1.4 Introduction to Design of Experiments (DoE)

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Digitalization Tools for the Chemical and Process Industries

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Outline

- Motivation
- Procedure for applying DoE
  - factorial and central composite designs
  - response surface modelling
- Example

Objectives of this lesson

- Brief introduction to **science-based decision making in experimental activities** (either in a lab, a pilot plant, or a full-scale plant):
  - performing **experiments** efficiently
    - defining the problem
    - identifying the experimental domain
    - planning experiments to create informative data
  - **analyzing data** from the experimentation
  - **interpreting the results** of the analysis
    - building and analyzing a *mathematical model* of the system under study
  - translating the outcomes interpretation into **action**

Why performing experiments?

- Answers to general questions:
  - what are the factors in a process that mostly impact on the product?
  - how can we find optimum of a process?
  - what is the best combination of *factors* (combination of raw materials, inputs, settings, etc…) to ensure a predetermined *response*, i.e., product quality?

- Motivations:
  - **development of new products/processes**
  - **screening important factors** in a chemical, physical or biological phenomenon
  - **improvement** of existing products/processes
  - **optimization**
    - **maximization** of productivity, profit, etc…
    - **minimization** of the effect of external and unknown variability sources, production costs, waste/scraps, reworks, pollution, etc…
  - testing **robustness** of products/processes/analytical instrumentation

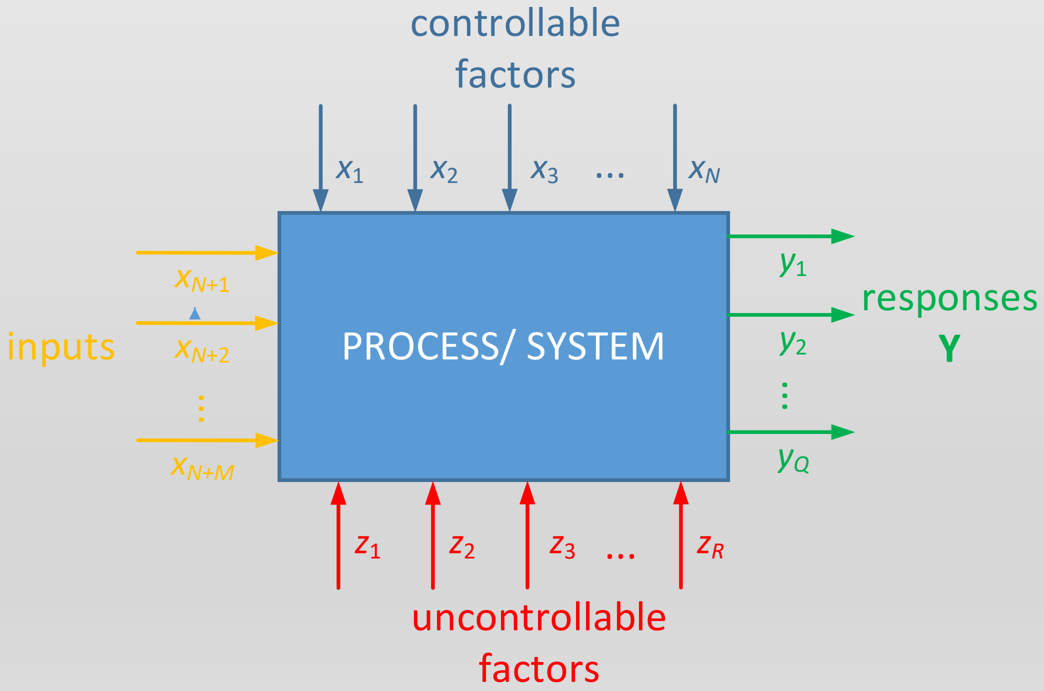
Experiments

- General objective: understanding the cause-and-effect relationships in a system

- **Experiment**: a test or series of runs in which *purposeful changes* are made to the *input variables* of a process/system to identify the reasons for the output *response* changes
- DoE involves making a set of *experiments* which are meaningful with regard to *a given question*

Processes and experimental strategy

- Experiments are used to study the performance of a process/system
  - understanding the combination of operations, machines, people, resources, settings, etc… that transform the inputs into an output characterized through *observable* variables
- Variables:
  - inputs
  - controllable variables
  - uncontrollable variables
  - responses



Experimentation strategy

Factors and responses

- **Responses *y***: variables which are highly informative about **the general conditions of the system**

- **Factors x_1, x_2, ...**: variables which **manipulate the system** under study and exert an influence on the response

Understanding the **relationship** between factors and responses through **mathematical modelling**:

- understanding important mechanisms of the reality
- manipulating the factors to manage the responses

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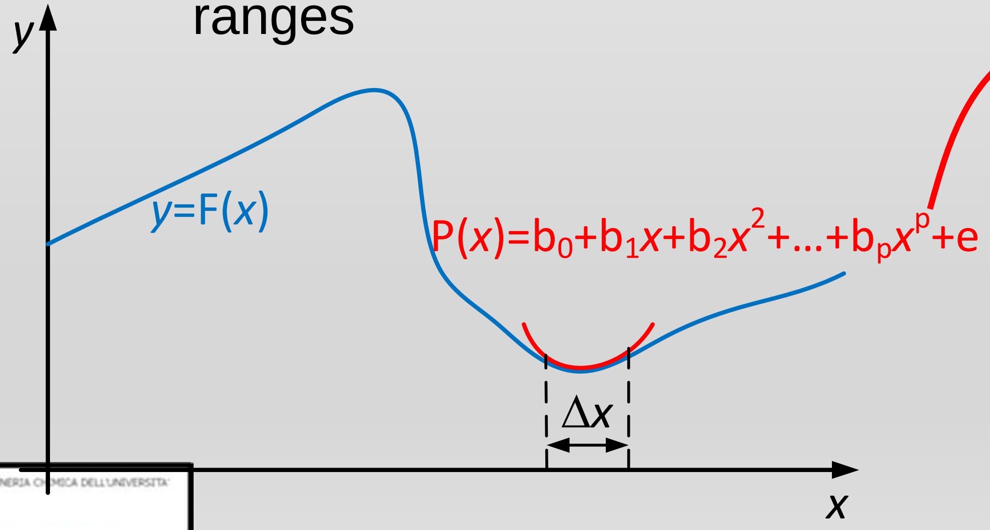
Empirical models for DoE

