Assignment Experimental Design
2014 - 2015

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Part 1: Mixture Experiments

Question 1.1

The three-component second-order Scheffé model is given as

$$E\{\mathbf{Y}\} = \beta_1\,\mathbf{x}_1 + \beta_2\,\mathbf{x}_2 + \beta_3\,\mathbf{x}_3 + \beta_{12}\,\mathbf{x}_1\,\mathbf{x}_2 + \beta_{13}\,\mathbf{x}_1\,\mathbf{x}_3 + \beta_{23}\,\mathbf{x}_2\,\mathbf{x}_3 \tag{1}$$

It is clear that we need to estimate six parameters to be able to fit this model. Having three mixture components and six parameters to estimate, 18 experimental runs seems like a reasonable choice between 15 and 20, leaving two unused runs in the experimental budget. These can be used afterwards e.g. for confirmation runs. Table 1a shows the (ordered) design matrix for a D-optimal design with 18 runs. Table 1b shows the (ordered) design matrix for an I-optimal design with 18 runs.

The I-optimal design showed in table 1b is not the I-optimal design as produced by *JMP*, but a slightly changed version of this design. Because the cost in terms of relative I-efficiency was very small ($\approx 99\%$), the decision was made to change some points to *a*) increase readability; *b*) increase balancedness in design; and *c*) decrease variance of parameter prediction.

Table 1: Generated optimal designs for $q = 3$ and $n = 18$

(a) D-optimal design

	x_1	x_2	x_3
1	1.0	0.0	0.0
2	1.0	0.0	0.0
3	1.0	0.0	0.0
4	0.0	1.0	0.0
5	0.0	1.0	0.0
6	0.0	1.0	0.0
7	0.0	0.0	1.0
8	0.0	0.0	1.0
9	0.0	0.0	1.0
10	0.5	0.5	0.0
11	0.5	0.5	0.0
12	0.5	0.5	0.0
13	0.5	0.0	0.5
14	0.5	0.0	0.5
15	0.5	0.0	0.5
16	0.0	0.5	0.5
17	0.0	0.5	0.5
18	0.0	0.5	0.5

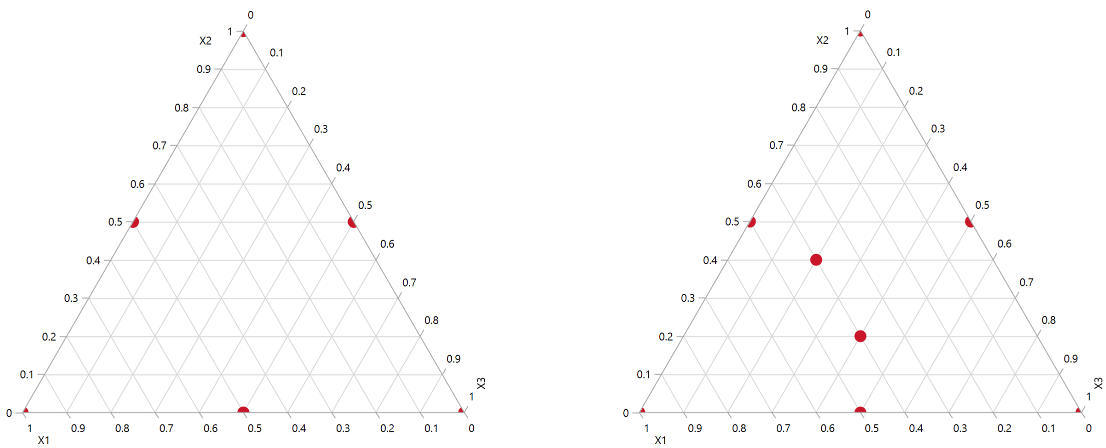
(b) I-optimal design

	x_1	x_2	x_3
1	1.0	0.0	0.0
2	1.0	0.0	0.0
3	0.0	1.0	0.0
4	0.0	1.0	0.0
5	0.0	0.0	1.0
6	0.0	0.0	1.0
7	0.5	0.5	0.0
8	0.5	0.5	0.0
9	0.5	0.5	0.0
10	0.5	0.0	0.5
11	0.5	0.0	0.5
12	0.5	0.0	0.5
13	0.0	0.5	0.5
14	0.0	0.5	0.5
15	0.0	0.5	0.5
16	0.0	0.5	0.5
17	0.4	0.4	0.2
18	0.4	0.2	0.4

To compare these two designs, we will use *a*) the overall structure of the designs; *b*) the fractional increase in the confidence interval length; *c*) the relative variances of factor-effect estimates; *d*) the average variance of prediction; and *e*) the FDS-plots of the two designs.

