Design of Experiments

by
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Experimentation is an old discipline, but modern design of experiments theory dates back to the pioneering work of Ronald Aylmer Fisher (1890-1962) at the Rothamsted Experimental Station, where he became a statistician in 1919. Rothamsted Experimental Station was an agricultural research institute. Fisher soon experienced the problems by trying to analyse haphazardly collected data and realized the advantage it would be to collect these in a planned and controlled manner. In 1935 he published his famous book *Design of Experiments*. Surprisingly fast his ideas found its way into industry, but there they seemed to have an obstacle for success. Agricultural experiments tend to be large in scale, having several variables with many levels for each variable that needed to be replicated. And they may take a long time to complete. Experiments in industry can be expensive, thereby cost considerations need to be taken into account. On the other side, in contrast to agriculture where one sows in the spring and harvests in the autumn, experiments in industry often give immediate response and new experiments can be planned and performed the next week. In the late 1940s George Box (1919-2013) discovered that sequential experimentation, where in each step smaller experiments with few levels for each factors were performed, much faster could bring a production process closer to optimal operational conditions. The analysis of such designs also relies more heavily on regression modelling. So, despite the evolution we will start with introducing the ideas for industrial experimentation first and then move on to more classic Design of Experiments theory.

Two-level factorial designs

In the regression model $\boldsymbol{Y} = \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}$ the design matrix $\mathbf{X}$ has a decisive impact on how easy it is to find a good model. Especially we have seen (chapter 12.7) that if the columns in the design matrix, $\mathbf{1}, \boldsymbol{x}_1, \boldsymbol{x}_2, \ldots \boldsymbol{x}_k$, are orthogonal, the vector of the estimators for the coefficients is given by:

$$\hat{\boldsymbol{\beta}} = \left(\boldsymbol{X}^t\boldsymbol{X}\right)^{-1}\boldsymbol{X}^t\boldsymbol{Y} = \begin{bmatrix} 1/n & 0 & 0 & 0 \\ 0 & \left(\boldsymbol{x}_1^t\boldsymbol{x}_1\right)^{-1} & 0 & 0 \\ 0 & 0 & \ddots & 0 \\ 0 & 0 & 0 & \left(\boldsymbol{x}_k^t\boldsymbol{x}_k\right)^{-1} \end{bmatrix} \begin{bmatrix} \sum_{i=1}^{n} Y_i \\ \boldsymbol{x}_1^t\boldsymbol{Y} \\ \vdots \\ \boldsymbol{x}_k^t\boldsymbol{Y} \end{bmatrix} = \begin{bmatrix} \sum_{i=1}^{n} \frac{Y_i}{n} \\ \left(\boldsymbol{x}_1^t\boldsymbol{x}_1\right)^{-1}\left(\boldsymbol{x}_1^t\boldsymbol{Y}\right) \\ \vdots \\ \left(\boldsymbol{x}_k^t\boldsymbol{x}_k\right)^{-1}\left(\boldsymbol{x}_k^t\boldsymbol{Y}\right) \end{bmatrix} \qquad (1)$$

Orthogonal columns give minimum variance in the estimators for the coefficients.

When an experiment is conducted we can choose values for the explanatory variables $x_1, x_2, \ldots, x_k$. One should choose these such that it is as favourable for the estimation as possible.

Example 1

We want to investigate how the yield of chemical process depends on the two factors temperature and concentration. It was conducted four experiments where two values for each of the factors were used. This gives four possible level combinations of the two factors to test out the yield of the process. The experiment is given below where also the registered yield of the process is given.

Experiment number	Temperature	Concentration	Yield
1	160	20	60
2	180	20	72
3	160	40	54
4	180	40	68

A model of the form $E(Y) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_{12} x_1 x_2$ can then be estimated from the data where the four values for the yield are the observed response values and the design matrix $\boldsymbol{X}$ consists of a column of four ones, a column with the values for the temperature, one column with the concentration values and one with the values of the product of the temperature and the concentration values.

$$\boldsymbol{X} = \begin{bmatrix} 1 & 160 & 20 & 3200 \\ 1 & 180 & 20 & 3600 \\ 1 & 160 & 40 & 6400 \\ 1 & 180 & 40 & 7200 \end{bmatrix}$$

A Regression Analysis in R of yield versus temperature (x1); concentration (x2) and temperature $\times$ concentration gave.

```
Call:
lm.default(formula = y ~ x1 + x2 + x1x2)

Residuals:
ALL 4 residuals are 0: no residual degrees of freedom!

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  -14.000         NA      NA       NA
x1             0.500         NA      NA       NA
x2            -1.100         NA      NA       NA
x1x2           0.005         NA      NA       NA
```

First we will only be concerned with the estimated coefficients

$$\begin{bmatrix} b_0 = -14 \\ b_1 = 0.5 \\ b_2 = -1.1 \\ b_{12} = 0.005 \end{bmatrix}$$

Let us now recode the factors by introducing new factors $z_1 = \frac{x_1 - 170}{10}$ and $z_2 = \frac{x_2 - 30}{10}$. The values of the new factors are thus centred and we have divided down by half the distance between the high and the low levels of the factors.

The new design matrix becomes:

$$\begin{bmatrix} 1 & -1 & -1 & 1 \\ 1 & 1 & -1 & -1 \\ 1 & -1 & 1 & -1 \\ 1 & 1 & 1 & 1 \end{bmatrix}$$

Notice that the new design matrix has only orthogonal columns and if we now compute the estimated coefficients we get from (1) that

$$b_0^* = \frac{60 + 72 + 54 + 68}{4} = 63.5$$
$$b_1^* = \frac{-60 + 72 - 54 + 68}{4} = 6.5$$
$$b_2^* = \frac{-60 - 72 + 54 + 68}{4} = -2.5$$
$$b_{12}^* = \frac{60 - 72 - 54 + 68}{4} = 0.5$$

Controlling the calculations by R gives for the recoded values of temperature and concentration:

```
Call:
lm.default(formula = y ~ z1 + z2 + z1z2)

Residuals:
ALL 4 residuals are 0: no residual degrees of freedom!

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)     63.5         NA      NA       NA
z1               6.5         NA      NA       NA
z2              -2.5         NA      NA       NA
z1z2             0.5         NA      NA       NA
```

To check if we have the same model we may substitute for z_1, z_2 and z_{12} which gives:

$$\hat{y} = 63.5 + 6.5\frac{(x_1 - 170)}{10} - 2.5\frac{(x_2 - 30)}{10} + 0.5\frac{(x_1 - 170)(x_2 - 30)}{10 \cdot 10}$$
$$= 63.5 - 110.5 + 7.5 + 25.5 + 0.65x_1 - 0.15x_1 - 0.25x_2 - 0.85x_2 + 0.005x_1x_2$$
$$= -14 + 0.5x_1 - 1.1x_2 + 0.005x_1x_2$$

When we are analyzing a two-level factorial design, it is normally simplest and most practical to recode the factor levels to 1 and –1 as above. Then we obtain orthogonal factor columns and it is simple to compute the coefficients.
One other argument is that we often have qualitative variables as for instance we are going to test out two different brands or we want to test out what happens with or without any treatment. In the last case it is of interest to be able to measure the effect of the treatment on the response. Let the factor value 1 correspond to treatment and the factor value -1 correspond to no treatment. It is then of interest to calculate the average value of the response when the factor value is 1 and when the factor value is -1.

Definition of main effect:

For two-level designs we define the main effect of a factor as: Expected average response when the factor is on the high level – expected average response when the factor is at the low level.

it is natural to estimate this effect by $\bar{y}_H - \bar{y}_L$ and for temperature this becomes:

$$\frac{72+68}{2} - \frac{60+54}{2} = 13 = 2b_1^*$$

and for concentration

$$\frac{54+68}{2} - \frac{72+60}{2} = -5 = 2b_2^*$$

Estimated main effect of a factor will always be the corresponding main regression coefficient multiplied by 2, since a main effect measure change in the expected response when we move from the low-level, -1, to the high level, +1, of the factor or when the recoded factor changes two units. The regression coefficients, however, measure the change in the expected response when the factor changes from 0 to 1.

In our example the coefficient in front of the x_1x_2 term, b_{12}, is small. This coefficient tells us if there is any interaction between the two factors or not.

Definition

The interaction between two factors is defined as: Half the main effect of a factor when the other is on the high level – half the main effect of a factor when the other factor is at its low level.

