Aalto University
School of Chemical
Technology

Design of experiments

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”The best time to plan an experiment is after you've done it.”
- Fisher

Introduce yourself

- Who are you?
- What do you do?
- Why are you here?
- Tell something funny about your name?

What to expect?

- Background and philosophy
- Theory
- Nomenclature
- Practical demonstrations and exercises

What not?

- Matrix algebra
- Statistical basics
- Detailed listing of possible designs

Intended learning outcomes

After the course you will be able to:

- Identify the basic principles of experimental design
- Use different programs for experimental design
- Recognise and use different design types
- Determine a suitable regression model based on design data
- Identify and apply different tools for model diagnostics

Course contents

Five sessions

- Introduction and factorial design
- Factorial design and diagnostics
- Central composite designs and optimization
- Mixture design and miscellaneous
- Practical groupwork

Requirements

Completed assignments and exam (pass/fail):

- Participation in all the sessions
- Given assignments and group work
- Course reader
- Individual exam (return by email)

Session 1

Introduction

- Why experimental design

Factorial design

- Design matrix
- Model equation = coefficients
- Residual
- Response contour

Some history

Originally by Fisher within agriculture and biology

- Fisher (1925) Statistical Methods for Research Workers (14th ed. reprint 1973: Hafner Publishing Company; New York)
- Fisher (1935) Design of Experiments (8th ed. reprint 1971: Hafner Publishing Company; New York)
- Box & Wilson (1951) On the experimental attainment of optimum conditions, *J Royal Stat Soc, Ser B*, 13, 1-45.
- Hill & Hunter (1966) A review of response surface methodology: a literature survey, *Technometrics*, 8, 571-590.

Experimental design or RSM?

Design →  → **Analysis**

Experimental design

- Planning and analysing experiments
- Emphasis on meaningful variation

Response Surface Methodology (RSM)

- Mathematical and statistical tools for the design and analysis of response surfaces
- Emphasis on optimization

Response surfaces

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If the current location is known, a response surface provides information on

- Where to go
- How to get there
- Local maxima/minima

Is there a difference?

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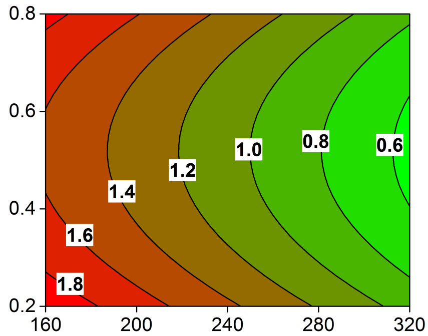
vs.



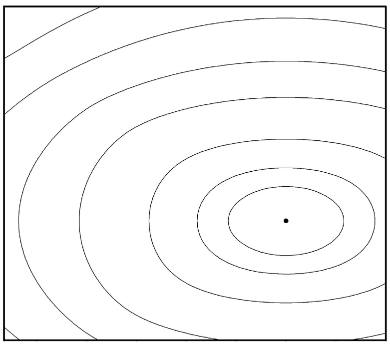
Research problem

$$A + B \xrightarrow{T,P} C$$

- A and B constant reagents
- C reaction product (response), to be maximized
- T and P reaction conditions (continuous factors), can be regulated

Response as a contour plot

P



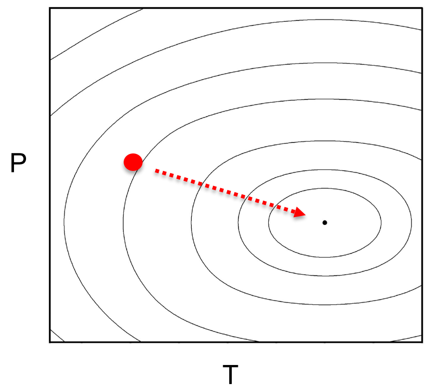
T

What kind of equation could describe C behaviour as a function of T and P?

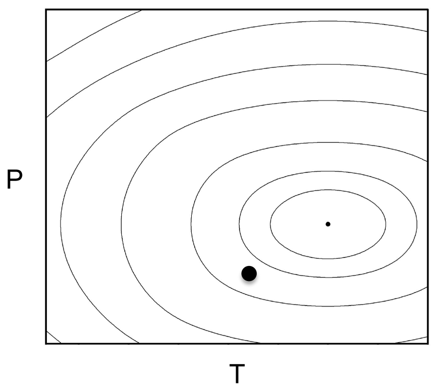
- C = f(T,P)

What else do we want to know?