When looking closely to the designs in table 1, we see that for the D-optimal design the design is nicely balanced. Each formulation returns exactly three times, which is off course why we choose $n = 18$ in the first place. To use the classic DoE terminology, the D-optimal design shown in table 1 are three replications of a $\{3, 2\}$ Simplex Lattice design. Again, this is not unexpected as most of the designs in classic textbooks are also D-optimal. The I-optimal design in table 1b has a less balanced feel, although there still is balance left to some extend. We see that the three pure mixtures all appear two times; the two first binary mixtures appear three times, while the last appears four times and there are two kinds of ternary mixtures.

Ternary plots, as shown below in figure 1, are a useful way of visualizing the differences between the two designs. For the D-optimal design we see in figure 1a that all the design points are located either at the vertices or at the edge centroids. For the I-optimal design, shown in figure 1b, we find next to the vertices and the centroids also two ternary mixtures, placed close to but not dead spot in the overall centroid of the simplex.



(a) D-optimal design

(b) I-optimal design

Figure 1: Ternary plots of generated designs

When a design is not orthogonal there will be an increase in the length of the confidence interval for the estimated parameters. For a mixture experiment, the proportion of one component in the mixture is unavoidable correlated with the proportions of the other component in the mixture, which makes it impossible to design perfect orthogonal designs. Therefore the increase in the length of the confidence interval will always be larger than zero. It is however interesting to keep this increase as small as possible to have less uncertainty on the estimated parameters. The fractional increase in CI length can be extracted from *JMP*, which we can use to calculate the VIF by means of the following relation:

$$\text{VIF} = (\text{Fractional Increase in CI Length} + 1)^2 \tag{2}$$

In table 2 the fractional increase in CI length and corresponding VIF are given for both the D-optimal design (table 2a) and the I-optimal design (table 2b). It should be noted that, due to the unavoidable perfect collinearity between the mixture components, the standard rule of thumbs for the VIF's are not very helpful. We can however use these figures to compare two designs. When looking at the table we see that

- all main effects and two-factor interactions in the D-optimal design have the same fractional increase in CI length. This is due to the balancedness of the design;

- this property does not returns for the I-optimal design, because this design is not balanced anymore and hence the estimation efficiency is different; and
- apart for the $x_2\,x_3$ interaction term, the D-optimal design outperforms the I-optimal design judging on these numbers.

Table 2: Fractional increase in CI length and VIF for the generated designs

(a) D-optimal design

Term	Fractional Increase in CI Length	VIF
x_1	1.449	6
x_2	1.449	6
x_3	1.449	6
$x_1\,x_2$	11.000	144
$x_1\,x_3$	11.000	144
$x_2\,x_3$	11.000	144

(b) I-optimal design

Term	Fractional Increase in CI Length	VIF
x_1	1.993	8.958
x_2	1.989	8.932
x_3	1.989	8.932
$x_1\,x_2$	11.216	149.220
$x_1\,x_3$	11.216	149.220
$x_2\,x_3$	10.703	136.971

Another useful way of comparing two designs is by using the relative variances of the factor estimates, as given in table 3. Again we see the same trends as observed already in table 2b. For the D-optimal design the relative variance of the estimates is the same for terms of the same order due to the balance in the design. Because the I-optimal design is less balanced, the relative variances are different. We also see that the D-optimal design outperforms the I-optimal design in terms of the relative variance on the estimates. This is not unexpected, because the D-optimal design is optimized to do exactly this.

