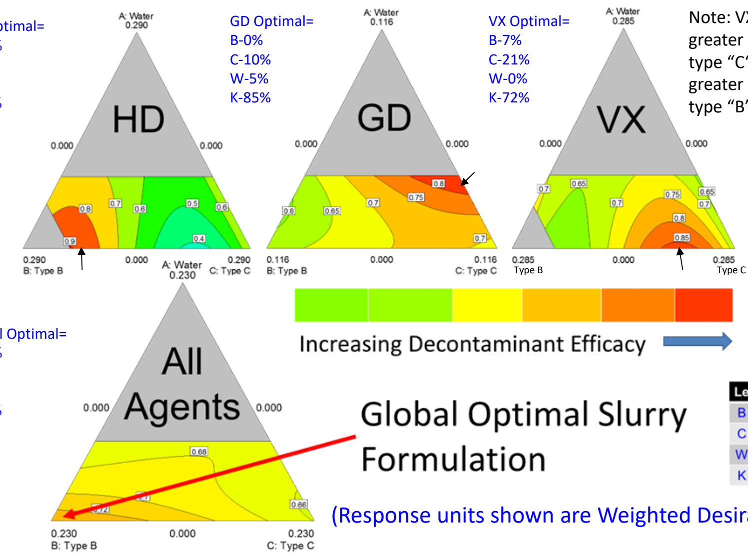
HD Optimal=
B-23%
C-6%
W-0%
K-71%

GD Optimal=
B-0%
C-10%
W-5%
K-85%

VX Optimal=
B-7%
C-21%
W-0%
K-72%

Note: VX shows greater efficacy with type "C" while HD has greater efficacy with type "B".

Global Optimal=
B-23%
C-0%
W-0%
K-77%



Global Optimal Slurry Formulation

Legend	
B	Type B $Zr(OH)_4$
C	Type C $Zr(OH)_4$
W	Added Water
K	Kerosene

(Response units shown are Weighted Desirability)

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CBC USES DOE FOR SLURRY FORMULATION (2016)

News Story

ECBC Team Slashes Time, Cost of Getting Better Decontamination Solution to Warfighters

ECBC RESEARCHERS HAVE DEVELOPED A DECONTAMINATION SPRAY THAT ENABLES SOLDIERS TO DECONTAMINATE VEHICLE SURFACES, EVEN VERTICAL ONES, IN THE FIELD IMMEDIATELY AFTER EXPOSURE.

RDECOM C&B Public Affairs | June 30th, 2016

Formulation DOE initially used in 2016 for "proof of concept" formulation.

DOE accelerates screening/development for $Zr(OH)_4$ decon slurry, conserving resources to be used for advanced development.

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CBC USES DOE FOR FINAL SLURRY FORMULATION (2020)

In 2020-21 CBC used Formulation Mixture-Process DOE for final Slurry formulation.

"Sprayable Slurry Offers The Missing Piece of Decon Puzzle"
https://www.dvidshub.net/news/308788/sprayable-slurry-offers-missing-piece-decon-puzzle
Photo accessed 9-12-22

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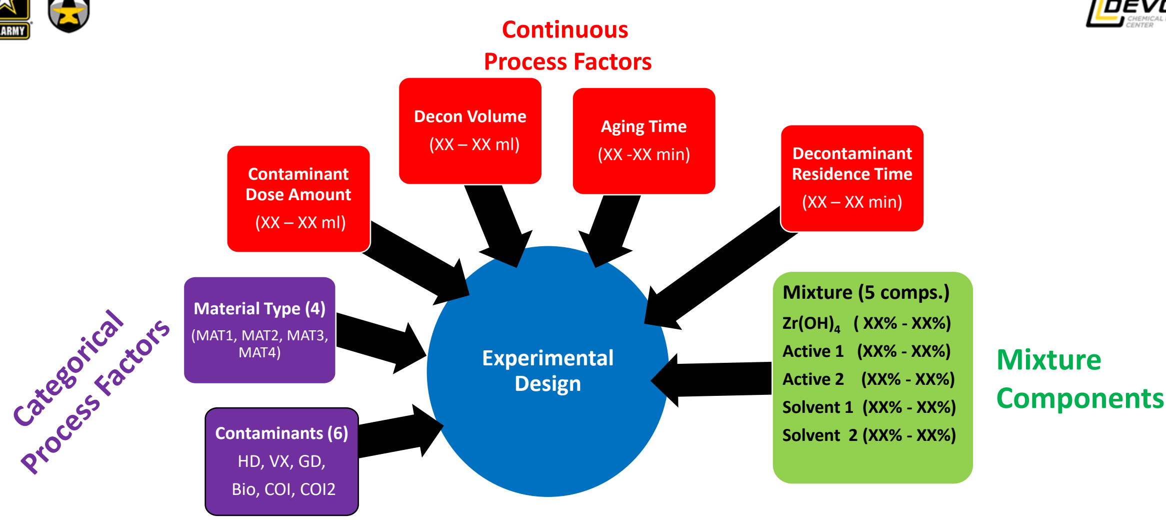
SLURRY FORMULATION COMPONENTS/PROCESS FACTORS