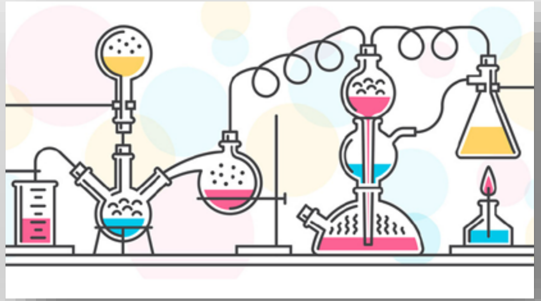
- Empirical modelling:
  - a function *y* can be approximated by a **polynomial** P(*x*) in a limited domain Δx
  - *p* is the **complexity** of the model:
    - bear in mind to find the trade-off between model complexity and investigation ranges



The higher the complexity *p* of the model we want to have, the larger the number of the experiment we must perform

How can you perform experiments?

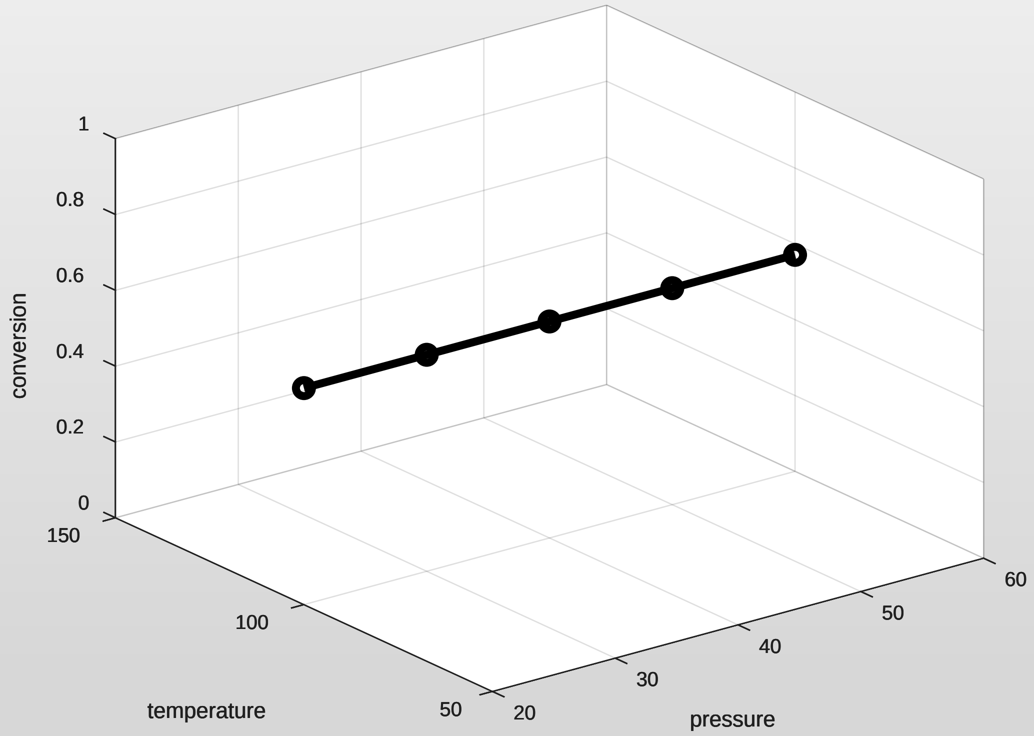
- Consider the case you have to industrialize a product of a reaction



- The experimentation is carried out changing 2 of the most influential factors on the product conversion
  - temperature
  - pressure
- Then the domain in which factors are varied is chosen

Reaction dependence on T and P (1/3)

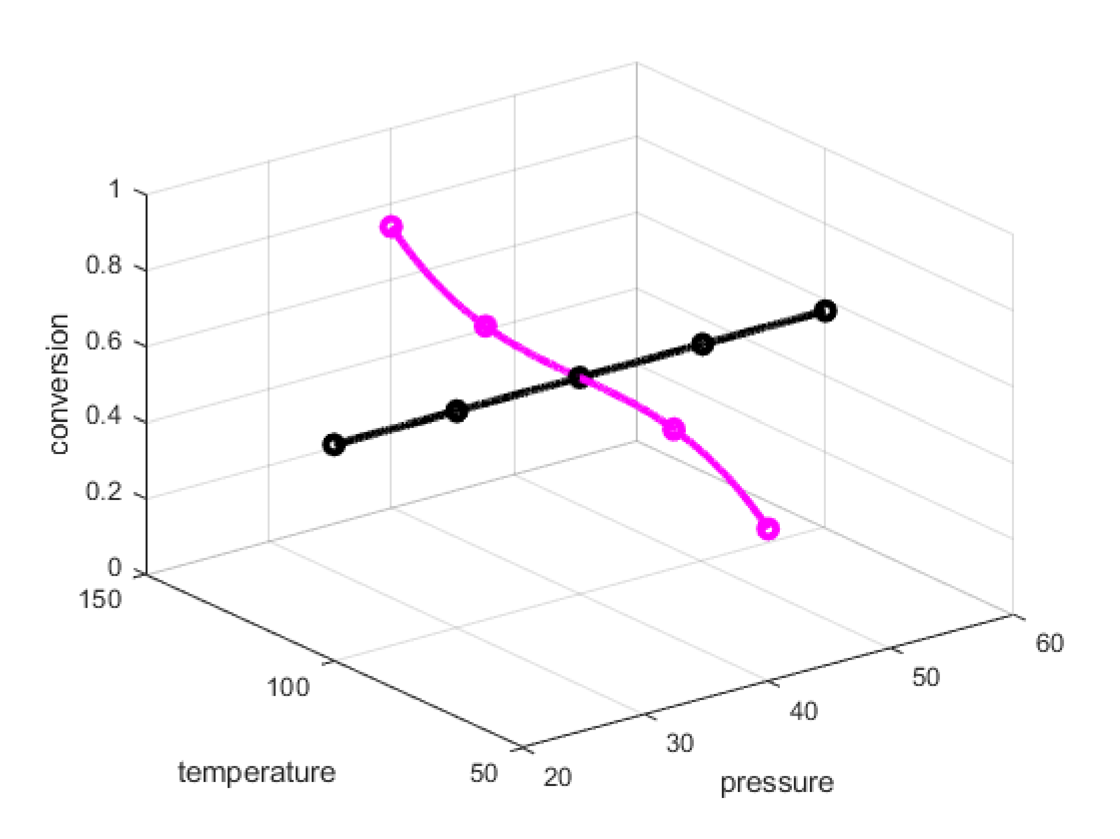
- The reaction is carried out changing:
  - temperature
    - domain: 50°C – 150°C
  - pressure
    - domain: 20 bar – 60 bar
- **OFAT method** (one factor at a time):
  - keep unchanged the temperature at 100°C
  - start with pressure at 20 bar
  - go up with pressure at 30, 40, 50, and 60 bar
- Results:
  - **no sensitivity to the pressure changes!**
  - conversion at 0.57