Table 3: Relative variance of Estimates for the generated designs

(a) D-optimal design

Term	Relative variance of Estimate
x_1	0.333
x_2	0.333
x_3	0.333
$x_1\,x_2$	8.000
$x_1\,x_3$	8.000
$x_2\,x_3$	8.000

(b) I-optimal design

Term	Relative variance of Estimate
x_1	0.498
x_2	0.496
x_3	0.496
$x_1\,x_2$	8.290
$x_1\,x_3$	8.290
$x_2\,x_3$	8.290

The Fraction of Design Space plot shown in figure 2 gives the variance of prediction for a given percentage of the design space. When moving to the right of the x-axis, more points are included in the design space. Basically we are looking for a line as low as possible (low variance on prediction) and as “flat” as possible (even variance of prediction over the entire design space). The lower blue line is the curve for the I-optimal design, while the upper red line is the one for the D-optimal design. It is no surprise that the I-optimal design outperforms the D-optimal design, because it is optimized just to do this. However it should be noted that there is little difference between the two designs.

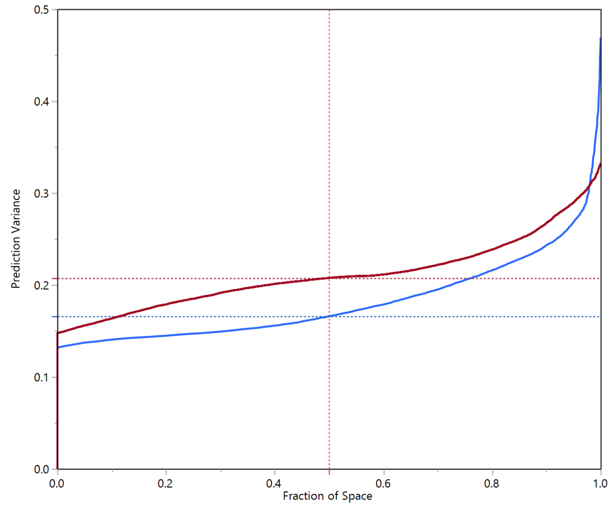


Figure 2: Fraction of Design Space plot for D-optimal (upper line) and I-optimal (lower line) design

We can compare the two designs based on the relative I-optimality of the D-optimal design in function of the I-optimal design, or

$$\begin{aligned}\text{Relative I-efficiency} &= \frac{\text{Average variance of prediction I-optimal design}}{\text{Average variance of prediction D-optimal design}} \\ &= \frac{0.180718}{0.210547} \\ &= 0.86\end{aligned} \tag{3}$$

which means that the I-optimal design is the better option in terms of average prediction variance and which is of course the same result as seen visually in figure 2.

Question 1.2

The three-component special cubic Scheffé model is given as

$$E\{\mathbf{Y}\} = \beta_1\,\mathbf{x}_1 + \beta_2\,\mathbf{x}_2 + \beta_3\,\mathbf{x}_3 + \beta_{12}\,\mathbf{x}_1\,\mathbf{x}_2 + \beta_{13}\,\mathbf{x}_1\,\mathbf{x}_3 + \beta_{23}\,\mathbf{x}_2\,\mathbf{x}_3 + \beta_{123}\,\mathbf{x}_1\,\mathbf{x}_2\,\mathbf{x}_3 \tag{4}$$

Based on this model, it is clear that only the I-optimal design can be used to estimate all the necessary parameters. This is because only the I-optimal designs contains ternary blends, and at least one is needed to estimate β_{123}.

A possible work-around regarding the D-optimal design would be to assign the two remaining runs to the centroid of the simplex and create as such a 20 run experiment. One should be aware however that by doing so any possible variation between the two experiments (day-to-day variation, ...) is completely confounded with the cubic interaction effect which could lead to wrong conclusions regarding this effect.