To estimate the interaction between temperature and concentration we therefore need to compute:

Estimated main-effect of temperature when concentration is on its high level is given by:

$$68 - 54 = 14$$

Estimated main-effect of temperature when concentration is on its low level is given by:

$$72 - 60 = 12$$

The estimated interaction then becomes: $\frac{14}{2} - \frac{12}{2} = 1 = 2b_{12}^{*}$.

Signs for computing the contrasts.

For two level experiments we have: All quantitative levels can be recoded to –1 and 1. All qualitative level can naturally be set to these values. If we agree upon that the high level of a factor corresponds to 1 and the low level corresponds to –1, we notice from above that estimation of effects can be done by adding together the response values with signs decided by the signs in the design matrix and thereafter divide by half the number of observations. We therefore construct a sign matrix where the necessary signs for computing the effects are given. In our case this matrix becomes:

Temp	Concentration	Temp*Conc
-	-	+
+	-	-
-	+	-
+	+	+

Other notation for level combinations.

High level is marked with the letter for the factor. Low level is marked with 1. 1 is left out if other letters are used.

Example:

A	B	Level code
-	-	1
+	-	a
-	+	b
+	+	ab

2^3 experiments.

A 2^k experiment has k factors, each at two levels. In example 1 our concern was a 2^2 experiment and how we can estimate the effects in such an experiment. Actually there was a third qualitative factor in this experiment, catalyst. With three factors each at two levels it is possible to construct 8 possible level combinations of high and low or + and – as we normally recode the levels to. Let A be temperature, B concentration and C catalyst. Then we get the following sign matrix extended with level codes and response values.

A	B	C	AB	AC	BC	ABC	levelcode	y
-	-	-	+	+	+	-	1	60
+	-	-	-	-	+	+	a	72
-	+	-	-	+	-	+	b	54
+	+	-	+	-	-	-	ab	68
-	-	+	+	-	-	+	c	52
+	-	+	-	+	-	-	ac	83
-	+	+	-	-	+	-	bc	45
+	+	+	+	+	+	+	abc	80

Estimated main effects becomes:

$$\hat{\mathrm{A}} = \frac{72+68+83+80}{4} - \frac{60+54+52+45}{4} = 23$$
$$\hat{\mathrm{B}} = \frac{54+68+45+80}{4} - \frac{60+72+52+83}{4} = -5$$
$$\hat{\mathrm{C}} = \frac{52+83+45+80}{4} - \frac{60+72+54+68}{4} = 1.5$$

For computing the interaction between A and B, AB, we need to find the main effect of A when B is at its high level and subtract the main effect of A when B is at its low level and thereafter divide by two. This corresponds to adding together the response values with the same sign as in the column for factor A when B is at its high level and adding them together with the opposite sign of what is in column A when B is at its low level and thereafter divide by half the number of observations. This is equivalent to use a factor column for calculation of effects where the signs in the columns for factor A and factor B are multiplied together or the signs in the column for AB above. In the same way we can compute the signs in the other two-factor interaction columns. The signs in the column for the three-factor interaction ABC is obtained by multiplying together the signs in the columns for A, B and C. This gives

$$\hat{\mathrm{AB}} = \frac{60+68+52+80}{4} - \frac{72+54+83+45}{4} = 1.5$$
$$\hat{\mathrm{AC}} = \frac{60+54+83+80}{4} - \frac{72+68+52+45}{4} = 10$$
$$\hat{\mathrm{BC}} = \frac{45+80+60+72}{4} - \frac{83+52++68+54}{4} = 0$$
$$\hat{\mathrm{ABC}} = \frac{80+52+54+72}{4} - \frac{83+45+60+68}{4} = 0.5$$

In R the analysis involves the function linear models.

```
Call:
lm.default(formula = y ~ (.)^3, data = plan)

Residuals:
```

```
ALL 8 residuals are 0: no residual degrees of freedom!

Coefficients:
                     Estimate       Std. Error    t value    Pr(>|t|)
(Intercept)      6.425e+01          NA           NA            NA
A1               1.150e+01          NA           NA            NA
B1              -2.500e+00          NA           NA            NA
C1               7.500e-01          NA           NA            NA
A1:B1            7.500e-01          NA           NA            NA
A1:C1            5.000e+00          NA           NA            NA
B1:C1           -4.017e-15          NA           NA            NA
A1:B1:C1         2.500e-01          NA           NA            NA
```

and in order to obtain the estimated effects we have to multiply the coefficients with 2.

```
  (Intercept)      A1              B1              C1
 1.285000e+02  2.300000e+01 -5.000000e+00  1.500000e+00

   A1:B1          A1:C1         B1:C1        A1:B1:C1
1.500000e+00 1.000000e+01 -8.033653e-15  5.000000e-01
```

Evaluation of significant effects in unreplicated experiments

The estimators for the effects are given by the following formula:

$\hat{Effekt} = \dfrac{\sum_{i=1}^{n} \delta_i Y_i}{n/2}$ where n is the number of observations and δ_i is either 1 or –1 dependent on the signs in the columns for the effect we are calculating. Since all Y_i, $i = 1, 2, \ldots, n$ are independent we get:

$$Var\left(\hat{Effekt}\right) = \sigma^2_{effekt} = \frac{\sum_{i=1}^{n} \delta_i^2 Var(Y_i)}{n^2/4} = \frac{4\sum_{i=1}^{n} \sigma^2}{n^2} = \frac{4\sigma^2}{n}.$$

If all the effects are zero and the data are normally distributed with the same variance, we get that all the estimators are $N\left(0, \dfrac{4\sigma^2}{n}\right)$. In a normal probability plot they should all be lying on a straight line. Those who fall off the line can be considered to be significant. The motivation for this is as follows.

Normalplot based on nscores.

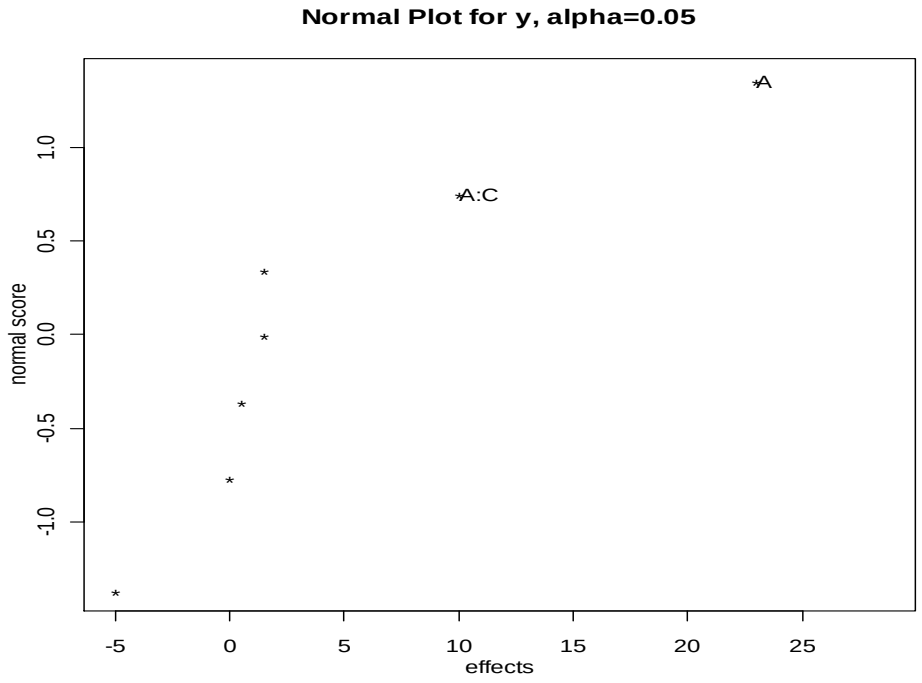
Such plots can be constructed as follows. Suppose we have n independent observations $x_1, x_2, \ldots, x_n$ that all come from the same distribution Let the ordered values of these according to algebraic size be: $x_{(1)}, x_{(2)}, \ldots, x_{(n)}$. A direct estimate of their distribution function

$P\left(X \le x_{(i)}\right), i = 1,2,...,n$ is given by i/n. Theoretically it can be shown that $F_i = \frac{i - 3/8}{n + 1/4}$ is a better choice. For the estimated effects from the 2^3 experiment with temperature, catalyst and concentration we can construct the following table:

$x_{(i)}$:	-5	0	0.5	1.5	1.5	10	23
F_i :	0.086	0.224	0.362	0.500	0.638	0.776	0.914
$\Phi^{-1}(F_i)$	- 1.37	-0.76	-0.35	0	0.35	0.76	1.37

The motivation for the third row is as follows. For normal distributed data $F\left(x_{(i)}\right) = \Phi\left(\frac{x_{(i)} - u}{\sigma}\right)$. It is therefore to be expected that $\Phi^{-1}(F_i) \approx \frac{x_{(i)} - \mu}{\sigma}$ such that a plot of $\Phi^{-1}(F_i) \approx \frac{x_{(i)} - \mu}{\sigma}$ against $x_{(i)}$ approximately becomes a straight line.