- Which factors and interactions are important
- Positions of local optima (if they exist)
- Direction towards an optimum
- Surface and surface function around an optimum
- Statistical significance



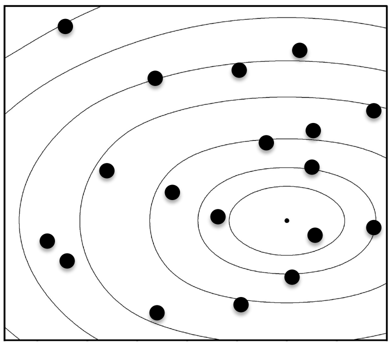
How can we do it?



The expert method

How can we do it?

P

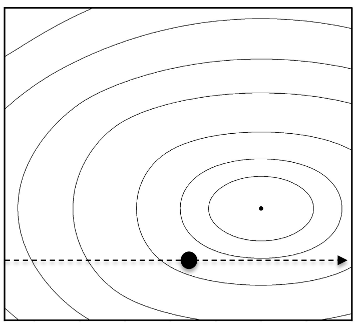


T

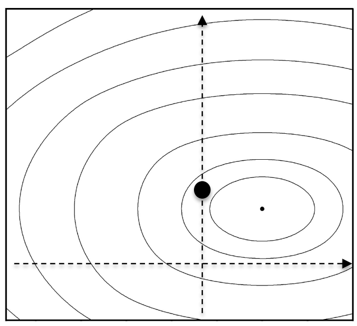
The PhD student method

How can we do it?

P fixed

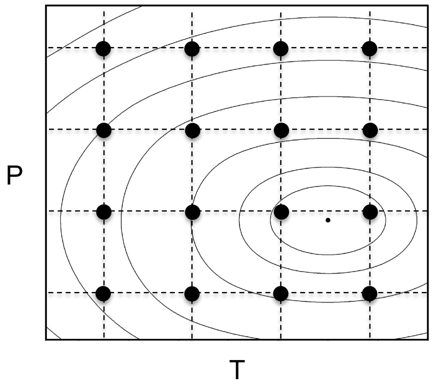


The classical method



T fixed

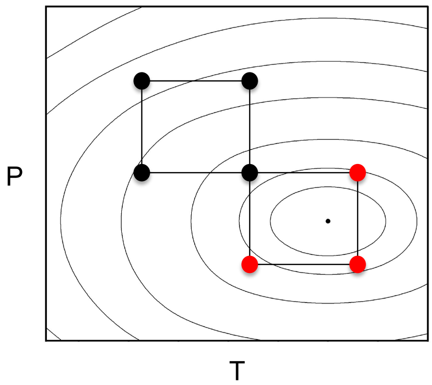
How can we do it?



The ”Soviet” method

- x^k possibilities with k factors on x levels
- 2 factors on 4 levels = 16 experiments

How can we do it?



The best method - factorial design

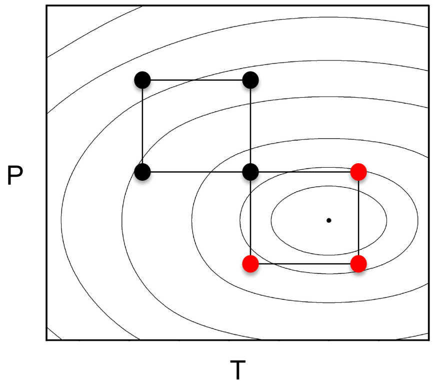
- ΔT, ΔP
- Factor interaction (diagonal)

Why experimental design?

- Reduce the number of experiments

→ Cost, time

- Extract maximal information
- Understand what happens
- Predict future behaviour