Question 1.3

For a blocked experiment we have to add a blocking factor to the second-order Scheffé model as defined in Question 1.1. For an additive block effect, denoted as γ, the adapted second order Scheffé model is given as

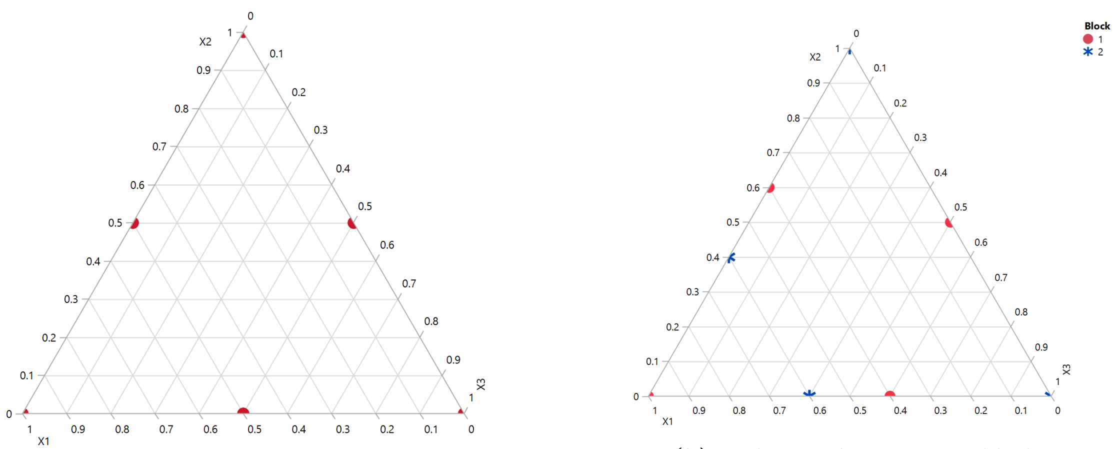
$$E\{\mathbf{Y}\} = \beta_1\,\mathbf{x}_1 + \beta_2\,\mathbf{x}_2 + \beta_3\,\mathbf{x}_3 + \beta_{12}\,\mathbf{x}_1\,\mathbf{x}_2 + \beta_{13}\,\mathbf{x}_1\,\mathbf{x}_3 + \beta_{23}\,\mathbf{x}_2\,\mathbf{x}_3 + \gamma\,\mathbf{z} \tag{5}$$

In table 4 a D-optimal eight-run design in two blocks is given for the second-order Scheffé model as defined above. Compared with the D-optimal design without blocks (see table 1a) we see that new formulations are included in the design (run 3, 4, 6, and 7). These points are selected most likely to reduce the confounding of the blocks with the interaction effects.

Table 4: Eight-run D-optimal design in two blocks

	Block	x_1	x_2	x_3
1	1	0.0	1.0	0.0
2	1	0.0	0.0	1.0
3	1	0.6	0.0	0.4
4	1	0.6	0.4	0.0
5	2	1.0	0.0	0.0
6	2	0.4	0.6	0.0
7	2	0.4	0.0	0.6
8	2	0.0	0.5	0.5

Below the ternary plots of both the 18-run D-optimal design without blocks (figure 3a) and the eight-run D-optimal design in two blocks (figure 3b) is given.



(a) D-optimal design

(b) Eight-run design in two blocks

Figure 3: Ternary plots of generated designs

In table 5 we can compare the fractional increase in CI length and the VIF's of the two designs. Firstly, the block effect has a fractional increase close to zero, which tells us that the block effect is relatively orthogonal to the other effects. It seems that for the three main effects the CI length does not increases dramatically, going from ≈ 1.5 to ≈ 1.90. Thus, blocking does not increases the uncertainty on the estimation too much. For the interaction effects two of the interaction parameters have a CI that is lower when blocking is used, but the third is substantial higher than the same when the design without blocks is used. The observation that the fractional increases in CI length for terms of the same order (main effects, ...) are not the same any more when a blocked design is used is because we lose the balance that was included in the original design, making the estimation of some effects more prone to uncertainty than others.

Table 6 shows more or less the same thing as table 5. There is a small increase in the relative variance for the main effects estimates, while the relative variance of the interactions is somewhat lower. The variances differ between terms of the same order in table 5b due to the loss of balance in the design.

