TTK31 - Design of Experiments (DoE), metamodelling and Quality by Design (QbD)
Autumn 2021

Big Data Cybernetics Gang

NTNU

Lecture overview

1. DoE: Introduction and motivation
2. ANalysis Of VAriance (ANOVA)
3. **Factorial designs and Fractional factorial designs**
4. Response surface designs
5. Optimal designs
6. Metamodelling
7. Combining DoE with multivariate analysis/machine learning
8. QbD – PAT
9. Practical examples of DoE related to cybernetics

Reminder: Reference group - VERY IMPORTANT

- at least 3 students (two or more seats free!)
- will do 4 meetings (1 after the exam)
- shall represent the whole class $\Longrightarrow$ you will have meetings among yourselves too
- shall lead to a referansegrupperapport containing suggestions for improvements

Experimental Work: The Basic Questions - recap

- Which design factors in my system are the most important?
- Are there any interactions?
- How can I get maximum information at minimum cost?
- Where is the optimal region?
- Where is the stable region?
- How can I span the variation of my calibration variables?
- How can I build a good calibration / validation data set?

Factorial designs

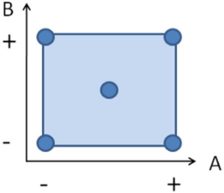
The full factorial design

Motivation for use

- Simplest design situation
- Basis for many other designs
- Optimal for detecting main effects and their interactions

2-level full factorial designs

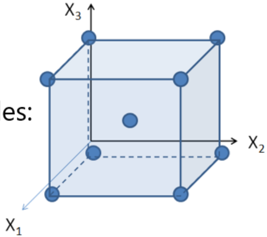
2 X-variables:



run #	X_1	X_2
2	-	-
4	-	+
6	+	-
1	+	+
3	0	0
5	0	0

2^2 experiments (+ centre samples)

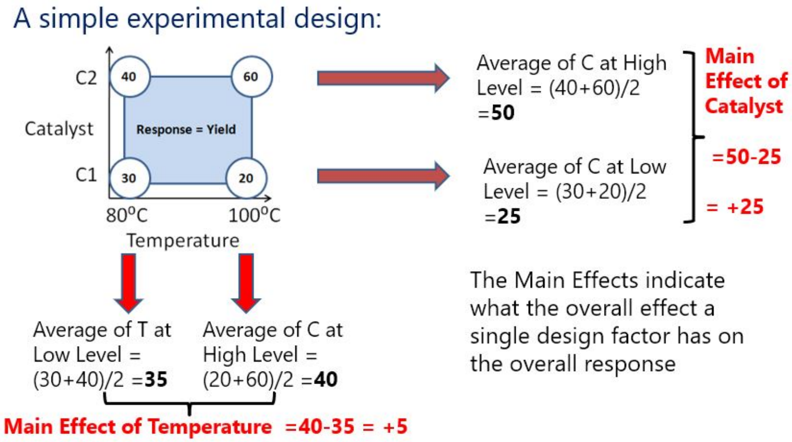
3 X-variables:



run #	X_1	X_2	X_3
2	-	-	-
11	-	-	+
5	-	+	-
8	-	+	+
4	+	-	-
1	+	-	+
9	+	+	-
7	+	+	+
3	0	0	0
6	0	0	0
10	0	0	0

2^3 experiments (+ centre samples)

Calculating effects - main effects



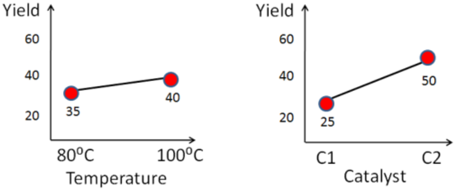
Calculating effects - interaction effects

The simplest way to find how to calculate the various effects is to use the design table: An example for 2^3 full factorial design

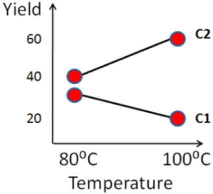
Std	A	B	C	AB	AC	BC	ABC	
1	–	–	–	+	+	+	–	y_1
2	+	–	–	–	–	+	+	y_2
3	–	+	–	–	+	–	+	y_3
4	+	+	–	+	–	–	–	y_4
5	–	–	+	+	–	–	+	y_5
6	+	–	+	–	+	–	–	y_6
7	–	+	+	–	–	+	–	y_7
8	+	+	+	+	+	+	+	y_8