A normal plot for the 2^3 experiment with temperature, catalyst and concentration is shown below:



We notice that estimated effects of temperature and the interaction between temperature and catalyst clearly separate from the others.

In the normal-plot a * is placed at those effects that are judged significant. The judgement of significance is done by means of Lenth's method.

Lenth's method.

For a random variable $Z \sim N(0, \tau^2)$, the median of $|Z|$ approximately equals 0.675τ and hence $1.5 \cdot (\text{median of } |Z|) \approx 1.5 \cdot 0.675\tau \approx 1.0125\tau \approx \tau$. Now let $\hat{\theta}_1, \hat{\theta}_2, \ldots, \hat{\theta}_m$ be independent estimators of the effects obtained from orthogonal contrasts and let their variance be τ^2. An estimator for τ is then given by:

$$\hat{\tau} = 1.5 \cdot \text{Median}\left(|\hat{\theta}_i|, i = 1, 2, \ldots, m\right)$$

and a more refined estimator

$$\hat{\tau}^* = 1.5 \cdot \text{Median}\left(|\hat{\theta}_i| : |\hat{\theta}_i| < 2.5\hat{\tau}\right)$$

For testing $H_0: \theta_i = 0 \quad H_1: \theta_i \neq 0$

we use that $T = \dfrac{\hat{\theta}_i}{\hat{\tau}^*}$ is approximately t-distributed with $m/3$ degrees of freedom. If more accurate inference is needed, a table of critical values is given in the book Experiments, Planning, Analysis and Optimization by Hamada and Wu (2009), p 702.

Using higher order interactions to test for significance of effects.

Often it is assumed that three-factor and higher order interactions are zero. If the assumption is true, these can be used to estimate the variance of the effects. In a 2^4 experiment we can estimate 4 three-factor and one four-factor interaction. By averaging the five squared three-factor and four-factor interactions, we get an estimate for the variance of the effects with 5 degrees of freedom. This can be used in evaluating the significance of the effects. For instance, factor A is significant if

$$\left|\frac{\hat{A}}{s_{\hat{A}}}\right| \geq t_{\frac{\alpha}{2},5}.$$

Example
A 2^4 experiment in the four factors A =catalyst charge, B = temperature, C = pressure and D = concentration was performed in a process development study. The 16 experiments set up in standard form are shown below. Here also all the interaction columns are included.

Row	A	B	C	D	AB	AC	AD	BC	BD	CD	ABC	ABD
1	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1
2	1	-1	-1	-1	-1	-1	1	1	1	1	1	1
3	-1	1	-1	-1	-1	1	1	-1	-1	1	1	1
4	1	1	-1	-1	1	-1	-1	-1	-1	1	-1	-1
5	-1	-1	1	-1	1	-1	1	-1	1	-1	1	-1
6	1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1
7	-1	1	1	-1	-1	-1	1	1	-1	-1	-1	1
8	1	1	1	-1	1	1	-1	1	-1	-1	1	-1
9	-1	-1	-1	1	1	1	-1	1	-1	-1	-1	1
10	1	-1	-1	1	-1	-1	1	1	-1	-1	1	-1
11	-1	1	-1	1	-1	1	-1	-1	1	-1	1	-1
12	1	1	-1	1	1	-1	1	-1	1	-1	-1	1
13	-1	-1	1	1	1	-1	-1	-1	-1	1	1	1
14	1	-1	1	1	-1	1	1	-1	-1	1	-1	-1
15	-1	1	1	1	-1	-1	-1	1	1	1	-1	-1

```
  16     1     1     1     1     1     1     1     1     1     1     1     1
```

```
 Row   ACD   BCD   ABCD

   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     1     1     -1
  10    -1     1      1
  11     1    -1      1
  12    -1    -1     -1
  13    -1    -1      1
  14     1    -1     -1
  15    -1     1     -1
  16     1     1      1
```

The 16 response values for percentage conversion are:

71 61 90 82 68 61 87 80 61 50
89 83 59 51 85 78

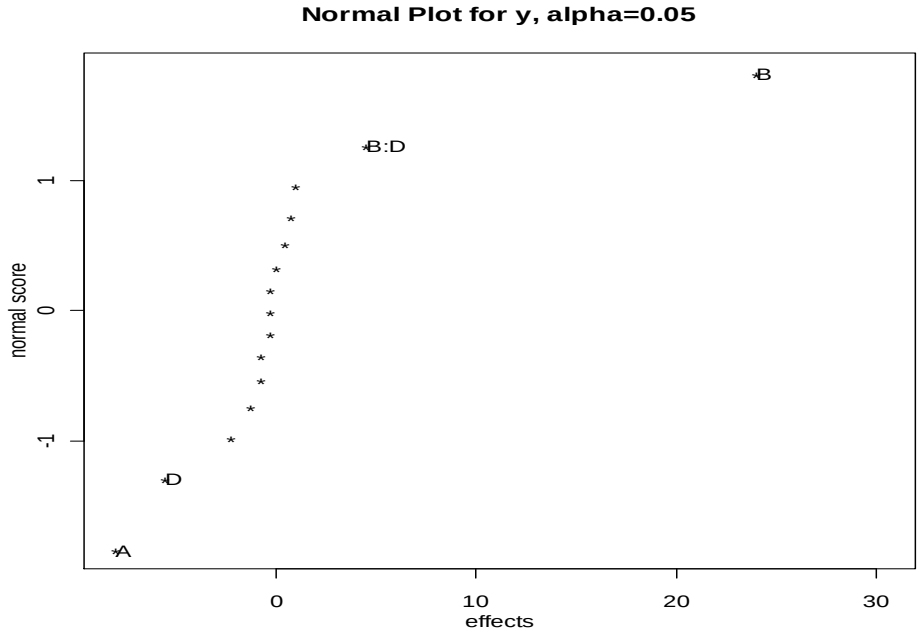
Fractional Factorial Fit: % Conversion versus A; B; C; D

```
Residuals:
ALL 16 residuals are 0: no residual degrees of freedom!

Coefficients:
              Estimate Std. Error t value Pr(>|t|)
(Intercept)  7.225e+01         NA      NA       NA
A1          -4.000e+00         NA      NA       NA
B1           1.200e+01         NA      NA       NA
C1          -1.125e+00         NA      NA       NA
D1          -2.750e+00         NA      NA       NA
A1:B1        5.000e-01         NA      NA       NA
A1:C1        3.750e-01         NA      NA       NA
A1:D1        2.229e-16         NA      NA       NA
B1:C1       -6.250e-01         NA      NA       NA
B1:D1        2.250e+00         NA      NA       NA
C1:D1       -1.250e-01         NA      NA       NA
A1:B1:C1    -3.750e-01         NA      NA       NA
A1:B1:D1     2.500e-01         NA      NA       NA
A1:C1:D1    -1.250e-01         NA      NA       NA
B1:C1:D1    -3.750e-01         NA      NA       NA
A1:B1:C1:D1 -1.250e-01         NA      NA       NA
```

And the estimated effects become:

```
  (Intercept)       A1           B1           C1           D1
 1.445000e+02 -8.000000e+00  2.400000e+01 -2.250000e+00 -5.500000e+00
     A1:B1        A1:C1        A1:D1        B1:C1        B1:D1
 1.000000e+00  7.500000e-01  4.458239e-16 -1.250000e+00  4.500000e+00
     C1:D1      A1:B1:C1     A1:B1:D1     A1:C1:D1     B1:C1:D1
-2.500000e-01 -7.500000e-01  5.000000e-01 -2.500000e-01 -7.500000e-01
  A1:B1:C1:D1
-2.500000e-01
```



The normal-plot indicates that the main effect of catalyst charge, temperature and concentration together with the interaction between temperature and concentration are significant.

We notice that all the estimated three-factor and four-factor interactions are small. If the true value for these interactions are zero, their estimators will have expected value 0 and the same equal variance σ^2_{effekt}.