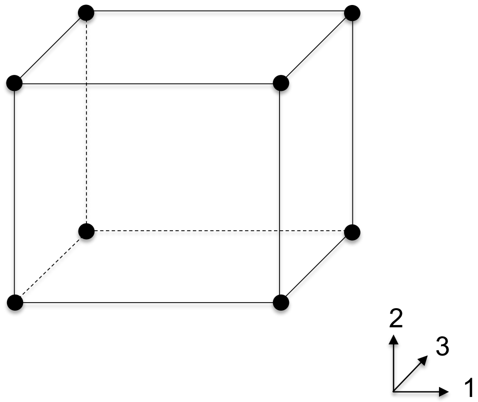
Challenges

- Multiple factors on multiple levels
- 6 factors on 3 levels, 3^6 experiments

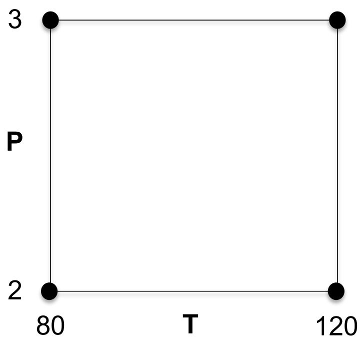
→ Only 2 levels

→ Discard factors

= SCREENING

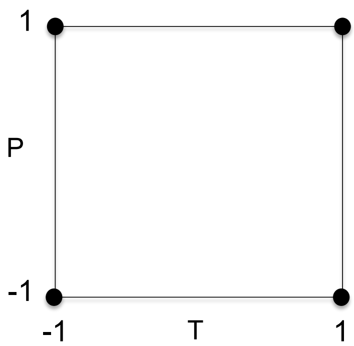


Factorial design



N:o	T	P
1	80	2
2	120	2
3	80	3
4	120	3

Factorial design

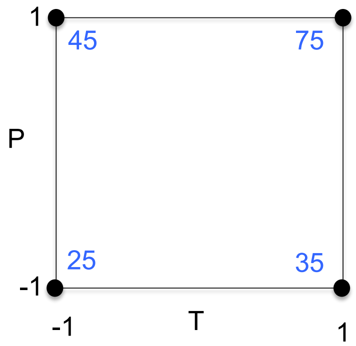


In coded levels:

N:o	T	T coded	P	P coded
1	80	-1	2	-1
2	120	1	2	-1
3	80	-1	3	1
4	120	1	3	1

The smallest possible full factorial design!

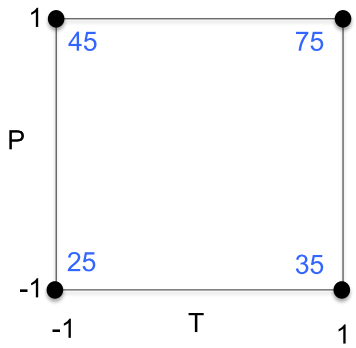
Factorial design



Design matrix:

N:o	T	P	C
1	-1	-1	25
2	1	-1	35
3	-1	1	45
4	1	1	75

Factorial design



Average T effect:

$$\mathrm{T} = \frac{75+35}{2} - \frac{45+25}{2} = 20$$

Average P effect:

$$\mathrm{P} = \frac{75+45}{2} - \frac{35+25}{2} = 30$$

Interaction (TxP) effect:

$$\mathrm{T{\times}P} = \frac{75+25}{2} - \frac{45+35}{2} = 10$$

Research problem

$$A + B \xrightarrow{T,P,K} C$$

- A and B constant reagents
- C reaction product (response), to be maximized
- T, P and K reaction conditions (continuous factors) at two different levels
- Number of experiments $2^3 = 8$ ($[\text{levels}]^{[\text{factors}]}$)

How to select proper factor levels?

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Factorial design

First step

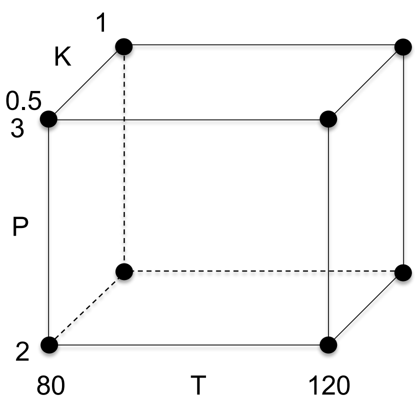
- Selection and coding of factor levels

→ Design matrix

T = [80, 120]

P = [2, 3]

K = [0.5, 1]



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Factorial design

N:o	Order	T	P	K
1		-1	-1	-1
2		1	-1	-1
3		-1	1	-1
4		1	1	-1
5		-1	-1	1
6		1	-1	1
7		-1	1	1
8		1	1	1

Randomize!