Interpreting effects - overview

Main effects

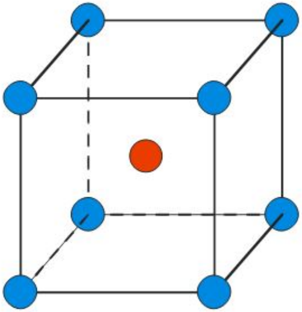


Interactions

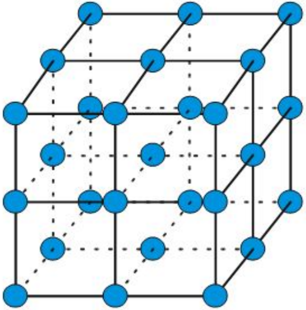


But what about adding more levels to the design factors?

- Adding more levels will rapidly increase the number of runs
- If the goal is to have a more precise description of the design space, other designs are more economical



2^3 factorial with center point
(8 runs plus 4 cp's = 12 pts)



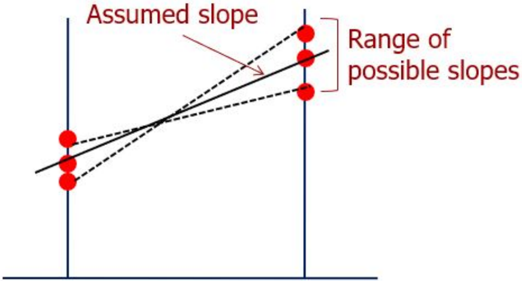
3^3 Three-level factorial
(27 runs + 5 cp's = 32 pts)

Additional experiments

- Center samples
  - To detect curvature
  - To estimate error variance
  - For category variables need one experiment for each level
- Replicated samples
  - Replication of factorial points
  - More precise estimate of error variance
- Remember the assumptions about the residuals, $N(0, \sigma^2)$:
  - Normally distributed
  - Mean of zero
  - Constant variance

Replicates and center samples

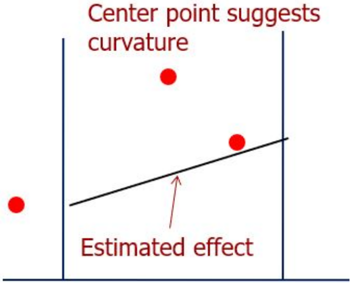
Replicates :



Precision

$SD_{\text{repl. samples}} << SD_{\text{whole design}}$?

Center samples :



Curvature check

$\overline{Y}_{\text{center samples}} = \overline{Y}_{\text{design}}$?

Power of an experimental design

- The power of a design *must* be calculated prior to performing any experiments!
- The calculation of power takes four inputs:
    1. Δ, what *you* regard as a significance difference for a given response
    2. σ, the noise in the measurement of the response variable
    3. The number of experiments
    4. The significance level α

Estimation of power

Power = (1−β)*100%

Power is the probability of revealing an active effect of size delta (Δ) relative to the noise (σ) as measured by signal to noise ratio (Δ/σ).

It should be high (at least 80%!) for the effect size of interest.

Effect?		ANOVA says:	
		Retain H_0	***Reject H_0***
Truth:	***No***	OK☺	Type I Error (alpha) *False Alarm*
	Yes	Type II Error (beta) *Failure to detect*	OK☺

How to Select Ranges of Variation

- Wide enough to generate response variation
- Narrow enough to avoid huge non-linearities
- Useful tip: Start with two extreme combinations
    - If too extreme results: narrow down
    - If different enough results: OK
    - If too close results: Check center samples

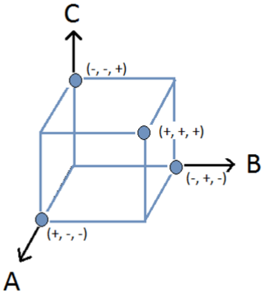
Fractional Factorial designs

Fractional Factorial designs

- Full factorial designs are expensive if many design factors
- Often higher order interactions can be neglected → Fractional factorial design
- Subset of the full factorial design
- Experiments are systematically chosen to cover the widest possible design space