Therefore an estimator for σ^2_{effekt} is given by: $\dfrac{\hat{ABC}^2 + \hat{ABD}^2 + \hat{ACD}^2 + \hat{BCD}^2 + \hat{ABCD}^2}{5}$

For our data the estimate becomes:

$$s^2_{effekt} = \frac{(-0.75)^2 + (0.5)^2 + (-0.25)^2 + (-0.75)^2 + (-0.25)^2}{5} = 0.3$$

and the standard deviation of the effect is estimated to $s_{effekt} = \sqrt{0.3} \approx 0.55$.

By evaluation of significance the absolute value of the estimated effects shall be compared to: $s_{effekt} \cdot t_{0.025,5} = 0.55 \cdot 2.571 = 1.41$. Therefore one may question if also the main effect of pressure is significant.

Estimation of variance by replication.

In order to get a model independent estimate of the variance we need to replicate our experiment. If one replicate is performed, we have two response values for each level combination and both of these have the same expected value.

Let y_{11} and y_{12} be the two observed response values for the first level combination. An estimate for the variance of the observations, σ^2, is then given by:

$$\sum_{j=1}^{2}\left(y_{1j}-\bar{y}_1\right)^2=\left(y_{11}-\frac{y_{11}+y_{12}}{2}\right)^2+\left(y_{12}-\frac{y_{11}+y_{12}}{2}\right)^2=$$

$$\left(\frac{y_{11}-y_{12}}{2}\right)^2+\left(\frac{-y_{11}+y_{12}}{2}\right)^2=\frac{\left(y_{11}-y_{12}\right)^2}{2}$$

Normally we get 2^k such estimates that can be used to estimate σ^2 by averaging.

Example. A 2^3 experiment with replicates.

A	B	C	y_{i1}	y_{i2}	$y_{i1}-y_{i2}$	$\frac{\left(y_{i2}-y_{i1}\right)^2}{2}$
-	-	-	59	61	-2	2
+	-	-	74	70	4	8
-	+	-	50	58	-8	32
+	+	-	69	67	2	2
-	-	+	50	54	-4	8
+	-	+	81	85	-4	8
-	+	+	46	44	2	2
+	+	+	79	81	-2	2
Total						64

The estimate for σ^2 then becomes: $s^2=\frac{64}{8}=8$.

$$\sigma^2_{effekt}=\frac{4\sigma^2}{n}\Rightarrow s^2_{effekt}=\frac{4\cdot s^2}{16}=\frac{4\cdot 8}{16}=2$$

By doing (m-1) replicates (in total m values for each level combination), an estimator for σ^2 for each i is given by $\sum_{j=1}^{m}\frac{\left(Y_{ij}-\bar{Y}_i\right)^2}{m-1}$. By averaging these we get an estimator for the variance with $\left(m-1\right)2^k$ degrees of freedom.

Interpretation of effects.

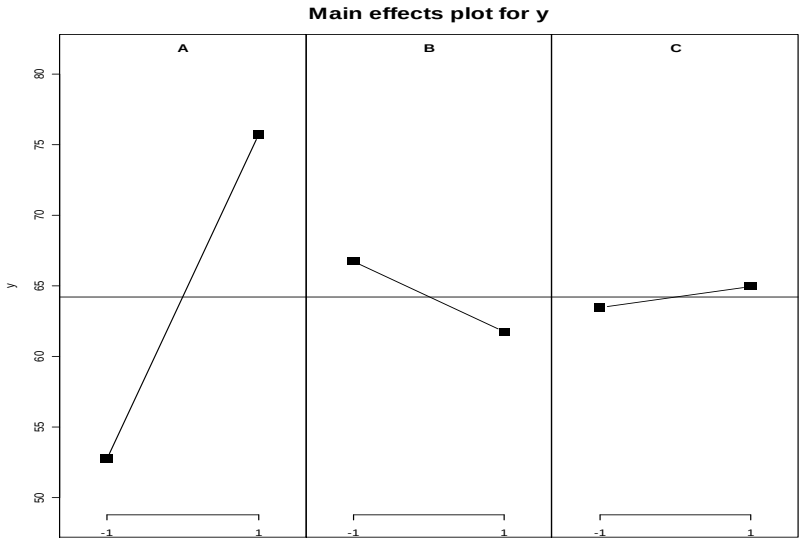
If a factor has no interaction with other factors we interpret estimated main effects as the estimated change in expected response when we go from low to high level of the corresponding factors. If a factor has interactions with other factors the effect on the expected response by going from low to high level will depend on the level of those factors that are involved in an interaction with this factor. The interpretation of the effect of this factor is then done by means of interaction-plot(s).

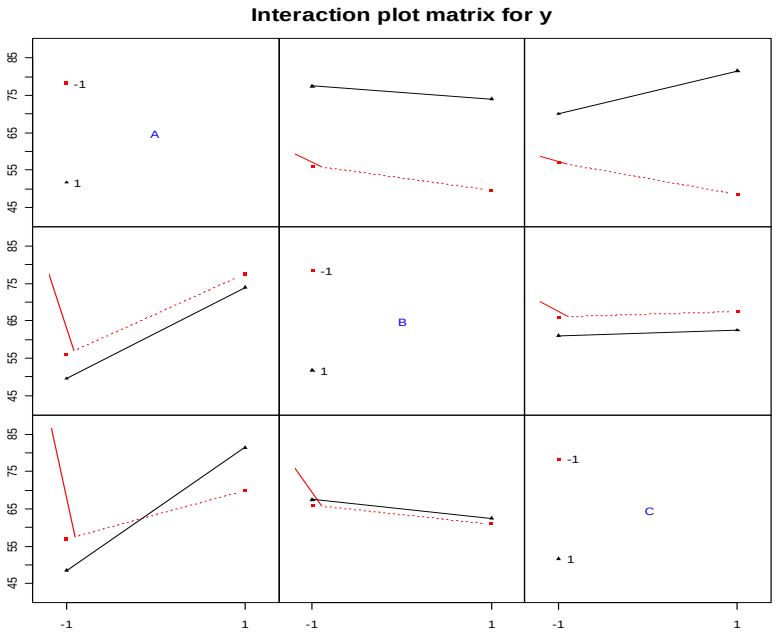
Example 2^3 experiment for chemical yield.

Here the estimated main-effect of temperature was 23 and the interaction between temperature and catalyst was estimated to 10. It is now possible to construct a table which illustrates what happens for the 4 level combinations of A and C. A graphical visualization of this table is called an interaction plot.

	C	
A	-	+
-	$\frac{60+54}{2}=57$	$\frac{52+45}{2}=48.5$
+	$\frac{72+68}{2}=70$	$\frac{83+80}{2}=81.5$

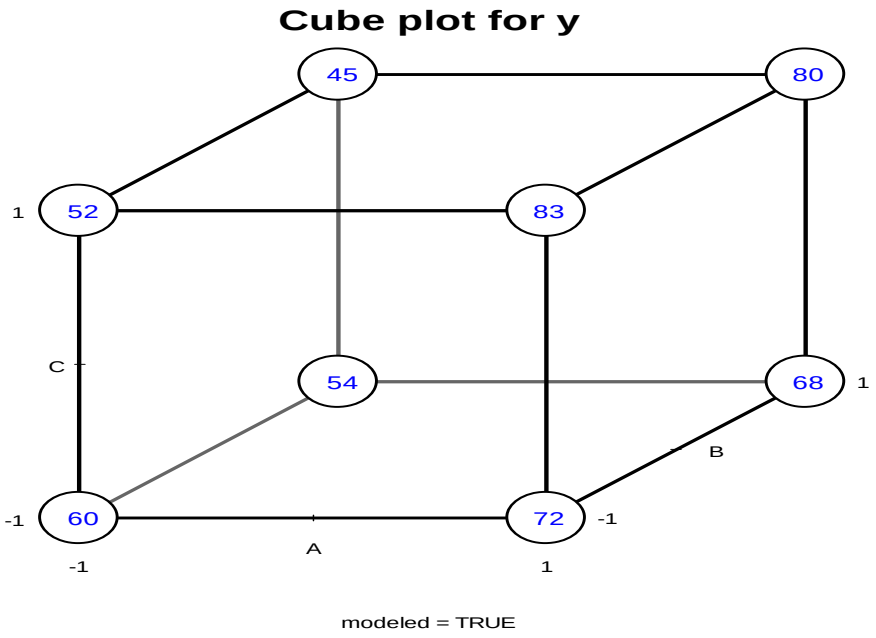
Main-effects plot and two-factor interaction plot is shown below. If there is no interaction between two factors the effect of one factor is the same independent of the level of the other factor. The lines in a two-factor interaction plot will then become parallel. This seems to be almost true for the factors A and B and for B and C, but not for the factors A and C.