Reaction dependence from T and P (2/3)

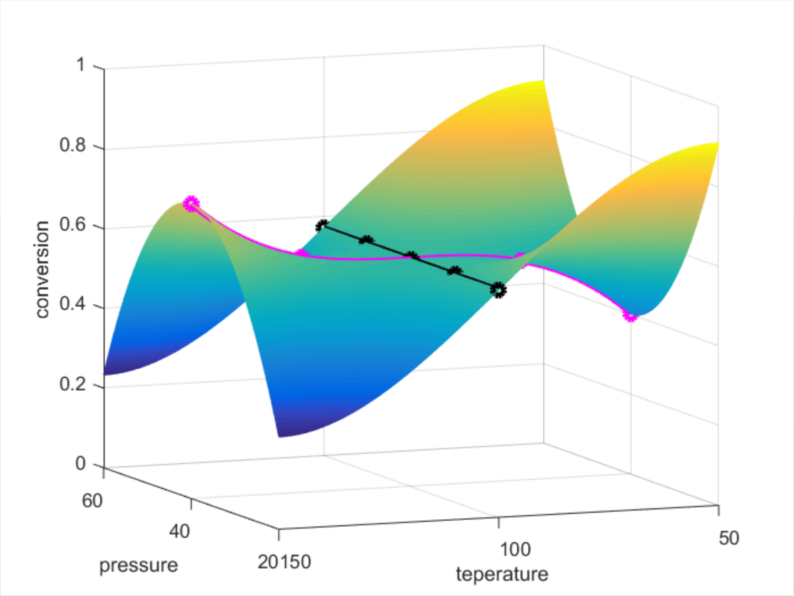
- **Continued OFAT method**:
  - then keep constant the pressure at 40 bar
  - change the temperature
    - 50, 75, 100, 125 and 150°C

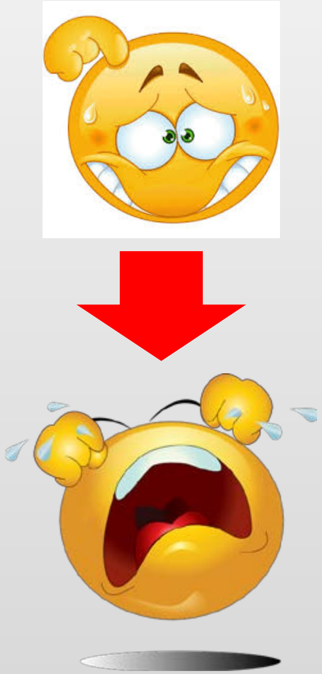
- Conclusions:
  - ***sensitivity to temperature***
  - ***maximum conversion 0.74***



Reaction dependence from T and P (3/3)

- **The sad reality**:
  - the maximum conversion that can be obtained is: 0.95
    - you are losing part of the product!
  - you are failing to consider a lot of information
    - pressure influences the conversion
    - there is a strong interaction among pressure and temperature





Suggestion: change your mind and properly design your experiments!

“Intuitive” approaches: pros and cons

- **Best-guess approach**: based on “expert” experience
  - **pros**:
    - it is easy
  - **cons**:
    - the optimal number of experiments can not be determined a priori
    - what is the strategy to stop the experimentation
- **One-factor-at-a-time** (OFAT) approach
  - **pros**:
    - straightforward interpretation of the results
  - **cons**:
    - inefficient
    - fails to consider interactions among factors
    - lower content of information with higher number of experiments

Science-based approach to experimentation

- **Statistical Design of Experiments**
  - objective approach to plan the experiments
  - appropriate data are *collected* and *analyzed* by statistical methods
  - valid and objective conclusions

- **organized approach**: it is a guided procedure for experimentation
- gives the most **parsimonious** experimental plan
- provides more useful and precise **information** on the factors relation and influence on the responses
- can be easily interpreted in a straightforward graphical manner

Effectiveness of statistical DoE

- Critical issues faced by statistical DoE:
  - provides informationally **optimal** arrangement of the experiments

- higher understanding on the system
  - multiple assessment of the **effect of each factor**
  - estimates correctly the factors' **interactions**
  - evaluates the whole experimental **domain**, also along the edges
- produces reliable and easy-to-interpret maps of the system under study
- considers correctly **the systematic and the non-systematic part of the variability**
  - **distinguishes *effects* from *noise***