Table 5: Fractional increase in CI length and VIF for the generated designs

(a) D-optimal design

Term	Fractional Increase in CI Length	VIF
x_1	1.449	6
x_2	1.449	6
x_3	1.449	6
$x_1\,x_2$	11.000	144
$x_1\,x_3$	11.000	144
$x_2\,x_3$	11.000	144

(b) 8 run D-optimal design

Term	Fractional Increase in CI Length	VIF
Block	0.213	1.472
x_1	1.853	8.139
x_2	1.954	8.727
x_3	1.954	8.727
$x_1\,x_2$	10.771	138.549
$x_1\,x_3$	10.771	138.549
$x_2\,x_3$	15.275	264.889

Table 6: Relative variance of Estimates for the generated designs

(a) D-optimal design

Term	Relative variance of Estimate
x_1	0.333
x_2	0.333
x_3	0.333
$x_1\,x_2$	8.000
$x_1\,x_3$	8.000
$x_2\,x_3$	8.000

(b) 8 run D-optimal design

Term	Relative variance of Estimate
Block	0.429
x_1	1.009
x_2	1.044
x_3	1.044
$x_1\,x_2$	4.162
$x_1\,x_3$	4.162
$x_2\,x_3$	5.754

Question 1.4

The model used to simulate the data is given as

$$\mathbf{Y} = 12.7\,\mathbf{x}_1 + 10.4\,\mathbf{x}_2 + 17.4\,\mathbf{x}_3 + 19.0\,\mathbf{x}_1\,\mathbf{x}_2 + 11.4\,\mathbf{x}_1\,\mathbf{x}_3 - 9.6\,\mathbf{x}_2\,\mathbf{x}_3 + \epsilon \tag{6}$$

for the imposed error we see that $\epsilon \sim \mathcal{N}(0, 2)$. Since our main interest is in maximizing Y and not so much in estimating the parameters correctly, we will use the I-optimal design as given in table 1b.

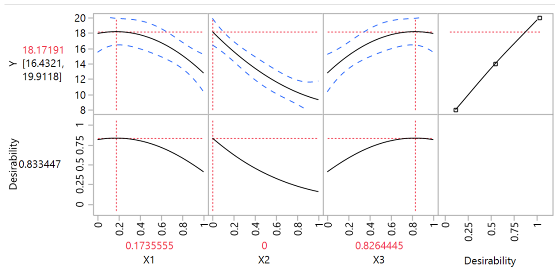
Table 7 gives a summary and some diagnostics of the fitted model. We see that the R^2 and the R_a^2 are satisfyingly high, the F-test suggests that the model parameters are highly significant different from zero and the high P-value of the lack-of-fit test is reassuring.

Table 7: Summary and diagnostics of fitted model

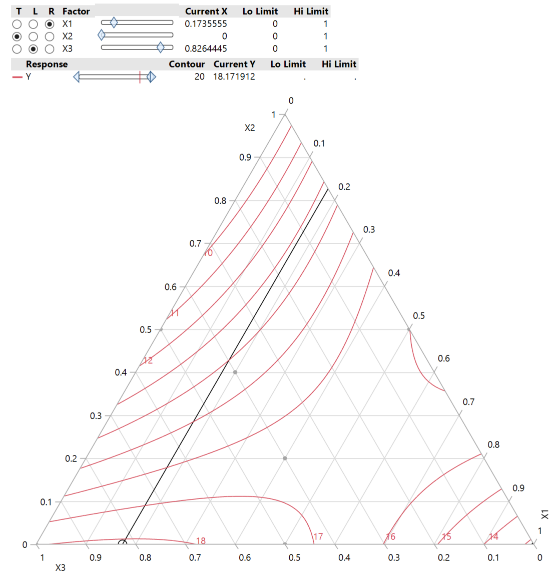
R^2	0.8475
R_a^2	0.7840
P-value F-test	$\leq$0.0001
P-value Lack-of-fit F-test	0.1760

Because we set the response variable Y to *"maximize"* when making the design, we can use the profiler and the *"desirability"* function of *JMP* to find the optimum formulation to achieve the highest yield. The profiler is shown in figure 4a. According to the profiler, the maximum yield lies between 16.43 and 19.91 and is achieved with the following formulation of the mixture: x_1: 0.17; x_2: 0.0; and x_3: 0.83.

