Definition 1. **Design of Experiments (DOE)**, is the design of any task that aims to describe and explain the variation of information under conditions (hypothesized to reflect the variation).

In its simplest form, an experiment aims at predicting the outcome by introducing a change of the preconditions, which is represented by one or more **independent variables** (or **input variables**, **predictor variables**). The change in one or more independent variables is generally hypothesized to result in a change in one or more **dependent variables**, (or **output variables**, **response variables**). The experimental design may also identify **control variables** that must be held constant to prevent external factors from affecting the results.

Main concerns in experimental design include **validity**, **reliability**, and **replicability**.

DOE Overview

1. ensure the level of scientific knowledge needed to drive the type of experiment;
2. conduct structured experiments, which can range in complexity depending on the goals and current knowledge of the system;
3. use statistical modeling to help analysis, draw conclusions and make predictions;
4. repeat the DOE process as necessary.

Definition 2. **Factors** are any condition that can be varied in an experiment, essentially the independent variables. **Levels** are the specific values or settings that a factor can take. If a factor is varied, it must be varied at two or more levels to understand its effect on the response variable.

A **full factorial experiment**, (or **full factorial design**, **fully crossed design**) is an experiment whose design consists of two or more factors, each with discrete possible values or "levels", and whose experimental units take on all possible combinations of these levels across all such factors. Such an experiment allows the investigator to study the effect of each factor on the response variable, as well as the effects of interactions between factors on the response variable. For a k-factor, L-level full factorial design, the total required # experiments (runs) $N = L^k$.

Example 1. full factorial design.

Experiment	Factor A	Factor B	Factor C
1	Low	Low	Low
2	Low	Low	High
3	Low	High	Low
4	Low	High	High
5	High	Low	Low
6	High	Low	High
7	High	High	Low
8	High	High	High

Table 1: 3-factor, 2-level design

A **fractional factorial design** consists of a carefully chosen subset (fraction) of the experimental runs of a full factorial design. This approach allows for the estimation of the most important effects and interactions while ignoring those runs that are redundant, providing little or no new information about the system. For a k-factor, L-level, $1/L^p$ fractional factorial design, the total required # experiments (runs) $N = L^{(k-p)}$.

Definition 3. Full factorial designs belong to a class of experimental designs, called **classical designs**.

Classical designs are optimal in a sense that allow for complete exploration of all possible combinations of factors at different levels. This comprehensive approach ensures that interactions between factors are fully captured, providing sufficient information about the system being studied.

However, in most cases, classical designs are restrictive in terms of the number of runs required, which can make them impractical for experiments involving a large number of factors or when resources are limited.

Optimal designs are a class of experimental designs that are optimal depending on the statistical model and w.r.t. some statistical criterion. It aims to maximize the information gained from an experiment while minimizing costs of experimentation.

Optimal designs are optimal in a way that allow for a more efficient and targeted approach to experimentation, especially in situations where classical designs are not feasible. In particular, they may make parameters to be estimated without bias and with minimum variance under fewer experimental runs, than non-optimal designs with the same precision.

Definition 4. **D-optimal designs** represent a specific category of optimal designs that focus on the "determinant" optimality criterion. The goal of a D-optimal design is that, for given numbers of experimental runs n and factors k, we would like to choose the D-optimal design (factor settings) $\mathbf{X}$ s.t. it solves the following optimization problem:

$$\max_X |\mathbf{X}'\mathbf{X}| \quad \text{s.t. } x \in \mathcal{X},$$

where $\mathcal{X}$ is the set of all possible design matrices that could be constructed under the experimental conditions.

OLS Overview

OLS equation: $\mathbf{Y} = \mathbf{X}\beta + \varepsilon$,
parameters estimator: $\hat{\beta} = (\mathbf{X}'\mathbf{X})^{-1}\mathbf{X}'\mathbf{Y}$,
estimator variance: $\text{Var}(\hat{\beta}) = \sigma_\varepsilon^2(\mathbf{X}'\mathbf{X})^{-1}$.

$\mathbf{Y}$ - vector of observed responses,
$\mathbf{X}$ - design matrix of experimental settings,
β - vector of unknown parameters,
ε - vector of random errors,
$\hat{\beta}$ - vector of estimated parameters,
σ_ε^2 - variance of the error.