DoE tasks

EARLY STAGES

CONSOLIDATION

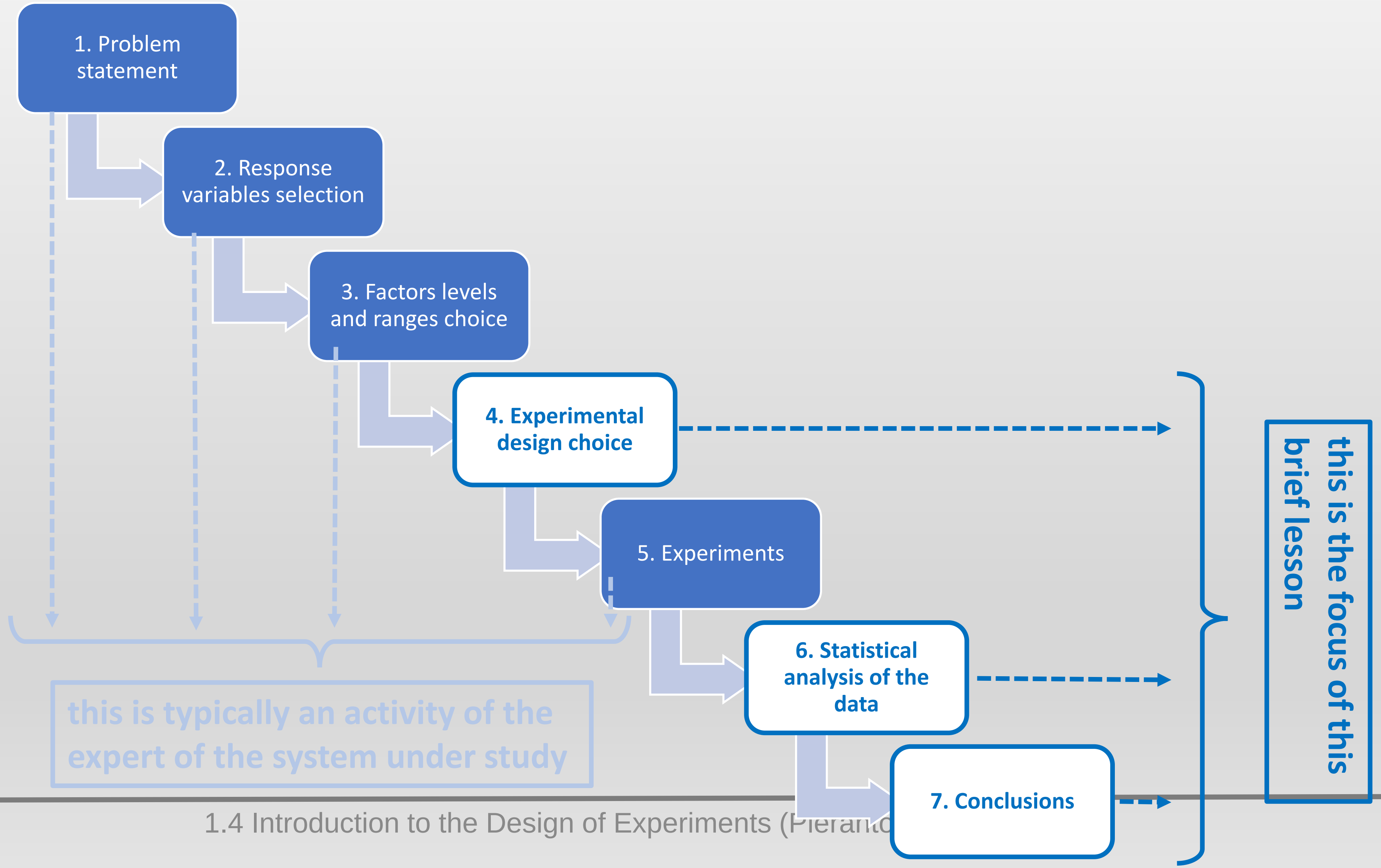
1. **discovery**
   - determine what happens when exploring new systems
2. **screening** (not complicated, extremely important when a process/technology is new, usually requires few experiments)
   - uncover the most influential *factors* affecting the process/product
   - determine in which *ranges* the factors should be investigated
3. **optimization** (complex task, requires much effort)
   - determine a model to predict the response from all the possible combinations of factors
   - define which combination of the factors will result in optimal products/operating conditions
4. **confirmation** (could be extremely useful in scale-up)
   - verify that the system operates/behaves in a consistent way with respect to theories/past experience
5. **robustness testing** (last tests before the product/method release)
   - determine the sensitivity of a product/process to small changes in the factors settings (fluctuation occurring in a «bed day»)
   - ascertain that the process/system is robust to small fluctuations

COMPLEXITY

Basic principles

- **Randomization**
  - both the allocation of the experimental material and the order in which the individual runs of the experiment are to be performed are randomly determined
    - statistical methods require that the observations (or errors) be independently distributed random variables
    - “averaging out” the effects of extraneous factors
- **Replication**
  - making **independent repeated runs of each factor combination**
    - allows determining experimental error
  - replication is not repetition
    - **repeated measurements** reflect the inherent variability of the measurement system or gauge
    - **replications** reflect variability sources both within and between runs
- **Blocking**
  - separate experimental runs based on levels of nuisance factors
    - reduces or eliminates variability from nuisance factors
  - one block is a set of relatively homogeneous experimental conditions

Procedure for designing experiments



1. Recognition and statement of the problem

- Fix the overall and the **specific objectives** of the experimentation
  - team approach to design experiments: solicit inputs from all the involved parties
    - engineering
    - quality assurance
    - manufacturing
    - marketing
    - management
    - customers
    - operating personnel
- **Sequential approach**:
  - series of smaller experimental campaigns with specific objectives

2. Selection of the response variables

- **Response variables** (qualitative or quantitative in nature) provide valuable information about the process under study
  - multiple responses are often necessary
- Determine *how the response variables should be measured*
  - careful calibration and maintenance of the measurement system
- The **measurement error** is an important factor
  - if gauge capability is poor consider repeat several times the measurements

3.1 Choice of factors

- Identify the potential design factors
  - factors that the experimenter/process expert may wish to vary during the experiments
  - classify factors in:
    - **design factors**: selected for the study
    - **nuisance factors**: they must be accounted for because they exert a large effects on the responses
      - classification:
        - controllable: its levels can be set by the experimenter → blocking can deal with it
          - different raw materials, different days of the week
        - uncontrollable: cannot be manipulated, but can be measured → analysis of covariance is used to compensate this effect
          - environmental humidity
        - noise: natural and uncontrollable fluctuation that is not systematic → robustness studies usually minimize the noise effects
    - **held-constant factors**: despite exerting some effects on the response, they are not interesting for the purpose of the experimentation
    - **allowed-to-vary factors**: factors that are applied in an nonhomogeneous fashion (e.g.: differences among operating units, effects of materials, etc…)