In the mixture profiler as shown in figure 4b we have drawn the contour plots for yields between 7.0 and 20.0 and with an interval of 1.0. We see that the highest yields are above 18.0 and are achieved near the bottom left corner, indicating a very low proportion of x_2, a low proportion of x_1 and a high proportion of x_3 in the (yield-wise) most ideal mixtures.



(a) Prediction profiler (set on maximum desirability)



(b) Mixture profiler

Figure 4: *JMP* profilers

Part 2: Trend-robust Mixture Experiments

Question 2.1

In all experiments it is clear that runs will be separately and if only one test unit is available then these will be ran over time period. In some cases this time effect may be important, and the results may vary due to it. To account for this a time trend covariate can be added. In our model we assume a linear time trend. One should note that the inclusion of the term *linear* in linear time trend is very important here, if the time trend was not linear the design estimated would not be D-optimal. In the following a design will be generated for special cubic Scheffé model with 3 components and the inclusion of a time covariate. The special cubic Scheffé model with a time covariate is given as:

$$E\{\mathbf{Y}\} = \beta_1\,\mathbf{x}_1 + \beta_2\,\mathbf{x}_2 + \beta_3\,\mathbf{x}_3 + \beta_{12}\,\mathbf{x}_1\,\mathbf{x}_2 + \beta_{13}\,\mathbf{x}_1\,\mathbf{x}_3 + \beta_{23}\,\mathbf{x}_2\,\mathbf{x}_3 + \beta_{123}\,\mathbf{x}_1\,\mathbf{x}_2\,\mathbf{x}_3 \;+\; \gamma\, t \tag{7}$$

where t is the time at which the run is performed. Note that we assume that there is no interaction between the time trend and the mixture ingredient factors. From the model above it is clear that we need to specify eight parameters to be able to design an optimal experiment for this problem. As we can use 14 experimental runs, all parameters in this model are estimable. Table 8 shows the 14 run design matrix for a D-optimal design taking into account the linear time trend covariate.

When analysing the design in table 8, we see that it is nicely balanced. We see that the three pure mixtures, three binary mixtures and ternary mixture all appear twice. It also observe that the variable values from 1 - 7 are a mirror image of the values from 8 - 14, which indicates complete orthogonality for the linear time trend, this will be shown later by time trend robustness.

From the ternary plot of the D-optimal design in figure 5 we see all the design points are located either at the vertices, at the edge centroids or at the overall centroid of the simplex. This creates a very symmetrical design among the variables.

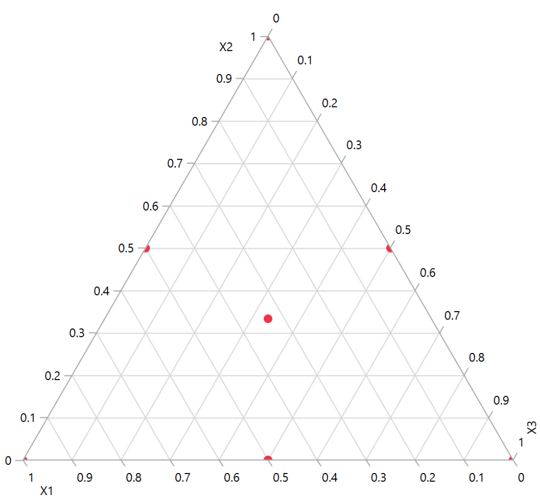


Figure 5: Ternary Plot of D-optimal design

Table 8: D-optimal design assuming a time trend (t)

x_1	x_2	x_3	t
0.50	0.00	0.50	−1.00
0.00	1.00	0.00	−0.85
0.00	0.50	0.50	−0.69
1.00	0.00	0.00	−0.54
0.33	0.33	0.33	−0.38
0.00	0.00	1.00	−0.23
0.50	0.50	0.00	−0.08
0.50	0.50	0.00	0.08
0.00	0.00	1.00	0.23
0.33	0.33	0.33	0.38
1.00	0.00	0.00	0.54
0.00	0.50	0.50	0.69
0.00	1.00	0.00	0.85
0.50	0.00	0.50	1.00