The interpretation of the analysis is then that the effect of catalyst is negative when the temperature is its low level, but positive when temperature is at its high level. The best result for the yield is obtained when both temperature and catalyst is on their high level.

A cube plot illustrates what level combinations are favourable.



Blocking in 2^p experiment.

An experiment should always be performed in a randomized order. Randomization is our best guarantee to obtain independent observations and reduces the chances for external factors (factors not included in the experiment) to influence our response such that we end up with wrong conclusions. It is also important to reset the level combinations for each experimental run to ensure that the observations have as equal variance as possible.

If we are going to do many experiments, it will often be the case that the experimental condition changes from the start of the experimentation until it is done. Change in experimental conditions may influence the response values leading to wrong estimates for the effects. This can be avoided if we block the experiment. Sometimes there are other constraints like restrictions on the raw material that makes the use of blocking desirable. When an experiment is blocked the randomization should always be performed in each block.

2^3 experiment in 2 blocks each block of sixe 4.

Assume we conduct the experiments where the three-factor interaction has a – in block 1 og the rest of the experiments in block 2.

Run	A	B	C	AB	AC	BC		ABC
1	-	-	-	+	+	+	Block 1	-
4	+	+	-	+	-	-		-
6	+	-	+	-	+	-		-
7	-	+	+	-	-	+		-
2	+	-	-	-	-	+	Block 2	+
3	-	+	-	-	+	-		+
5	-	-	+	+	-	-		+
8	+	+	+	+	+	+		+

We observe that if a number h is added to all runs in block 2, the calculated estimates of main effects and two-factor interactions remain unchanged since there are equally many + and – in each block. This is not true for the three-factor interaction that will be confounded with the block effect.

2^3 experiment in 4 blocks, each block of sixe 2

Assume we block the 2^3 experiment in blocks using the following sign pattern in the two-factor interaction columns for AB and BC.

Block 1	Block 2	Block 3	Block 4
(- -)	(- +)	(+ -)	(+ +)

The design will then be blocked into 4 blocks as shown below:

Block	A	B	C	Forsøk	AB	BC	AC	ABC
Block 1	- +	+ -	- +	3 6	- -	- -	+ +	+ -
Block 2	+ -	- +	- +	2 7	- -	+ +	- -	+ -
Block 3	+ -	+ -	- +	4 5	+ +	- -	- -	- +
Block 4	- +	- +	- +	1 8	+ +	+ +	+ +	- +

AB, BC and AC are confounded with the block effect.

How to decide which effects should be used for blocking

We should strive at being in a position such that main-effects and low order interactions can be estimated. Let I be a column with only + signs. We notice that.

$$I = AA=BB=CC$$

where AA, BB, … means the entry-wise product of signs in the respective columns.
Assume we block a 2^3 experiment letting D=ABC and E=AC be our blocking factors. The interaction between D and E then becomes: DE=ABCAC=B, i.e. one of the main effects are confounded with the block effect in addition to ABC and BC.

Blocking in general

Assume we are going to block a 2^6 experiment in 8 blocks using the blocking factors $B_1 = ACE$ $B_2 = ABEF$ and $B_3 = ABCD$. The blocking is then done using the following sign patterns in the corresponding three factor columns.

Block 1	Block 2	Block 3	Block 4	Block 5	Block 6	Block 7	Block 8
(- - -)	(+ - -)	(- + -)	(+ + -)	(- - +)	(+ - +)	(- + +)	(+ + +)

We get:

$$B_1B_2 = ACEABEF = BCF$$
$$B_1B_3 = ACEABCD = BDE$$
$$B_2B_3 = ABEFABCD = CDEF$$
$$B_1B_2B_3 = ACEABEFABCD = ADF$$

These four interactions will together with $B_1 = ACE$, $B_2 = ABEF$ og $B_3 = ABCD$ be confounded with the block effect.

The Analysis of variance table for 2^p experiments

In cases when an experiment is blocked it may be useful or even necessary to use an analysis of variance table to find an estimate for the variance of the response. If all columns in the design matrix are orthogonal, we have

$$SS_R = b_1^2 \sum_{i=1}^{n} x_{1i}^2 + b_2^2 \sum_{i=1}^{n} x_{2i}^2 + \cdots + b_k^2 \sum_{i=1}^{n} x_{ki}^2 \qquad (2)$$

In two-level experiments we have $2^p - 1$ effect columns and k becomes $2^p - 1$. If we use that that a regression coefficient is equal to the corresponding effect divided by two and that for a two-level experiment $\sum_{i=1}^{n} x_{ji}^2 = n$, j=1,2,…,k, we get:

$$SS_R = \frac{\hat{A}^2 \cdot n}{4} + \frac{\hat{B}^2 \cdot n}{4} + \cdots + \frac{\hat{A}BC....^2 \cdot n}{4}$$

Each of the terms above gives us the sum of squares for the effects.

For an 2^3 experiment this becomes:

Source	SS	DF
A	$SS_A = 2\hat{A}^2$	1
B	$SS_B = 2\hat{B}^2$	1
C	$SS_C = 2\hat{C}^2$	1
AB	$SS_{AB} = 2\hat{A}B^2$	1
AC	$SS_{AC} = 2\hat{A}C^2$	1
BC	$\mathrm{SS_{BC}} = 2\hat{\mathrm{B}}\mathrm{C}^2$	1
ABC	$SS_{ABC} = 2\hat{A}BC^2$	1
Total	$SS_T = SS_R = \sum_{i=1}^{n} \left(y_i - \bar{y}\right)^2$	7

Notice that here $SS_R = SS_T$. This is due to that when a model with a constant term and seven effects are fitted to the data, all residuals become zero.

If the three-factor interaction ABC is used as blocking factor, we can consider ABC to be a blocking factor instead of a three-factor interaction. The blocking factor has two levels which we can code to –1 and +1. The analysis of variance table therefore becomes:

Source	SS	DF
A	$SS_A = 2\hat{A}^2$	1
B	$SS_B = 2\hat{B}^2$	1

C	$SS_C = 2\hat{C}^2$	1
AB	$SS_{AB} = 2\hat{A}B^2$	1
AC	$SS_{AC} = 2\hat{A}C^2$	1
BC	$SS_{BC} = 2\hat{B}C^2$	1
Block	$SS_{Block} = 2\hat{A}BC^2$	1
Total	$SS_T = \sum_{i=1}^{n}(y_i - \bar{y})^2$	7

In order to perform the experiment in 4 blocks, one might wish to introduce a factor with four levels. But four levels may be represented with two two-level factors. Thus, we can pick two effect-columns and block according to the four possible level combination in these two columns. The interaction between these two factors will then also be confounded with the block effect.

For a 2^3 experiment divided into four blocks using two of the three two-factor interactions columns AB, AC and BC we get this analysis of variance table.

Source	SS	DF
A	$SS_A = 2\hat{A}^2$	1
B	$SS_B = 2\hat{B}^2$	1
C	$SS_C = 2\hat{C}^2$	1
Block	$SS_{Block} = 2\hat{A}B^2 + 2\hat{B}C^2 + 2\hat{A}C^2$	3
ABC	$SS_{ABC} = 2\hat{A}BC^2$	1
Total	$SS_T = \sum_{i=1}^{n}(y_i - \bar{y})^2$	7

Let us assume that a replicated 2^3 experiment is carried out in four blocks. It is then possible to block the experiment using ABC as the blocking factor in each replicate. The other blocking factor will have –1 for the first eight experiments and +1 for the eight last. Both block factor columns are orthogonal to the other columns. The same is true for their interaction column.