effect on the response is considered to be relatively small

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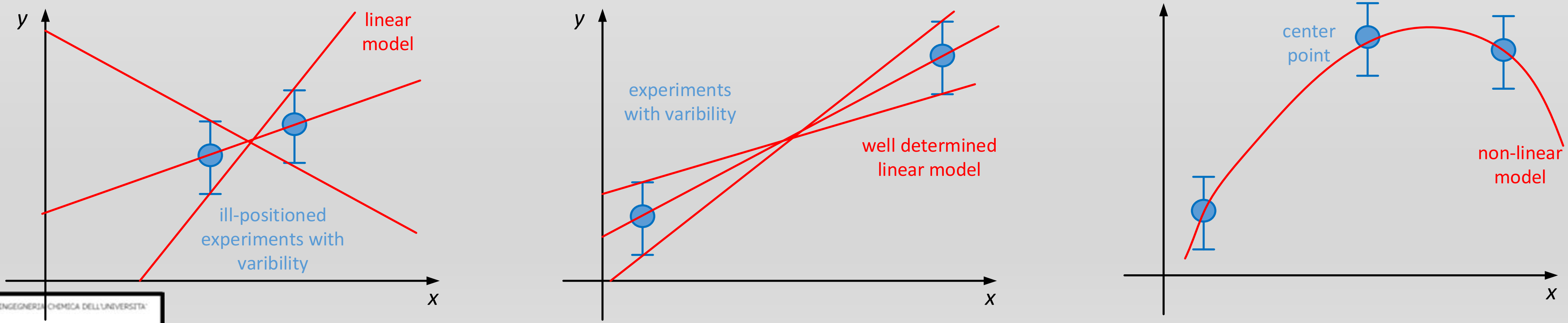
3.2 Choice of levels and ranges

- Choose the **experimental domain** and the region of interest for each variable
  - keep the experimental domain sufficiently large
  - use the process knowledge
    - practical experience, **not being overly influenced by past experience**
    - theoretical understanding
- Choose the **ranges** over which the factors are varied and the **specific levels** at which the experiments are run
  - select the way of *controlling* that the factors are maintained at the desired levels
  - choose the measurement system for the factors
  - the number of factors levels is usually kept **low**

Issues on variability addressed by DoE

- **Where and how** the experiments are performed matters a lot!!!
  - the investigation range of a factor should be considerably larger than the **experimental variability**
  - an extra point located in the **domain center** (center point) is favorable to identify non-linearity



4. Choice of the experimental design (1/3)

- Decide the **resources** that could be allocated for the experimental campaign:
  - **time** required for one experiment compared to the time available to obtain results
  - **cost** of the experiments (e.g.: raw materials, dedicated personnel, etc…)
  - number of experiment **replicates** needed
  - **order** of the experimental trials (managing blocking and randomization)
- Think about and select a tentative **empirical model** for describing the results

4. Choice of the experimental design (2/3)

- **Empirical model**: equation(s) describing the quantitative relation among DoE factors and responses
  - **first-order polynomial** which accounts for the main effects (simple model used in **screening and characterization**):
    - x's are design factors
    - y's are responses
    - β_i are parameters to be estimated
    - **main effects** are evaluated

$$y = \beta_o + \sum_{i=1}^{I} \beta_i x_i + \varepsilon$$

  - first-order model with **interactions** (widely used):
    - cross-product terms identify interactions
    - pertinent for **in-depth screening**

$$y = \beta_o + \sum_{i=1}^{I} \beta_i x_i + \sum_{i=1}^{I} \sum_{j=i+1}^{I} \beta_{ij} x_i x_j + \varepsilon$$

  - **second-order model**:
    - requires more experiments
    - adequate for **optimization**

$$y = \beta_o + \sum_{i=1}^{I} \beta_i x_i + \sum_{i=1}^{I} \sum_{j=i+1}^{I} \beta_{ij} x_i x_j + \sum_{i=1}^{I} \beta_{ii} x_i^2 + \cdots + \varepsilon$$

WARNING: the higher the number of model parameters is, the higher the number of the needed experiments

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4. Choice of the experimental design (3/3)

- **Design generation**:
  - **design and chosen model are intimately linked**
  - may be done by means of a commonly available commercial software
- Creation of an **experimental worksheet**:
  - reports the **selected experimental design**
  - additional information:
    - **randomized order** in which to perform the experiments
    - name the experiment
    - may be used to annotate uncontrollable factors

We will see how to do this in few minutes!

5. Carrying out the experiments

- Conduct, if possible, preliminary **pilot runs**: this can be helpful to:
  - check measurement system
  - verify consistency of the materials
  - evaluate the experimental error
  - reconsider the experimental plans and techniques
- Verify and monitor the process carefully to guarantee that the **experiments are performed exactly according to the plan**:
  - up-front planning is crucial to:
    - prevent mistakes
    - ensure the success of the experimental campaign
- **Perform experiments**!

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6. Statistical analysis of the data

- Analyze data obtained form the experiments by means of **statistical methods**
  - graphical methods help very much to visualize and interpret the outcomes of the study
  - evaluation of the empirical model:
    - analyze in a systematic manner the relation among factors and responses
    - residual analysis and model adequacy help to judge the model
  - the resulting analysis will lead to **objective conclusions** for **decision-making**:
    - measure the *likelihood* of the conclusions and the confidence of the outcomes
    - couple the results with *scientific judgement and process knowledge* lead to sound conclusions

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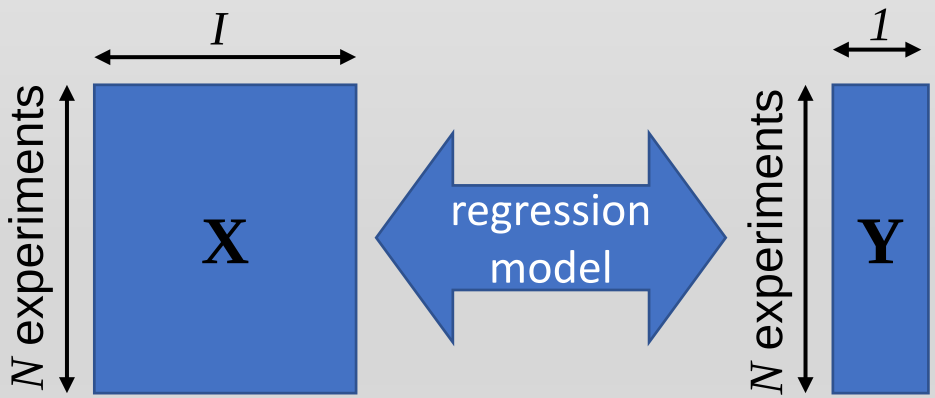
Response surface models through regression