Factorial design matrix

- Notice symmetry in diffent colums
- Inner product of two colums is zero
- E.g. **T'P** = 0

→ Orthogonality

Orthogonality

For a first-order orthogonal design, X'X is a diagonal matrix

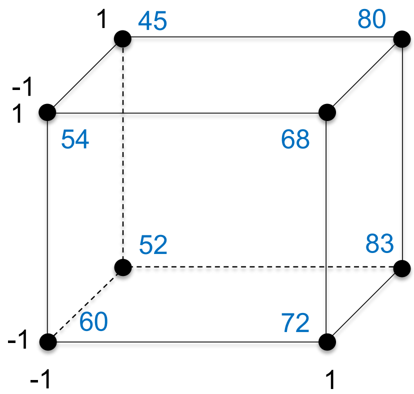
$$\mathbf{X} = \begin{bmatrix} -1 & -1 \\ 1 & -1 \\ -1 & 1 \\ 1 & 1 \end{bmatrix}, \mathbf{X}' = \begin{bmatrix} -1 & 1 & -1 & 1 \\ -1 & -1 & 1 & 1 \end{bmatrix}$$

$$\mathbf{X}'\mathbf{X} = \begin{bmatrix} -1 & 1 & -1 & 1 \\ -1 & -1 & 1 & 1 \end{bmatrix} \begin{bmatrix} -1 & -1 \\ 1 & -1 \\ -1 & 1 \\ 1 & 1 \end{bmatrix} = \begin{bmatrix} 4 & 0 \\ 0 & 4 \end{bmatrix}$$

If two columns are orthogonal, variable effects can be estimated independently

Factorial design

N:o	T	P	K	C
1	-1	-1	-1	60
2	1	-1	-1	72
3	-1	1	-1	54
4	1	1	-1	68
5	-1	-1	1	52
6	1	-1	1	83
7	-1	1	1	45
8	1	1	1	80



Empirical model

$y_c = f(T, P, K) + \varepsilon$

$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_k x_k + \varepsilon$

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{e} \rightarrow \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{bmatrix} = \begin{bmatrix} 1 & x_{11} & x_{12} & \cdots & x_{1k} \\ 1 & x_{21} & x_{22} & \cdots & x_{2k} \\ 1 & \vdots & \vdots & \ddots & \vdots \\ 1 & x_{n1} & x_{n2} & \cdots & x_{nk} \end{bmatrix} \underbrace{\begin{bmatrix} b_0 \\ b_1 \\ \vdots \\ b_k \end{bmatrix}}_{} + \begin{bmatrix} e_1 \\ e_2 \\ \vdots \\ e_n \end{bmatrix}$$

Measure **Choose** **Unknown! How to solve b?**

Least-squares regression

Minimize difference between measured and predicted values

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{e}$$
$$\rightarrow \mathbf{e} = \mathbf{y} - \hat{\mathbf{y}} = \mathbf{y} - \mathbf{X}\mathbf{b}$$

Cannot minimize a vector, minize the sum of squares (a scalar)

$$\frac{\partial \mathbf{e}'\mathbf{e}}{\partial \mathbf{b}} = \ldots = -2\mathbf{X}'\mathbf{y} + 2\mathbf{X}'\mathbf{X}\mathbf{b} = 0$$
$$\rightarrow \mathbf{b} = (\mathbf{X}'\mathbf{X})^{-1}\mathbf{X}'\mathbf{y}$$

→ Least-squares estimate of **b**

Linearity

Some confusion about multiple linear regression and linearity

- Linear in coefficients or variables?

$$y_i = b_0 + b_1 x_i + \varepsilon_i$$

- Linear in both coefficients and variables

$$y_i = b_0 + b_1 x_i + b_2 x_i^2 + \varepsilon_i$$

- Linear in coefficients (with a fixed *x*, *y* a linear function of b_0, b_1 and b_2)

Factorial design

N:o	T	P	K	C
1	-1	-1	-1	60
2	1	-1	-1	72
3	-1	1	-1	54
4	1	1	-1	68
5	-1	-1	1	52
6	1	-1	1	83
7	-1	1	1	45
8	1	1	1	80

Model equation, main terms:

$$y_i = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_k x_k + \varepsilon_i$$

where

y_i denotes a response

x_i a factor or a variable (T, P or K)

β_i a coefficient

ε_i a residual

β_0 the mean term (average level)

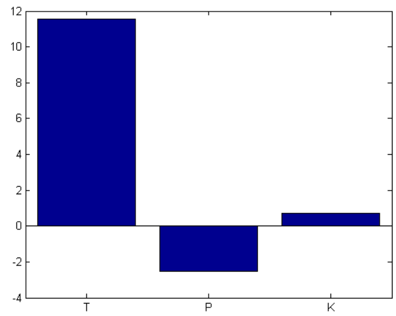
Factorial design

Model equation = coefficients

$$b = \begin{bmatrix} b_0 \\ b_1 \\ b_2 \\ b_3 \end{bmatrix} = \begin{bmatrix} 64.2 \\ 11.5 \\ -2.5 \\ 0.8 \end{bmatrix}$$