$|\mathbf{X}'\mathbf{X}|$, called **D-optimality criterion**, is the determinant of the information matrix $\mathbf{X}'\mathbf{X}$. It also indicates the magnitude of $\mathbf{X}'\mathbf{X}$. Maximizing $|\mathbf{X}'\mathbf{X}|$ would minimize $\text{Var}(\hat{\beta})$, indicating higher precision in the estimates of β.

$$\text{D-efficiency} = \left(\frac{|\mathbf{X}'\mathbf{X}|}{n^p}\right)^{1/p}$$

$$F_0 = \left(\left(\mathbf{L}\hat{\boldsymbol{\beta}}\right)' \left[\mathbf{L}\left(\mathbf{X}'\mathbf{X}\right)^{-1}\mathbf{L}'\right]^{-1} \left(\mathbf{L}\hat{\boldsymbol{\beta}}\right)\right) / (rMSE)$$

Under the null hypothesis, the test statistic F_0, has an F distribution on r and $n-p-1$ degrees of freedom.

If the true value of β is $\boldsymbol{\beta}^A$, then F_0 has a non-central F distribution with non-centrality parameter given by:

$$\lambda = \left(\left(\mathbf{L}\boldsymbol{\beta}^A \right)' \left[\mathbf{L} \left(\mathbf{X}'\mathbf{X} \right)^{-1} \mathbf{L}' \right]^{-1} \left(\mathbf{L}\boldsymbol{\beta}^A \right) \right) / \sigma^2$$

To compute the power of the test, first solve for the α-level critical value F_c:

$$\alpha = 1 - F\text{Dist}\left(F_c, r, n-p-1 \right).$$

Then calculate the power as follows:

$$\text{Power} = 1 - F\text{Dist}\left(F_c, r, n-p-1, \lambda \right)$$

Definition 5. **Blocking** is the arranging of experimental units that are similar to one another into groups (blocks) explicitly. The **blocking factor** is the condition that defines the grouping of the runs.

The goal of blocking is to control(minimize) variability introduced by specific factors that are not of primary interest but could influence the observed outcomes of experiment. This reduces reduces known but irrelevant sources of variation between units and thus allows greater precision in the estimation of the source of variation under study.

Blocks can be "fixed" or "random." **Fixed blocks** are used when the levels of the blocking factor are specifically chosen and are of interest to the experimenter. **Random blocks** are used when the levels are selected at random from a larger population, and the specific levels are not of interest

An important characteristic of a blocking factor is that such factors are not under direct control of the investigator. It is ideal to make the blocking factor orthogonal to the other factors. Real world constraints on model form, block sizes and the total number of runs can make this impossible. In such cases, optimal blocking is a useful alternative.

For making inferences about **future blocks**, it can be useful to model the characteristics that make one block different from another as random variation.
Characterizing the impact of the blocking factor as random variation requires the use of a mixed model (having both fixed and random components). Mixed models are better fit using GLS (generalized least squares) rather than OLS (ordinary least squares).

GLS Overview

$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}_{\text{ET}}\gamma_{\text{ET}} + \varepsilon,$

$\mathbf{Y}$ - vector of observed responses,
$\mathbf{X}$ - design matrix of experimental settings,
β - vector of unknown parameters/effects,
$\mathbf{Z}_{\text{ET}}$ - design matrix for the block effects,
γ_{ET} - vector of block effects,
ε - vector of random errors.

The matrix Z_{ET} is specifically structured to represent the blocks in the experiment, with rows corresponding to the different treatments and columns to the blocks. The "-1" entries denote the reference block against which other blocks are compared.

The variance of the estimator $\hat{\beta}$ is also given, showing how it depends on the variance of the blocks and the error variance. The variance equations show that if you have orthogonal blocking (meaning the blocks are independent of the treatments), the variance of the estimator of the treatment effects is reduced to the error variance only, which is the ideal scenario because it means that the blocks are not introducing additional variability into the estimation of treatment effects.

$$\text{Var}(\hat{\boldsymbol{\beta}}) = \sigma_\varepsilon^2 \left\{ \mathbf{X}'\mathbf{X} - \mathbf{X}'\mathbf{Z}_{\text{ET}} \left(\mathbf{Z}'_{\text{ET}}\mathbf{Z}_{\text{ET}}\right)^{-1} \mathbf{Z}'_{\text{ET}}\mathbf{X} \right\}^{-1} = \sigma_\varepsilon^2 \left\{ \left(\mathbf{X}'\mathbf{X}\right)^{-1} + \boldsymbol{\Delta} \right\},$$

Hence for orthogonal blocking

$$\text{Var}(\hat{\boldsymbol{\beta}}) = \sigma_\varepsilon^2 \left(\mathbf{X}'\mathbf{X}\right)^{-1}$$