Question 2.2

In the following question we will be evaluating the time trend robustness of the D-optimal design used in Question 2.1. As the time trend is rarely an important part of our design, we usually try to minimize its effect (bias) in the model, so we can reduce the errors and provide better conclusions for the important parameter effects. When we run a D-optimal design in *JMP*, the program will aim to output a design that meets these requirements, by minimising the determinant of the variance-covariance matrix of the non-covariate parameter estimates, instead of all parameters. This is shown by:

$$var\left(\hat{\beta}\right) = \sigma_\epsilon^2\{\mathbf{X}'\mathbf{X} - \mathbf{X}'\mathbf{Z}(\mathbf{Z}'\mathbf{Z})^{-1}\mathbf{Z}'\mathbf{X}\}^{-1} \tag{8}$$

To minimize this value we look for as small a value as possible for $\mathbf{X'Z(Z'Z)^{-1}Z'X}$. To evaluate if the model is trend robust, the technique observed in table 9 below can be used.

Table 9: Testing for a Time Trend Robust model

x_1	x_2	x_3	t	$t \times x_1$	$t \times x_2$	$t \times x_3$	$t \times x_1x_2$	$t \times x_1x_3$	$t \times x_2x_3$	$t \times x_1x_2x_3$
0.50	0.00	0.50	−1.00	−0.50	0.00	−0.50	0.00	−0.25	0.00	0.00
0.00	1.00	0.00	−0.85	0.00	−0.85	0.00	0.00	0.00	0.00	0.00
0.00	0.50	0.50	−0.69	0.00	−0.35	−0.35	0.00	0.00	−0.17	0.00
1.00	0.00	0.00	−0.54	−0.54	0.00	0.00	0.00	0.00	0.00	0.00
0.33	0.33	0.33	−0.38	−0.13	−0.13	−0.13	−0.04	−0.04	−0.04	−0.01
0.00	0.00	1.00	−0.23	0.00	0.00	−0.23	0.00	0.00	0.00	0.00
0.50	0.50	0.00	−0.08	−0.04	−0.04	0.00	−0.02	0.00	0.00	0.00
0.50	0.50	0.00	0.08	0.04	0.04	0.00	0.02	0.00	0.00	0.00
0.00	0.00	1.00	0.23	0.00	0.00	0.23	0.00	0.00	0.00	0.00
0.33	0.33	0.33	0.38	0.13	0.13	0.13	0.04	0.04	0.04	0.01
1.00	0.00	0.00	0.54	0.54	0.00	0.00	0.00	0.00	0.00	0.00
0.00	0.50	0.50	0.69	0.00	0.35	0.35	0.00	0.00	0.17	0.00
0.00	1.00	0.00	0.85	0.00	0.85	0.00	0.00	0.00	0.00	0.00
0.50	0.00	0.50	1.00	0.50	0.00	0.50	0.00	0.25	0.00	0.00
				0.00	0.00	0.00	0.00	0.00	0.00	0.00

It is relatively easy to check if the design is trend-robust. To do so, we need to calculate the cross-products of the time coded effect (t) by each of the main and interactions effects and verify that each sum to zero. The required calculations are shown in the last seven columns of the table. Thus time and the experimental factors are almost completely orthogonal to each other.

A more analytical way of evaluating the trend robustness of a model is to use the trend robustness factor given below:

$$\text{Trend Robustness} = \left(\frac{|\mathbf{X'X} - \mathbf{X'Z(Z'Z)^{-1}} - \mathbf{Z'X}|}{|\mathbf{X'X}|} \right)^{\frac{1}{p}} \tag{9}$$

The $\mathbf{Z'Z}$ matrix here measures the information on the covariates in the design. If the covariates in the design are seen as nuisance parameters and aren't seen as important to estimate, a D-optimal criterion will be chosen which prioritises the effects of the experimental factors. This is the case with the time factor we are observing in our design.