Additional Constraints: Solvent 1 /(Solvent 1 + Solvent 2)=XX% to XX%
Solvent 2/ (Solvent 1 + Solvent 2)=XX% to XX%

Full Factorial= 6x4x3x3x3x3x (5 Formulations) ≈ *9720 X 5 reps = 48,600 samples required!*

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POSSIBLE OPTIONS

- Reduce the design space, drop agents, materials, or formulation components.
  (Reduces the scope/relevancy of the study and falls short of stakeholder expectations.)
- Find a more efficient experimental design strategy.
  (Mixture-Process Formulation DOE)

STARTING STATISTICAL MIXTURE-PROCESS MODEL FOR SLURRY DOE

Starting model- Special Cubic on the Mixture side, Quadratic Process side.

Cross terms limited to Cubic (3way) (≈Kowalski/ Cornell/ Vining (KCV) design*.)

Starting model= 489 terms.

DOE= 584 samples total (10 lab days), 35 exact replicates, 35 check-points

Predicted Response= (Mixture model terms) + (Cross terms) + (Process model Terms)

Output is a fitted prediction model good for the entire design space.

Design included 24 different agent/material combinations with 5 formulation components across 4 process factors, by far the most ambitious ever attempted by CBC.

*S. Kowalski, J. Cornell, G. Vining (2000), *A New Model and Class of Design for Mixture Experiments with Process Variables, Communications in Statistics- Theory and Methods, 29:9-10, 2255-2280*

COVID RESTRICTIONS FORCE PLANS TO CHANGE

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Original Design (ambitious/high efficiency) :584 sample I-Optimal (10 day) DOE was Special Cubic on the Mixture side and Quadratic on the Process side with cross terms limited to Cubic (3way)

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FULL STARTING MODEL FOR ZR(OH)4 DOE

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Mixture model terms

Linear blending | Quadratic non-linear blending | Cubic non-linear blending

Predicted Response = $(\beta_1 A + \beta_2 B + \beta_3 C + \beta_4 D + \beta_5 E) + (\beta_{12} AB.....+ \beta_{45} DE) + (\beta_{123} ABC.....+\beta_{345} CDE)...$

Process model Terms
2Way interactions

$+ (\delta_{12} FH...+\delta_{56} KL)$

Cross terms

$+ (\alpha_{ii} AF.....+\alpha_{ii} EL) + \boxed{(\alpha_{ii} AF^2.....+\alpha_{ii} EL^2) + (\alpha_{jjj} ABF+.....\alpha_{jjj} EKL)}$

DOE allows for fitting of the β, δ, and α terms.

Formulation
A-$Zr(OH)_4$
B-Active 1
C-Active 2
D-Solvent 1
E-Solvent 2

Process Factors
F-Age Time
G-Res Time
H-Dose Amt.
J-Decon Vol.
K- Material (4)
L- Agent (6)

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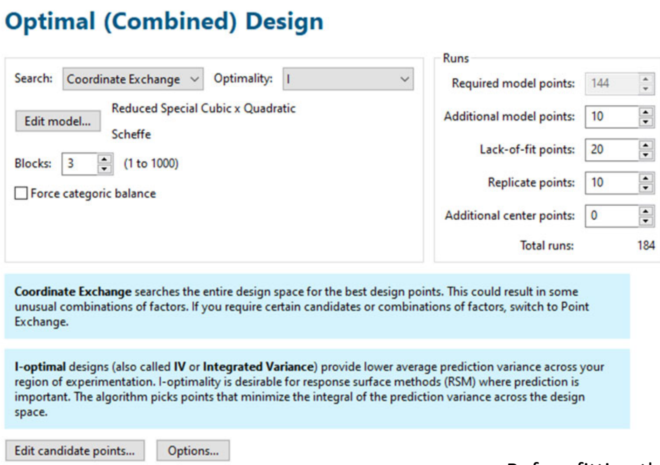
GENERATING CHECK-POINTS FOR IN-LINE MODEL VALIDATION