2-level fractional factorial design

- 3 design variables, A, B, C
- 2^{3-1} design, C $=$ AB
- All main effects are estimated in $2^{3-1} = 4$ runs
- The main effects are aliased with the interaction effects



Aliasing/Confounding

- The price to be paid for performing fewer experiments (fractional designs)
- $\rightarrow$ some effects cannot be studied independently of each other
- The degree of confounding is described by the *confounding pattern* and the *resolution*

Constructing a 2-level Fractional Factorial design: Aliasing

- Example: Constructing the 2^{4-1} Design from a 2^3 Design
- Write out the full design
- Let D $=$ ABC (aliasing with the highest interaction term)

A	B	C	AB	AC	BC	ABC
-	-	-	+	+	+	-
+	-	-	-	-	+	+
-	+	-	-	+	-	+
+	+	-	+	-	-	-
-	-	+	+	-	-	+
+	-	+	-	+	-	-
-	+	+	-	-	+	-
+	+	+	+	+	+	+

Aliasing/Confounding: Four design variables

Example: four design variables, can only afford 10 runs
2^{4-1} fractional factorial design + 2 center samples

The column for **D** equals the interaction **ABC**

Defining relation: **I=ABCD**, resolution=**IV**

This gives the following confounding pattern:

A=BCD
B=ACD
C=ABD
D=ABC
AB=CD
AC=BD
AD=BC

These effects cannot be estimated separately from each other

	A	B	C	D=ABC
1	-	-	-	-
2	+	-	-	+
3	-	+	-	+
4	+	+	-	-
5	-	-	+	+
6	+	-	+	-
7	-	+	+	-
8	+	+	+	+
9	0	0	0	0
10	0	0	0	0

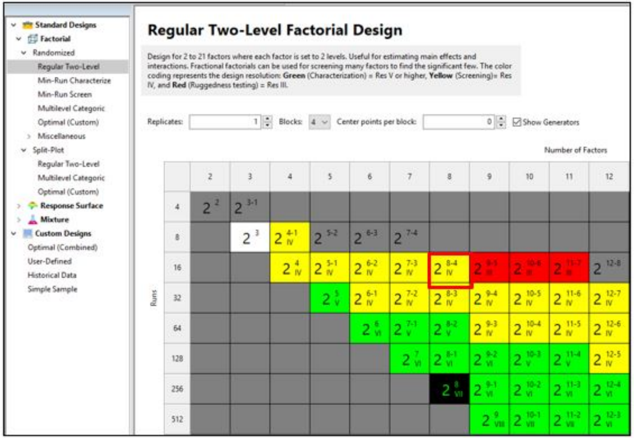
The resolution of a design

- Resolution V: Main effects are not confounded with 2-way interactions
- Resolution IV: 2-way interactions are confounded and main effects are confounded with three-factor interactions
- Resolution III: Main effects are confounded with 2-way interactions

Number of experiments for various designs

	Resolution		
Factors	Full	V	Runs
5	32	16	$^1/_2$
6	64	32	$^1/_2$
7	128	64	$^1/_2$
8	256	64	$^1/_4$
9	512	128	$^1/_4$
10	1,024	128	$^1/_8$
11	2,048	128	$^1/_{16}$
12	4,096	256	$^1/_{16}$
13	8,192	256	$^1/_{32}$
14	16,384	256	$^1/_{64}$
15	32,768	256	$^1/_{128}$

Resolution and confounding patterns for various designs



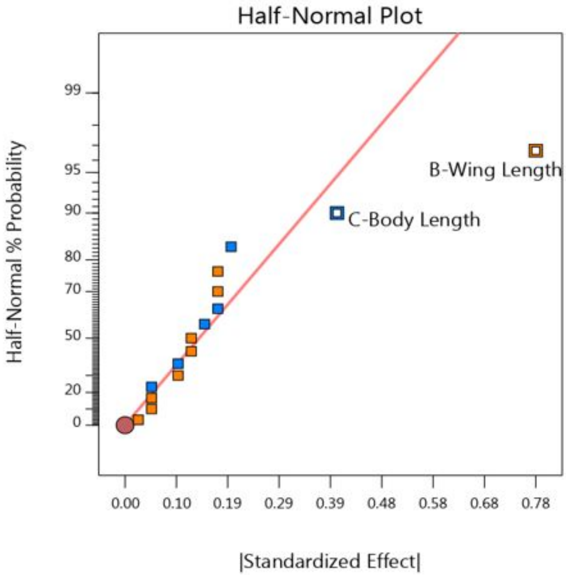
How to identify the important effects?