- The most appropriate modelling strategy is to build a **regression model**
  - the **relation between factors and responses** is described
- Data collected from the experimentation are used to **estimate the coefficients** $\boldsymbol{\beta}$ of the regression model
- The **estimated regression parameters** $\hat{\boldsymbol{\beta}}$ are used to **estimate/predict the response variable** $\hat{y}_{\mathrm{NEW}}$ for new combinations of factors $\mathbf{x}_{\mathrm{NEW}}$



$$y = \beta_o + \sum_{i=1}^{I} \beta_i x_i + \sum_{i=1}^{I} \sum_{j=i+1}^{I} \beta_{ij} x_i x_j + \sum_{i=1}^{I} \beta_{ii} x_i^2 + \cdots + \varepsilon$$

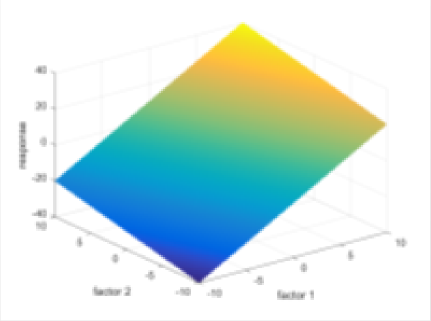
$$\mathbf{y} = \boldsymbol{\beta}\mathbf{X}$$

$$\hat{\boldsymbol{\beta}} = \left(\mathbf{X}^{\mathrm{T}}\mathbf{X}\right)^{-1}\mathbf{X}^{\mathrm{T}}\mathbf{y}$$

Response surface models

- First-order model

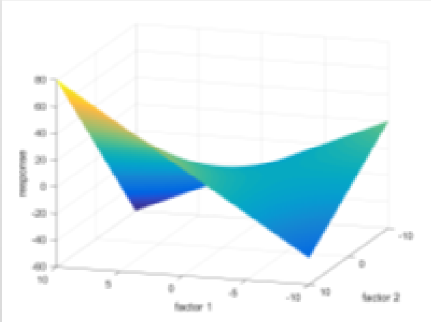
screening:
- what the important factors are
- where the domain of valuable y is



$$y = \beta_o + \sum_{i=1}^{I} \beta_i x_i + \varepsilon$$

- First-order with interactions

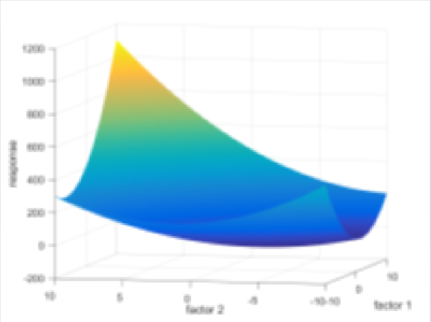
in-depth understanding:
- what are the interactions between factors that influence y



$$y = \beta_o + \sum_{i=1}^{I} \beta_i x_i + \sum_{i=1}^{I} \sum_{j=i+1}^{I} \beta_{ij} x_i x_j + \varepsilon$$

- Second-order model

optimization:
- where are the conditions which maximize/minimize y



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7. Conclusions

- Draw **practical conclusions** from the performed experiments and the statistical analysis of the data
  - a course of action is recommended
  - results should be validated through confirmation testing
- Experimental campaign should be **iterative**:
  - avoid large and comprehensive experiments
  - as experimental plan progresses:
    - some negligible factors are dropped
    - some new variables are considered
    - the experimental domain of the factors are varied, etc…

⬇

  - **sequential experimental campaigns** are preferable

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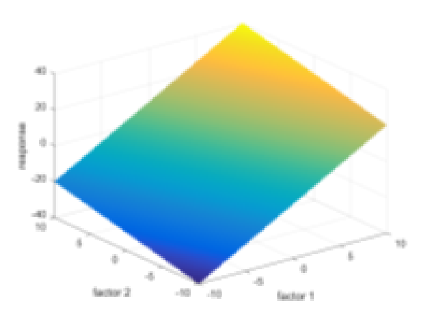
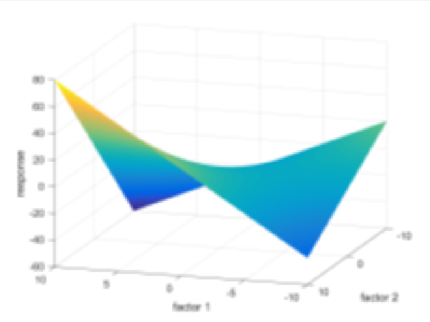
Sequential experimental campaigns

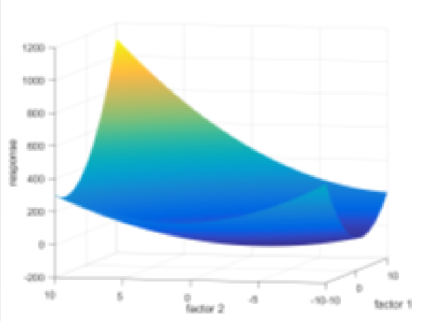
1st EXPERIMENTAL STEP: screening design
- selection of the important factors
- choice of the proper domain



2nd EXPERIMENTAL STEP: in-depth understanding
- understanding what are the interactions between factors impacting y



3rd EXPERIMENTAL STEP: system optimization
- finding the conditions which maximize/minimize y



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Suggested experimental plans

- Planning a properly designed experimental campaign requires:
  - **fractional factorial design** for the screening experimental campaigns
    - sufficiently parsimonious
    - identifies the **main effects** of the factors on the response
  - **full factorial design** to obtain enough information to identify
    - **main effects**
    - **factors interactions**
  - **central composite design** to carry out a wide experimentation and find the optimal conditions on the system under study
    - **main effect**
    - **factor interaction**
    - **quadratic effects**