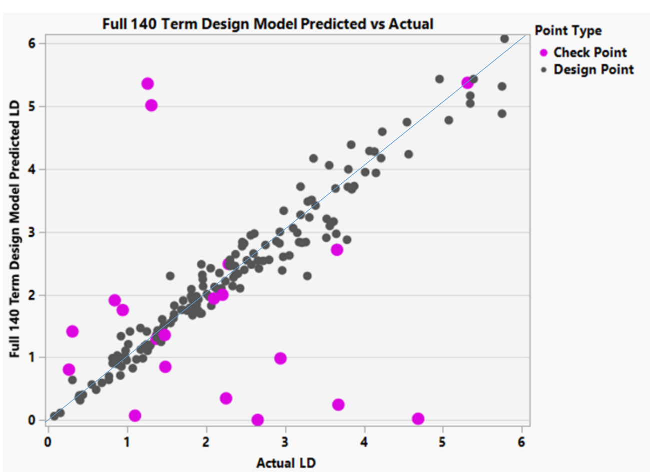


Use "Lack-of-Fit" to generate Check-points

Run	Build Type	Component 1 A:A	Comp
1	Model	0.491232	
2	Model	0	
3	Model	1	
4	Model	0	
5	Model	0	
6	Model	0.503759	
7	Model	1	
8	**Lack of Fit**	**0.174063**	
9	Model	0.483184	
10	Model	0.493826	
11	**Lack of Fit**	**0.532253**	
12	**Lack of Fit**	**0.183432**	

Before fitting the model, set the check-point rows' status to "verification". This will hold the points back from the model fitting.

EXAMPLE OF OVER-FITTING: FULL 142 TERM MODEL



Model fits design points great

Fit Statistics

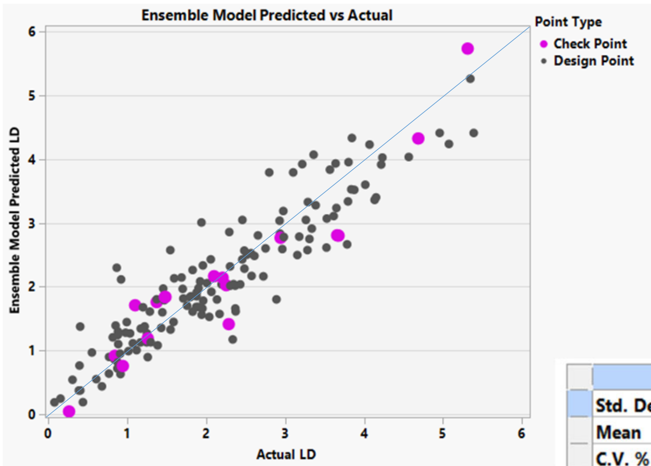
Std. Dev.	0.1462	**R^2**	0.9916
Mean	1.42	**Adjusted R^2**	0.8862
C.V. %	10.30	**Predicted R^2**	NA(1)
		Adeq Precision	14.4472

If we force a fit the full 142 term design model, we get a great R-Square, R-Square Adjusted and a super low RMSE.

However, model is over-fit; can predict the design points, but has no predictive capability at the check-points.

The model is useless away from the design points. Can't give us good predictions at the "untested" formulation/process factor combinations.

EXAMPLE OF PROPERLY FIT MODEL: REDUCED 48 TERM MODEL



This plot shows the actual experiment LD vs the model predicted LD

The plot shows that the model is predicting at the check-points and the design points with similar median errors of about 0.30 log units.

Model is capable of predicting at any "unknown' formulation or set of process factors within the design space.