- If all main and interaction effects are estimated, there are no degrees of freedom for the error, and thus no output for F-ratios and p-values in the ANOVA table.
- However, the effects can be visualized in various plots to make an assessment:
  - Half-Normal Plot
  - Normal Plot
  - Pareto Chart

Half-Normal Plot

- If there are no significant effect, they should follow a normal distribution
- One way of visualizing this is in the normal probability plot (ref. plot of residuals)
  1. Sort the effects
  2. Plot them on a logarithmic scale
- Effects that deviate from a straight line in this plot might be significant
- One can show the effects as absolute values (half-normal) or as is (normal plot)

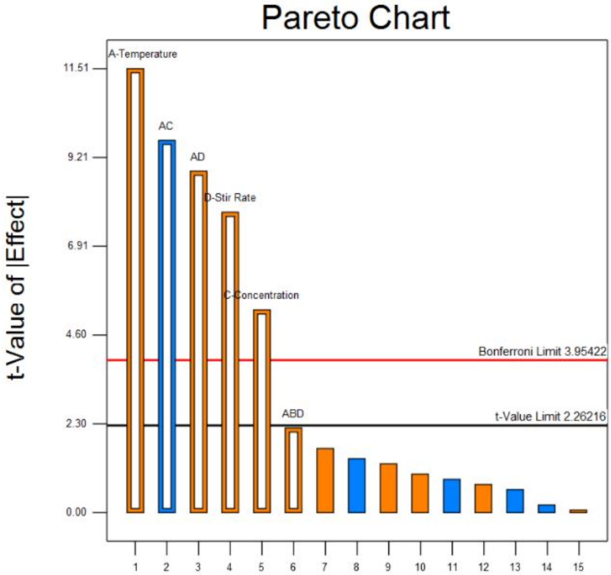
Half-Normal Plot - example



Pareto Chart

- The Pareto Chart is another option to show the importance of the effects
- It has two critical limits:
  - t-limit: A limit based on the t-distribution
  - Bonferroni limit: A conservative limit taking into account the number of terms in the model
- Selected Effects that are above the Bonferroni Limit are almost certainly important and should be left in the model.
- Effects that are above the t-value Limit are possibly important and should be added if they make sense to the experimenter
- Effects that are below the t-value limit should only be selected to support hierarchy. They can also be forced into the model by the analyst.

Pareto Chart - example



Small example Factorial design: Popcorn

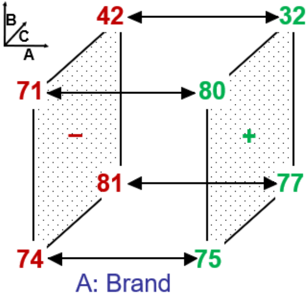
Popcorn example: Finding the best experimental settings

Multi-response optimization

Std	A: Brand expense	B: Time minutes	C: Power percent	R_1: Taste rating	R_2: UPKs oz.
1	Cheap	4.0	75.0	74	3.1
2	Costly	4.0	75.0	75	3.5
3	Cheap	6.0	75.0	71	1.6
4	Costly	6.0	75.0	80	1.2
5	Cheap	4.0	100.0	81	0.7
6	Costly	4.0	100.0	77	0.7
7	Cheap	6.0	100.0	42	0.5
8	Costly	6.0	100.0	32	0.3

Calculations of effects: Popcorn

Popcorn example



$$\text{Effect}(\Delta y) = \frac{\sum y_+}{n_+} - \frac{\sum y_-}{n_-}$$

$$\Delta y_A = \frac{75+80+77+32}{4} - \frac{74+71+81+42}{4} = -1$$

Small example 2: Factorial design

- Optimization of filtration rate in a chemical process
- A 2^4 full factorial design
- Four numerical design factors
  - Temperature
  - Pressure
  - Concentration
  - Stir rate
- Response variable: Filtration rate