- b_0 average value (mean term)
- Large coefficient → important factor
- Interactions usually present

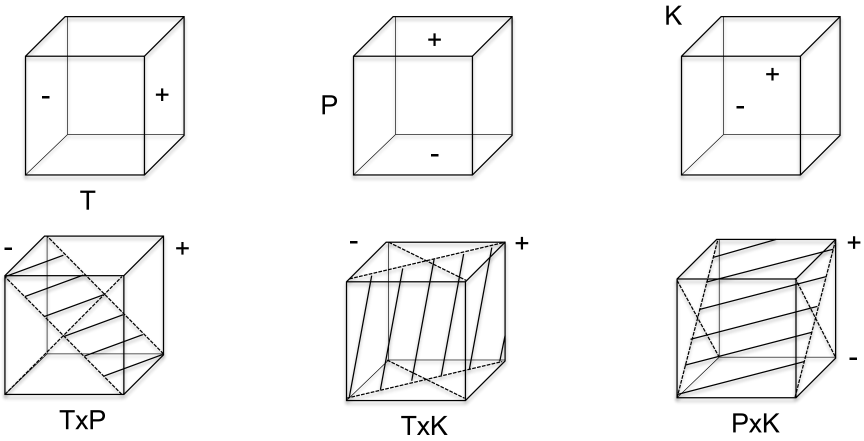
Due to coding, the coefficients are comparable!



Factorial design

N:o	T	P	K	TxP	TxK	PxK	TxKxP	C
1	-1	-1	-1		1		-1	60
2	1	-1	-1		-1		1	72
3	-1	1	-1		1		1	54
4	1	1	-1		-1		-1	68
5	-1	-1	1		-1		1	52
6	1	-1	1		1		-1	83
7	-1	1	1		-1		-1	45
8	1	1	1		1		1	80

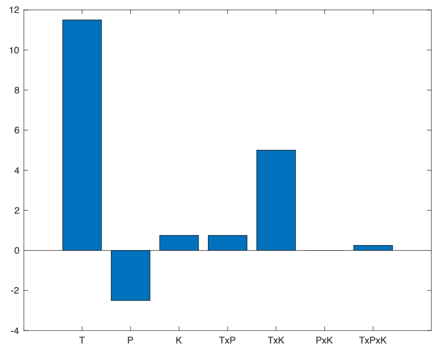
Factorial design



Factorial design

Model equation = coefficients

$$\mathbf{b} = \begin{bmatrix} b_0 \\ b_1 \\ b_2 \\ b_3 \\ b_{12} \\ b_{13} \\ b_{23} \\ b_{123} \end{bmatrix} = \begin{bmatrix} 64.3 \\ 11.5 \\ -2.5 \\ 0.8 \\ 0.8 \\ 5.0 \\ 0 \\ 0.25 \end{bmatrix}$$



- Large interaction b_{13} (TxK)
- Important interaction, main effects cannot be removed

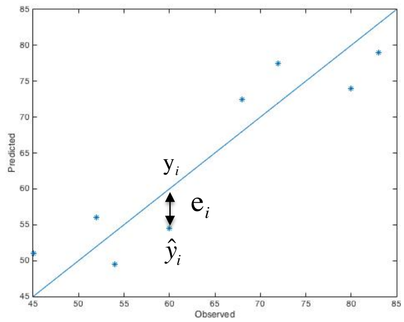
→ Which coefficients to include?