Std. Dev.	0.1958	**R^2**	0.8678
Mean	1.42	**Adjusted R^2**	0.7956
C.V. %	13.80	**Predicted R^2**	0.6610
		Adeq Precision	16.5898

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STARTING STATISTICAL MIXTURE-PROCESS MODEL

Design	Runs	# Test Days	Model Terms	Mixture Order	Process Order	Cross Terms
Original Design	584	10	489	Special Cubic	Quadratic	3 way
Contingency Design	184	3	142	Special Cubic	Quadratic	2 way

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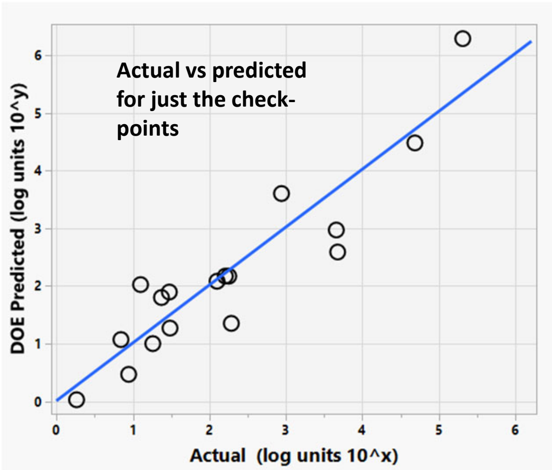
FITTED DOE MODEL CHECK-POINT ACTUAL VS PREDICTED



Check-Points not used to fit the model only to rate the predictive capability.

Check-points are a good indication of model predictive capability at "unknown" points.

DOE characterized the response across 6 orders of magnitude throughout the design space.

Reduced 45 term prediction model delivered a final formulation optimized across all process factors using only 3 laboratory days of data!

Fit Statistics

Std. Dev.	0.1971		**R^2**	0.8571
Mean	1.42		**Adjusted R^2**	0.7902
C.V. %	13.89		**Predicted R^2**	0.6852
			Adeq Precision	17.6452

The **Predicted R^2** of 0.6852 is in reasonable agreement with the **Adjusted R^2** of 0.7902; i.e. the difference is less than 0.2.

Good agreement between Adjusted and Predicted R^2

The strong R-Square pred. score, low design point fitted residuals, low and unbiased check-point residuals together provide strong evidence that the model is a capable predictor at "unknown" points throughout the design space.

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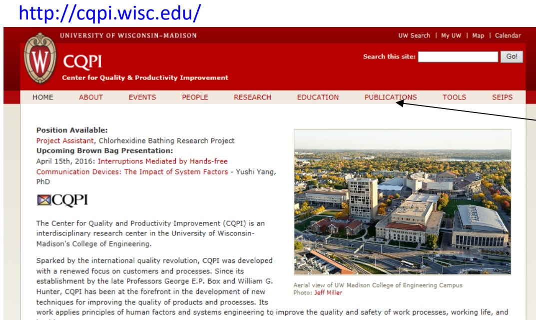
RESOURCES- APPLIED DESIGN, SOFT SIDE ISSUES

University of Wisconsin-
Center for Quality and Product Improvement
http://cqpi.wisc.edu/



Technical Reports

Statistics as a Catalyst to Learning (report #172) (1999), G.Box
Statistics for Discovery (report #179) (2000), G.Box

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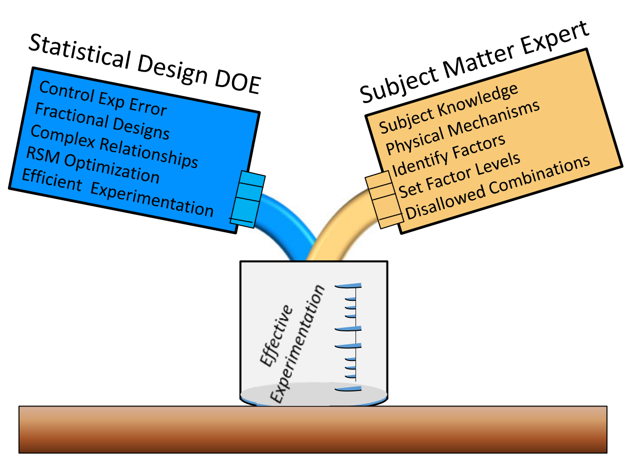
COMBINING THE EFFICIENCY OF DOE WITH SME EXPERTISE / KNOWLEDGE



DOE Efficiency + SME Expertise = Effective Experimentation

Questions?

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END

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