Let the average in each of the four blocks be: $\bar{y}_1, \bar{y}_2, \bar{y}_3$ and $\bar{y}_4$. In the sum of squares for the blocks the three estimated effects are given by:

$$\left(\frac{\bar{y}_2 + \bar{y}_4}{2} - \frac{\bar{y}_1 + \bar{y}_3}{2}\right),$$

$$\left(\frac{\bar{y}_3 + \bar{y}_4}{2} - \frac{\bar{y}_1 + \bar{y}_2}{2}\right) \text{ and}$$

$$\left(\frac{\bar{y}_1 + \bar{y}_4}{2} - \frac{\bar{y}_2 + \bar{y}_3}{2} \right)$$

The sum of squares for the blocks is:

$$SS_{Block} = 4(\frac{\bar{y}_2 + \bar{y}_4}{2} - \frac{\bar{y}_1 + \bar{y}_3}{2})^2 + 4(\frac{\bar{y}_3 + \bar{y}_4}{2} - \frac{\bar{y}_1 + \bar{y}_2}{2})^2 + 4(\frac{\bar{y}_1 + \bar{y}_4}{2} - \frac{\bar{y}_2 + \bar{y}_3}{2})^2$$

The analysis of variable table becomes:

Source	SS	DF
A	$SS_A = 4\hat{A}^2$	1
B	$SS_B = 4\hat{B}^2$	1
C	$SS_C = 4\hat{C}^2$	1
AB	$SS_{AB} = 4\hat{A}B^2$	1
AC	$SS_{AC} = 4\hat{A}C^2$	1
BC	$SS_{BC} = 4\hat{B}C^2$	1
Block	SS_{Block}	3
Error	$SS_E = SS_T - (SS_A + SS_B + \cdots + SS_{Block})$	6
Total	$SS_T = \sum_{i=1}^{n} (y_i - \bar{y})^2$	15

Partial confounding

A replicated experiment can be divided into blocks using different interactions each time. This is called partial confounding. If the experiment the first time is blocked using the ABC interaction and the next time the AB interaction it is possible to estimate the AB interaction the first time and the ABC interaction the next time and so on.

The block-effect should now be calculated using the general formulae:

$$SS_{Block} = k\sum_{i=1}^{m}\sum_{b=1}^{s}\left(\bar{y}_{ib} - \bar{y}\right)^2$$

where k is the number of observations in each block, m is the number of replicates, s is the number of blocks in each replicate, $\bar{y}_{ib}$ is the average in block b in replicate i and $\bar{y}$ is the average of all observations.

Suppose we want to do such a partial confounding for a replicated 2^3 experiment

The analysis of variance table for a replicated 2^3 experiment becomes:

Source	SS	DF
A	$SS_A = 4\hat{A}^2$	1
B	$SS_A = 4\hat{A}^2$	1
C	$SS_c = 4\hat{C}^2$	1
AB	$SS_{AB} = 2\hat{A}B^2$	1
AC	$SS_{AC} = 4\hat{A}C^2$	1
BC	$SS_{BC} = 4\hat{B}C^2$	1
ABC	$SS_{ABC} = 2\hat{A}BC^2$	1
Block	SS_{Block}	3
Error	$SS_E = SS_T - (SS_A + SS_B + \cdots + SS_{Block})$	5
Total	$SS_T = \sum_{i=1}^{n} (y_i - \bar{y})^2$	15

Fractional factorial designs.

To save effort and costs we may want to find out by means of a 2^p experiment if more than p factors have any influence on the response.

Example. Suppose we suspect that three factors influence the response but are only allowed to do 4 experiments.
The full 2^3 experiment, extended with interaction columns can be written as:

Run	A	B	AB	C	AC	BC	ABC
1	-	-	+	-	+	+	-
2	+	-	-	-	-	+	+
3	-	+	-	-	+	-	+
4	+	+	+	-	-	-	-
5	-	-	+	+	-	-	+
6	+	-	-	+	+	-	-
7	-	+	-	+	-	+	-
8	+	+	+	+	+	+	+

Let us carry out the 4 experiments with a + in the column for the three-factor interaction i.e.

Run	A	B	AB	C	AC	BC
2	+	-	-	-	-	+
3	-	+	-	-	+	-
5	-	-	+	+	-	-
8	+	+	+	+	+	+

For the four chosen experiments we notice that I = ABC, which implies that AB and C get the same signs. This is also true for A and BC and for B and AC. I = ABC is the defining relation for the 4 run design. If we instead had chosen the four runs with a – in the three-factor interaction column the defining relation would have been I = -ABC.

Now for the full 2^3 experiment we get

$$\widehat{A} = \frac{y_2 + y_4 + y_6 + y_8 - (y_1 + y_3 + y_5 + y_7)}{4}$$

$$\widehat{BC} = \frac{y_1 + y_2 + + y_7 + y_8 - (y_3 + y_4 + y_5 + y_6)}{4}$$

From the four run or 2^{3-1} experiment we obtain

$$l_A = \frac{y_2 + y_8 - (y_3 + y_5)}{2} = \widehat{A} + \widehat{BC}$$

In the same way

$$l_B = \widehat{B} + \widehat{AC}$$

$$l_C = \widehat{C} + \widehat{AB}$$

$$l_I = \bar{y} + \widehat{ABC}/2$$

where $l_I = \frac{1}{4}\sum_{ABC+} y_i = \frac{1}{8}\sum_{i=1}^{8} y_i + \frac{1}{8}\sum_{ABC+} y_i - \frac{1}{8}\sum_{ABC-} y_i$

If all two- and three-factor interactions are small we would in theory be able to estimate all the three main-effects.

Generator for the design

In the 2^{3-1} experiment the signs in the AB column and the C column are the same i.e. C=AB This relation is called the generator for the design. $C=AB \Leftrightarrow C^2=I=ABC$ which means that equivalently can say that I=ABC is the defining relation for the experiment (ABC is defining contrast). In order to find out which effects that are aliased (have the same signs in the factor columns) we may multiply the effects by the defining relation. Hence for the 2^{3-1} experiment we get

$AI = AABC = BC \Rightarrow A \equiv BC$
$BI = BABC = AC \Rightarrow B \equiv AC$
$CI = CABC = AB \Rightarrow C \equiv AB$

About half fractions of 2^p designs

A half fraction of a 2^p design is called a 2^{p-1} design. This is to be read that we are going to experiment with p two-level factors in 2^{p-1} runs. It can be constructed as follows:
Number the factors $1, 2, \ldots, p$. Then construct a 2^{p-1} design in the factors $1, 2, \ldots, p-1$ and let the design column for the last factor be the interaction column $\pm 123\cdots(p-1)$. If we remove one of the factor columns we will have a complete fractional factorial design in the $p-1$ others.

Example of a half-fraction.

The following example is the often cited Reactor Example from Box, Hunter and Hunter (1978), page 377. The goal was to find out how five factors affected % reacted, y. Factors levels and the full 2^5 design is given below.

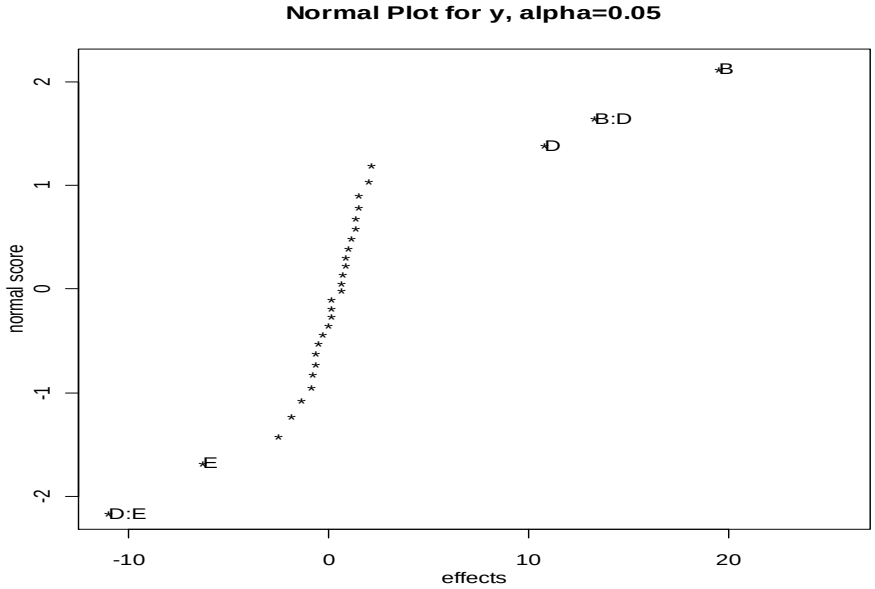
Factors	-	+
A: Feed rate conversion	10	15
B: Catalyst (%)	1	2
C: Agitation rate (rpm)	100	120
D: Temperature $\left({}^0C\right)$	140	180
E: Concentration (%)	3	6

	A	B	C	D	E	y
1	-1	-1	-1	-1	-1	61
*2	1	-1	-1	-1	-1	53
*3	-1	1	-1	-1	-1	63
4	1	1	-1	-1	-1	61
*5	-1	-1	1	-1	-1	53
6	1	-1	1	-1	-1	56
7	-1	1	1	-1	-1	54
*8	1	1	1	-1	-1	61
*9	-1	-1	-1	1	-1	69
10	1	-1	-1	1	-1	61
11	-1	1	-1	1	-1	94
*12	1	1	-1	1	-1	93
13	-1	-1	1	1	-1	66
*14	1	-1	1	1	-1	60
*15	-1	1	1	1	-1	95
16	1	1	1	1	-1	98
*17	-1	-1	-1	-1	1	56
18	1	-1	-1	-1	1	63
19	-1	1	-1	-1	1	70
*20	1	1	-1	-1	1	65
21	-1	-1	1	-1	1	59
*22	1	-1	1	-1	1	55
*23	-1	1	1	-1	1	67
24	1	1	1	-1	1	65
25	-1	-1	-1	1	1	44
*26	1	-1	-1	1	1	45
*27	-1	1	-1	1	1	78
28	1	1	-1	1	1	77
*29	-1	-1	1	1	1	49
30	1	-1	1	1	1	42
31	-1	1	1	1	1	81
*32	1	1	1	1	1	82

The estimated effects are given below together with a normal plot.