Factorial design

An estimate of standard error needed

- Replicates
- Model residual

$$\mathbf{e} = \mathbf{y} - \mathbf{Xb} = \mathbf{y} - \hat{\mathbf{y}}$$

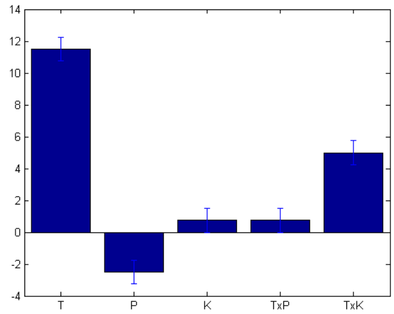


Factorial design

Error estimation allows significant testing

Remove insignificant coefficients

- Leave main effects
- Important interaction, main effect cannot be removed



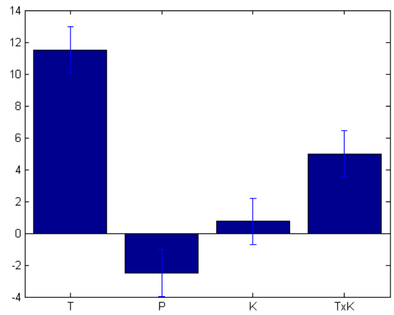
Factorial design

Error estimation allows significant testing

Remove insignificant coefficients

- Leave main effects
- Important interaction, main effect cannot be removed

Recalculate upon removal!



Factorial design

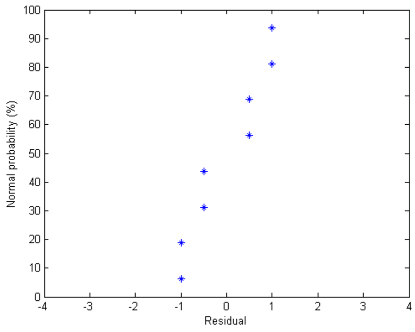
Model residuals

- Finding outliers
- If normally distributed

→ Random error

Several ways to present residuals

- Can a suggest response transformation



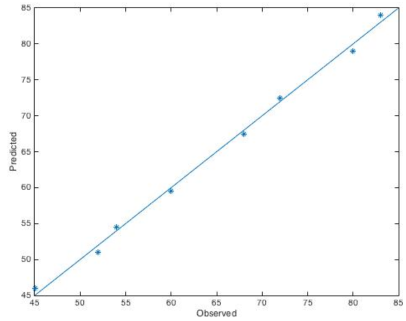
Factorial design

R^2 statistic

- Explained variation in measured response

$R^2 = 0.996$

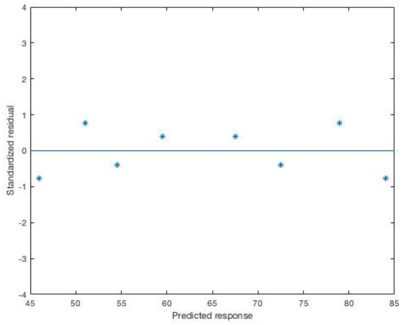
- 99.6% explained



Factorial design

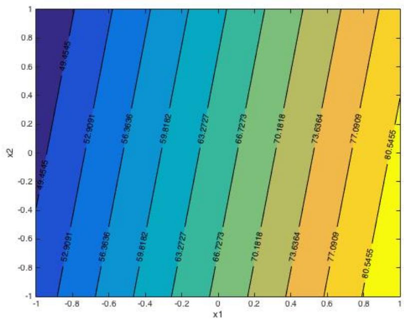
More things to look at

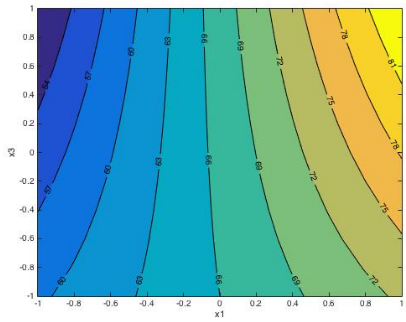
- Normal distribution of coefficients
- Residuals
- ANOVA



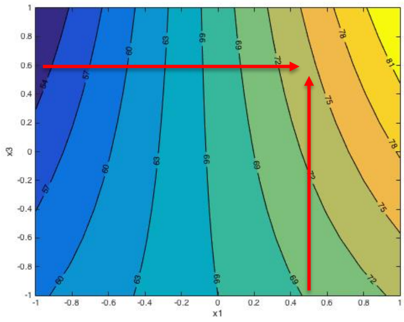
Factorial design

For three factors, 2D contours require one constant factor





Factorial design



Prediction

T = 110

P = 2 (min. level)

K = 0.9

Coded location

$\mathbf{x_m}$ = [1 0.5 -1 0.6 0.3]

Predicted response

y_m = 74.5

Session 1

Introduction

- Why experimental design

Factorial design

- Design matrix
- Model equation = coefficients
- Residual
- Response contour

Nomenclature

Factorial design
Screening
Design matrix
Model equation
Response
Effect (main/interaction)
Coefficient
Significance
Residual
Contour

Thank you!