Factorial designs

Full factorial designs

- **Factorial designs** are widely used in experiments involving several factors where it is necessary to study the **joint effect of the factors on a response**
- **Full factorial designs** perform experiments on **all the possible combinations of the levels of all the factors**
- When *L* levels are considered for *K* variables, the total number of experiments *M* to be carried out is:

$$\boxed{N = L^K}$$

- The most important of these special case is that of ***K* factors** moved on ***L* = 2 levels**, where factors may be:
  - **quantitative**
    - temperature, pressure, time, etc…
  - **qualitative**
    - machines, operators, the “high” and “low” levels of a factor, presence/absence of a variable

$$y = \beta_o + \sum_{i=1}^{I} \beta_i x_i + \sum_{i=1}^{I} \sum_{j=i+1}^{I} \beta_{ij} x_i x_j + \varepsilon$$

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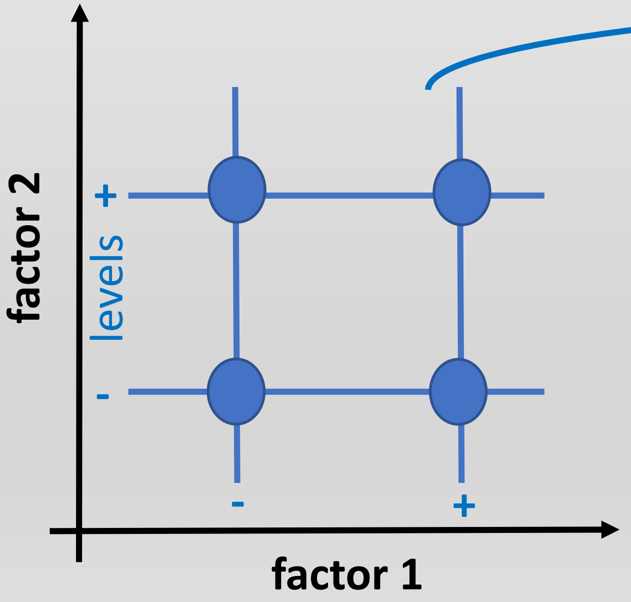
Experimental plan and design notations

- Alternative experimental design notations can be adopted:
  - **geometric coding**
  - **orthogonal coding** +/- or +1/-1
  - effects coding

2^2 experimental design



2^3 experimental design

run	factor 1	factor 2	factor 3
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
9	0	0	0

What if we do not have enough resources to complete a full factorial?

Fractional factorial designs

- As the number of factors *K* increases in a 2^K factorial design, the number of runs required for a complete full factorial experimentation rapidly outgrows the resources
    - a complete run of a 2^6 design requires 64 runs
- **Fractional factorial designs**: information on the main effects and low-order interactions may be obtained by running a ***fraction of the complete factorial*** (1/2, 1/4, …) experiment
    - based on the reasonable assumption that *certain high-order interactions are negligible*
    - **warning**: aliasing is present and some effects can be confounded

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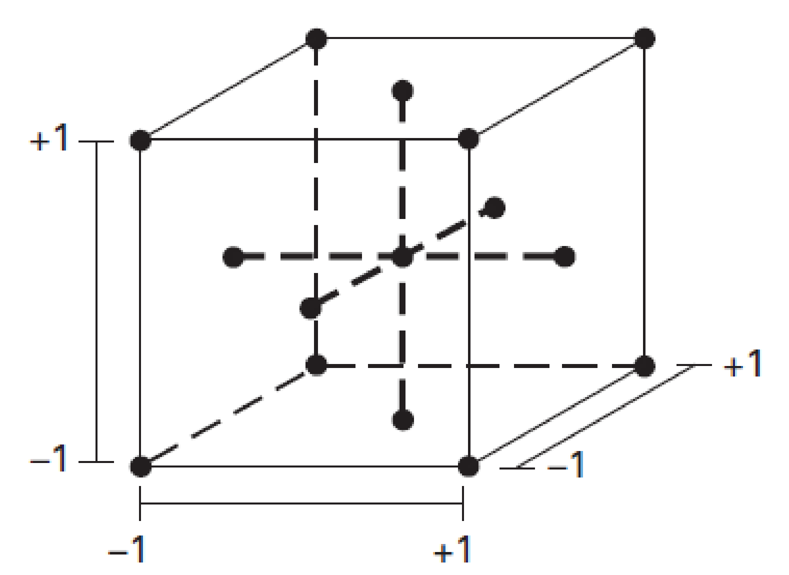
What if we need to optimize a system?

Central composite designs

- **Central composite designs**
  - cubic design with the center of the cube and of the faces (a total of 2^K+2K+n_C experiments)
    - circumscribed in a spherical domain
    - faced in a cubic domain
  - the best method to estimate the nonlinear effects



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Conclusions

- **DoE** gives you an added value!
  - science-based objective procedure
  - you know a priori the experimental burden base on your objective
  - maximum information from experiments is guaranteed with the most parsimonious campaign
- **Factorial designs** and **central composite designs** are valuable tool to plan experiments
- **Response surface models** are used to understand through “simple” regression models the relation among factors and responses

References

- **Montgomery, D. C. (2001), *Design and Analysis of Experiments*, John Wiley & Sons, Inc., New York.**
- **Eriksson, Johansson, Kettaneh-Wold, Wikström, Wold, S. (2008). *Design of Experiments - Principles and Applications,* Umetrics Inc.**
- Box, G. E. P., Hunter, W. G., and Hunter, S. J. (1978), *Statistics for Experimenters*, John Wiley & Sons, Inc., New York.
- Fisher, R. A. (1966), The Design of Experiments, Hafner Publishing Company, New York.
- Myers, R. H., and Montgomery, D. C., (1995), *Response Surface Methodology: Process and Product Optimization Using Designed Experiments,* John Wiley & Sons, New York.
- *and many others…*

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Example:
cake recipe and taste

Industrial production of cakes

- The case study is related to a food industry which produces cakes
- <u>Objective</u>: to map a process producing a cake mix to be sold in a box at a supermarket or shopping malls
- Factors:
  - flour
  - shortening
  - egg powder
- Response:
  - taste (from a panel)

0 = awful

6 = excellent

flour [g]	shortening [g]	egg powder [g]	taste
200	50	50	3.52
400	50	50	3.66
200	100	50	4.74
400	100	50	5.2
200	50	100	5.38
400	50	100	5.9
200	100	100	4.36
400	100	100	4.86
300	75	75	4.73
300	75	75	4.61
300	75	75	4.68