(Intercept)	A1	B1	C1	D1
1.310000e+02	-1.375000e+00	1.950000e+01	-6.250000e-01	1.075000e+01

```
      E1          A1:B1          A1:C1          A1:D1          A1:E1
-6.250000e+00  1.375000e+00  7.500000e-01 -8.750000e-01  1.250000e-01
     B1:C1          B1:D1          B1:E1          C1:D1          C1:E1
 8.750000e-01  1.325000e+01  2.000000e+00  2.125000e+00  8.750000e-01
     D1:E1         A1:B1:C1       A1:B1:D1       A1:B1:E1       A1:C1:D1
-1.100000e+01  1.500000e+00  1.375000e+00 -1.875000e+00 -7.500000e-01
    A1:C1:E1       A1:D1:E1       B1:C1:D1       B1:C1:E1       B1:D1:E1
-2.500000e+00  6.250000e-01  1.125000e+00  1.250000e-01 -2.500000e-01
    C1:D1:E1    A1:B1:C1:D1    A1:B1:C1:E1    A1:B1:D1:E1    A1:C1:D1:E1
 1.250000e-01 -7.031454e-15  1.500000e+00  6.250000e-01  1.000000e+00
  B1:C1:D1:E1 A1:B1:C1:D1:E1
-6.250000e-01 -5.000000e-01
```



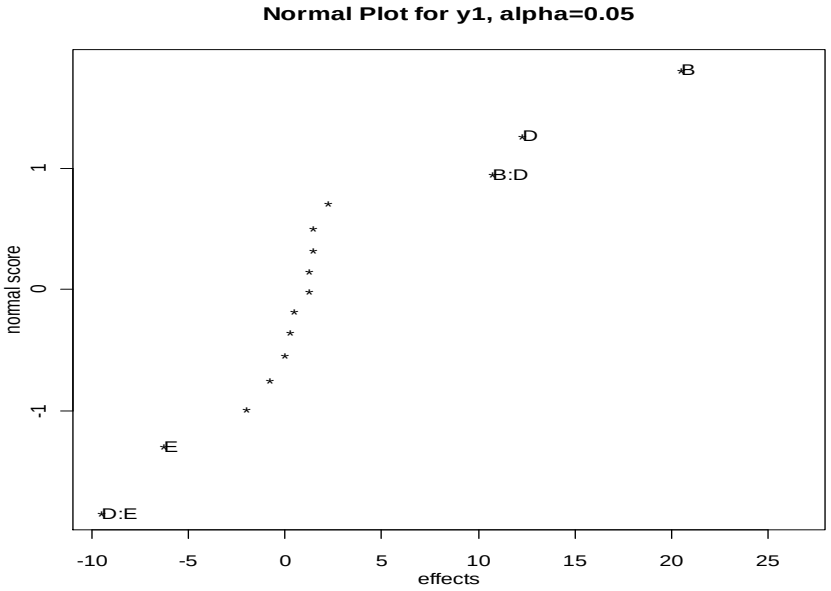
The normal plot indicates that the main-effects of B, D and E and the interactions BD and DE are the essential ones.

Now assume we instead only run the 16 experiments that are marked with a *. This corresponds to running those 16 experiments for which I=ABCDE or equivalently letting E=ABCD. The experimental runs would then be as follows.

```
    A  B  C  D  E  y
1  -1 -1 -1 -1  1 53
2   1 -1 -1 -1 -1 63
3  -1  1 -1 -1 -1 53
4   1  1 -1 -1  1 61
5  -1 -1  1 -1 -1 69
6   1 -1  1 -1  1 93
7  -1  1  1 -1  1 60
8   1  1  1 -1 -1 95
9  -1 -1 -1  1 -1 56
10  1 -1 -1  1  1 65
11 -1  1 -1  1  1 55
12  1  1 -1  1 -1 67
13 -1 -1  1  1  1 45
14  1 -1  1  1 -1 78
15 -1  1  1  1 -1 49
16  1  1  1  1  1 82
```

Estimated main effects and two-factor interactions are given below together with a normal plot.

```
  (Intercept)         A1             B1             C1             D1
 1.305000e+02 -2.000000e+00  2.050000e+01  9.158391e-16  1.225000e+01
       E1          A1:B1          A1:C1          A1:D1          A1:E1
-6.250000e+00  1.500000e+00  5.000000e-01 -7.500000e-01  1.250000e+00
     B1:C1          B1:D1          B1:E1          C1:D1          C1:E1
 1.500000e+00  1.075000e+01  1.250000e+00  2.500000e-01  2.250000e+00
     D1:E1
-9.500000e+00
```



We note that the same effects are judged significant by the normal plot and that their sizes are about the same as we obtained from the full 32 run experiment. The success of the half fractions in this case is due to fact that main effects are only aliased with four-factor interactions and two-factor interactions are only aliased with three-factor interactions.

Resolution in fractions of 2^p experiments.

Definition. A design is said to be of resolution R if no p-factor effect is aliased with an effect containing less than R- p factors.

In a resolution R design we have: Main effects are aliased with R-1 factor interactions
Two-factor interactions are aliased with R-2 factor interactions.

Resolution III

Main effects are aliased with two-factor interactions. Example 2^{3-1}, I=ABC.

Resolution IV

Main-effects are aliased with three-factor interactions. Two-factor interactions are aliased with two-factor interactions. Example 2^{4-1}, I=ABCD.

Resolution V

Main-effects are aliased with four-factor interactions. Two-factor interactions are aliased with three-factor interactions. Example 2^{5-1}, I=ABCDE.

For short the resolution of the design is always the length of the shortest word in the defining relation.

Fractions of 2^p experiments.

A quarter fraction of a 2^5 experiment. i.e. a 2^{5-2} experiment can be constructed as follows. Construct a 2^3 experiment in the factors A, B and C. let D=AB and E=AC. We notice that I=ABD and I=ACE and also that I^2=I=ABDACE=BCDE. Hence the defining relation is I=ABD=ACE=BCDE and the design will be of resolution III.

Designs of resolution III

A design where you assign factors to all possible 2^p-1 orthogonal columns of plus and minuses is called a saturated designs. Such designs will always be resolution III designs.

An Example. The Bicycle experiment (BHH 1978). In this example we have 7 factors each at two levels and we just want to do 8 experiments. It was constructed as follows: First a 2^3 experiment was constructed in the factors A, B and C. Thereafter the four other factors were assigned to factor columns in the following way: D=AB, E=AC, F=BC and G=ABC.