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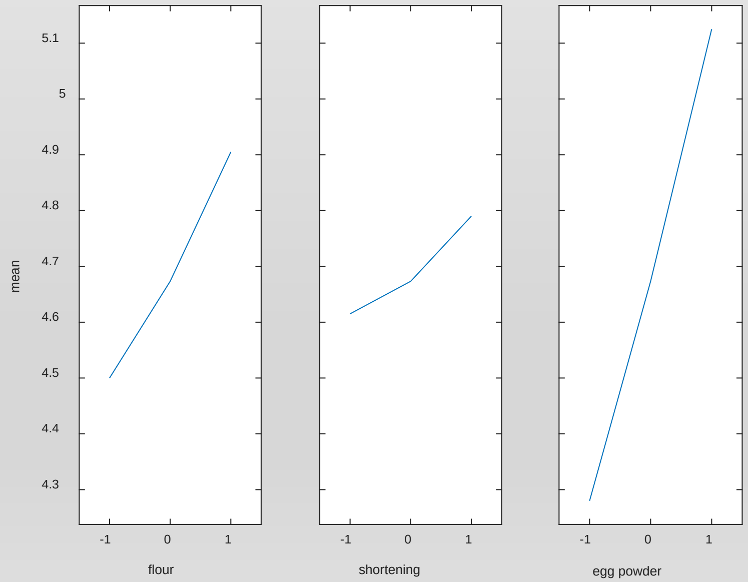
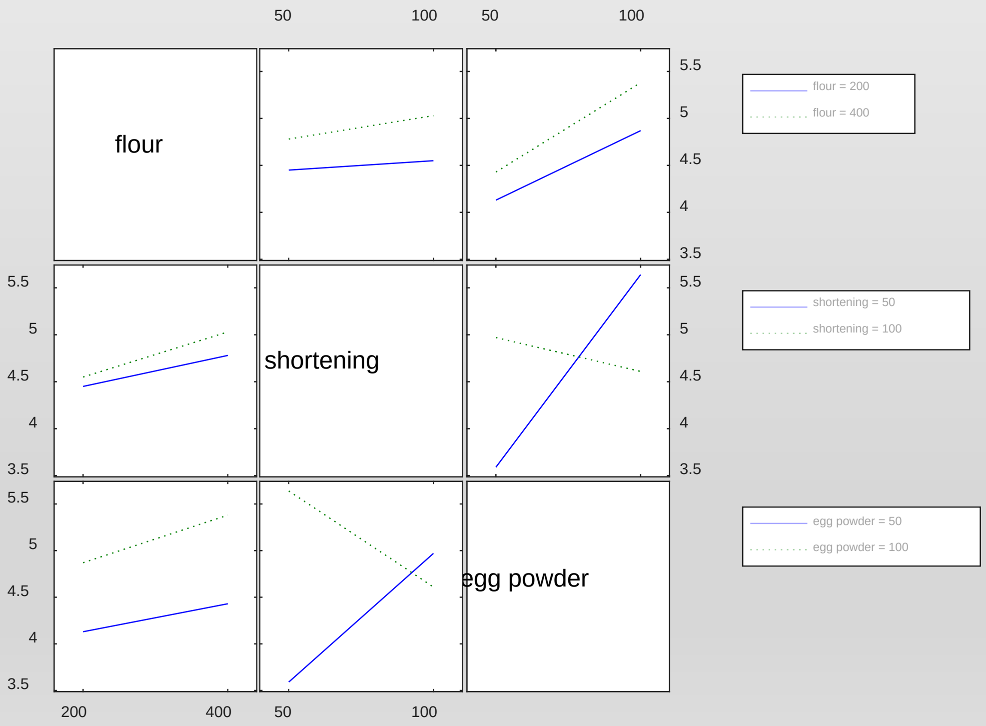
Main effects

- The **main effect plot** confirms that:
  - increasing the dosage of all the ingredients increases the cake taste
  - the main effect is the one of egg powder
  - the effect of shortening is low



Interactions

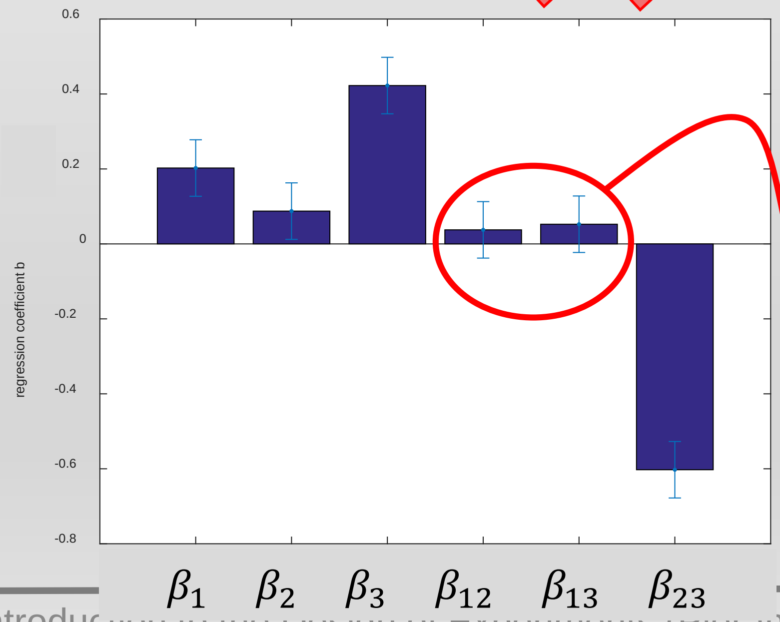
- The **interaction plot** highlights that:
  - there is a strong interaction among shortening and egg powder



Response surface modelling

- The bar plot of the regression coefficients confirms the abovementioned results
  - this result suggests to refine the model excluding the interactions between the flour and the other two factors

$$y = \beta_o + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \cancel{\beta_{12} x_1 x_2} + \cancel{\beta_{13} x_1 x_3} + \beta_{23} x_2 x_3$$



these interactions are affected by high uncertainty and can be removed from the model

Updated response surface model

- Main actions to improve the cake taste:
  - increase the flour content
  - increase the egg powder content
  - decrease the shortening content