Run	A:Seat up/down	B:Dynamo off/on	C:Handlebars up/down	D:Gear low/medium	E: Rain-coat on/off	F: Break fast yes/no	G: Tires hard/soft	Time to climb hill (sec) y
1	-	-	-	+	+	+	-	69
2	+	-	-	-	-	+	+	52
3	-	+	-	-	+	-	+	60
4	+	+	-	+	-	-	-	83
5	-	-	+	+	-	-	+	71
6	+	-	+	-	+	-	-	50
7	-	+	+	-	-	+	-	59
8	+	+	+	+	+	+	+	88

The seven estimated effects are shown below, but to know what we actually are estimating we need to find the defining relations for this design:

```
(Intercept)     A1     B1      C1     D1      E1      F1      G1
      133.0   3.5   12.0   1.0   22.5   0.5    1.0    2.5
```

From the four generators we obtain:

I = ABD=ACE=BCF=ABCG

which gives

I^2=I=BCDE=ACDF=CDG=ABEF=BEG=AFG

I^3=I=DEF=ADEG=BDFG=CEFG

I^4=I=ABCDEFG

In order to find out how the estimates of an effect are aliased with other effects we need to multiply the effect by all these 15 words. Let us assume that all interactions of order three and higher are negligible. Then we get for the estimators of the main effects

$\widehat{l}_{\mathrm{A}} \rightarrow$ A+BD+CE+FG

$\widehat{l}_{\mathrm{B}} \rightarrow$ B+AD+CF+EG

$\widehat{l}_{\mathrm{C}} \rightarrow$ C+AE+BF+DG

$\widehat{l}_{\mathrm{D}} \rightarrow$ D+AB+CG+EF

$\widehat{l}_{\mathrm{E}} \rightarrow$ E+AC+BG+DF

$\widehat{l}_{\mathrm{F}} \rightarrow$ F+BC+AG+DE

$\widehat{l}_{\mathrm{G}} \rightarrow$ G+CD+BE+AF

where the $\rightarrow$ points to which effects that are aliased or the expected value of the estimators.

We notice that the estimates for l_B and l_D are larger than the others. If the factors A,C,E,F and G are inert, the 2^{7-4} design can be interpreted as a repeated 2^2 design in the factors B and D. All interactions where the factors A,C,E,F and G are involved disappear and we get $\widehat{l}_{\mathrm{B}} \rightarrow$ B, $\widehat{l}_{\mathrm{D}} \rightarrow$ D and $\widehat{l}_{\mathrm{A}} \rightarrow$ BD. It is possible to construct 16 2^{7-4} design by choosing + or – signs for the four generators.

D = $\pm$AB F= $\pm$ BC

E = $\pm$ AC G= $\pm$ ABC

Often in a highly fractionated design we would like to be able to estimate the main effects free of aliasing with two-factor interactions. It is then possible to run a follow-up design with the generators D = -AB, E=-AC, F=-BC and G=ABC. For this design we obtain:

I=-ABD=-ACE=-BCF=ABCG

I^2=BCDE=ACDF=-CDG=ABEF=-BEG=-AFG

I^3=-DEF=ADEG=BDFG=CEFG

I^4=-ABCDEFG

which gives when we neglect interactions of order higher than 2.

$$l_A^* \rightarrow \text{A-BD-CE-FG}$$
$$l_B^* \rightarrow \text{B-AD-CF-EG}$$
$$\vdots$$
$$l_G^* \rightarrow \text{G-CD-BE-AF}$$

and

$$\frac{\hat{l}_A + l_A^*}{2} \rightarrow A$$
$$\vdots$$
$$\frac{\hat{l}_G + l_G^*}{2} \rightarrow G$$

If we instead were interested in examining one particular main effect, say D, and all interactions involved with this main effect we could run a follow-up design with generators $D = -AB$, E=AC, F=BC and G=ABC i.e., we switch all the signs in the column for factor D. Thereby we obtain

$$I=-ABD=ACE=BCF=ABCG$$
$$I^2=-BCDE=-ACDF=-CDG=ABEF=BEG=AFG$$
$$I^3=-DEF=-ADEG=-BDFG=CEFG$$
$$I^4=-ABCDEFG$$

If third and higher order interactions are inert we get

$$\tilde{l}_A \rightarrow \text{A-BD+CE+FG}$$
$$\tilde{l}_B \rightarrow \text{B-AD+CF+EG}$$
$$\vdots$$
$$\tilde{l}_D \rightarrow \text{D-AB-CG-EF}$$
$$\vdots$$

Thus

$$\frac{\hat{l}_D + \tilde{l}_D}{2} \rightarrow D$$
$$\frac{\hat{l}_A - \tilde{l}_A}{2} \rightarrow BD$$
$$\vdots$$

Example. A follow up design to the bicycle example was conducted to investigate how factor D affected the response. The signs in the column for factor D were changed as shown in the table below.

Run	A:Seat up/down	B:Dynamo off/on	C:Handlebars up/down	D:Gear low/medium	E: Rain-coat on/off	F: Break fast yes/no	G: Tires hard/soft	Time to climb hill (sec) y
1	-	-	-	-	+	+	-	47
2	+	-	-	+	-	+	+	74

3	-	+	-	+	+	-	+	84
4	+	+	-	-	-	-	-	62
5	-	-	+	-	-	-	+	53
6	+	-	+	+	+	-	-	78
7	-	+	+	+	-	+	-	87
8	+	+	+	-	+	+	+	60

The estimated effects are:

```
(Intercept)     A1      B1      C1      D1      E1      F1      G1
     136.25   0.75   10.25    2.75   25.25   -1.75   -2.25   -0.75
```

By combining these estimates with the ones from the first fraction we could obtain unbiased estimates for the main effect of factor D and all interactions involved with factor D. Here the two fractions gave very similar results and would strengthen our believes that B and D are the two really important factors.

Constructing fold-over of resolution III designs

Suppose we have constructed a 2^{7-4}_{III} design where D=AB, E=AC, F=BC and G=ABC. For the first eight runs we have $I_8 = ABD=ACE=BCF=ABCG=H$.

Now add eight more runs from a 2^{7-4}_{III} design where D=-AB, E=-AC, F=-BC, G=ABC and $H = -I_8$, i.e we add eight more runs where we have changed signs in each column. The 16 run design is shown below. Such a way of constructing designs where we first add a column of plus signs and thereafter double the run size by adding a new design where all the signs are switched is called construction by fold-over. If the resolution of a design is odd (3, 5, ...) we can always improve the resolution by one in this way. If the resolution is even (2, 4, ...), it will not be improved.

Run	A	B	C	D	E	F	G	H
1	-	-	-	+	+	+	-	+
2	+	-	-	-	-	+	+	+
3	-	+	-	-	+	-	+	+
4	+	+	-	+	-	-	-	+
5	-	-	+	+	-	-	+	+
6	+	-	+	-	+	-	-	+
7	-	+	+	-	-	+	-	+
8	+	+	+	+	+	+	+	+
9	+	+	+	-	-	-	+	-
10	-	+	+	+	+	-	-	-
11	+	-	+	+	-	+	-	-
12	-	-	+	-	+	+	+	-
13	+	+	-	-	+	+	-	-
14	-	+	-	+	-	+	+	-
15	+	-	-	+	+	-	+	-
16	-	-	-	-	-	-	-	-

For the last eight runs we have $I_8 = -ABD=-ACE=-BCF=ABCG=-H$. For the whole 16 runs design we get the following identity relationship: $I_{16} = ABCG=ABDH=ACEH=BCFH$. Multiplying these four words together two by two, three by three and finally all four, all the words are of length four and we have a resolution IV design.

Blocking in fractionated factorial designs.

When we block a fractionated design we need to take into account the defining relations. Let us illustrate this by two examples.
Example: A 2^{5-1} is to be run in two blocks each of size 8 run. For the half-fraction the defining relation is I=ABCDE. Suppose we block after the AB interaction. Then also IAB=ABCDEAB=CDE is confounded with the block effect.

Example: The same design is to be run in four blocks using AC and BC. AB will then be confounded with the block effect. The same will be true for IAC, IAB and IBC or BDE, ADE and CDE.

Final remarks and further reading

The techniques you have learned about two-level experimentation can be used to "improve almost everything", but not to optimize. In order to optimize a process you need to approximate the response by what we call a response surface which normally will be a second order function. And you need designs that can estimate such functions. These are called response surface designs. The most well-known is the central composite designs that add centre points and two-points on the axis for each factor to a two-level design. The distance from the centre to the points on the axis is often $-\sqrt{k}$ and $\sqrt{k}$ where k is the number of factors. Though, you can obtain a lot by basic two-level experimentation and in a dynamic and rapidly changing world the focus may equally well be on "never ending improvement" instead of optimization. For those who want to learn more about this interesting and challenging topic the "classics" are:

Box, G. E. P., Hunter, J. S. & Hunter, W. G.: Statistics for Experimenters (1978, 2005)
Montgomery, D. C.: Design and Analysis of Experiments (2077, 9th edition)
Wu, C. F. & Hamada, M.S.: Experiments, Planning, Analysis, and Optimization (2009, 2 th edition) .
Box, G. E. P. & Draper, N. R.: Response Surfaces, Mixtures, and Ridge Analyses (2007).
Myers, R. H. & Montgomery, D. C. & Anderson-Cook, C. M.: Response Surface Methodology (2016).