As mentioned above instead of minimizing the variance-covariance matrix for both the covariate and experimental factors, will choose to solely minimize the experimental factors variance covariance matrix. This is found by maximizing the numerator of the equation for trend robustness factor (essentially allowing $\mathbf{X'X} - \mathbf{X'Z(Z'Z)^{-1}} - \mathbf{Z'X}$ equal to 0). If this is the case we will obtain a value of 1 for trend-robustness. For the model in question we find a trend robustness factor of 1 and hence observe a completely trend robust design.

Question 2.3

In this section we will compare the Time Trend Robust design from Question 2.1, with a randomly ordered design that also includes the time trend. When we ran the D-optimal design for the new model, we excluded the time trend initially and added it after the design was formulated. Table 10a shows the random order design for said model.

The design in Table 8 is time trend robust, thus we find no inflation of the standard errors of the main-effect and interaction effects estimates compared to a situation in which there is no time trend. With the random ordered model however we do observe an inflation. Table 10b compares the relative variances for the effect estimates in the presence of a linear time trend for the design generated in question 2.1 and the newly generated randomly ordered design. As can be seen the randomised design shows more variance than time trend robust model, indicating that the time trend covariate factor is correlated to other factors.

Table 10

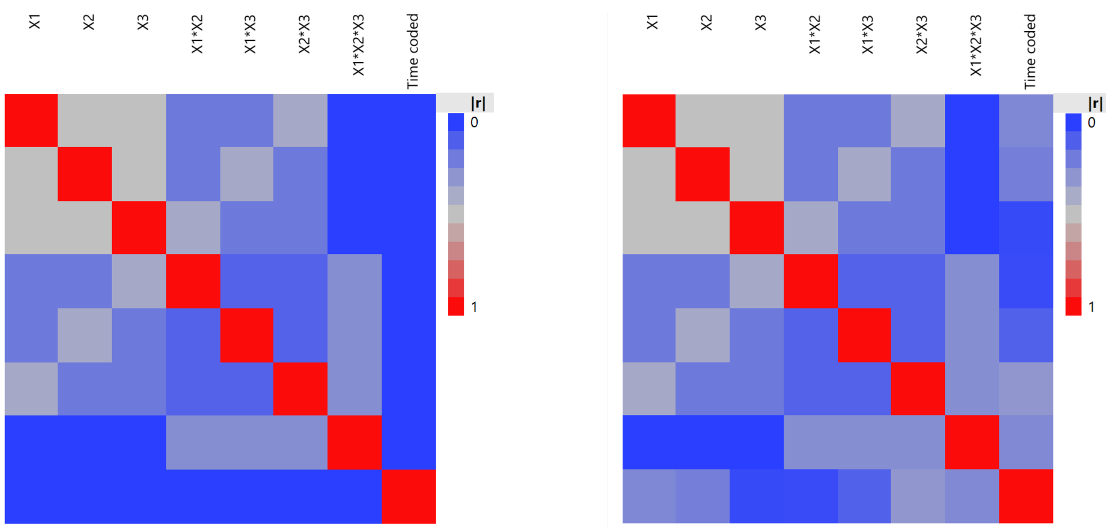
(a) D-optimal design for $q = 3$ and $n = 14$, ignoring the time trend (t)

x_1	x_2	x_3	t
0.33	0.33	0.33	−1.00
0.00	1.00	0.00	−0.85
0.00	0.50	0.50	−0.69
0.50	0.50	0.00	−0.54
0.50	0.00	0.50	−0.38
0.00	0.00	1.00	−0.23
1.00	0.00	0.00	−0.08
0.00	0.50	0.50	0.08
0.33	0.33	0.33	0.23
0.50	0.00	0.50	0.38
0.00	1.00	0.00	0.54
0.00	0.00	1.00	0.69
1.00	0.00	0.00	0.85
0.50	0.50	0.00	1.00

(b) Relative variance of estimates

Effect	Absence	Presence
x_1	0.534	0.500
x_1	0.506	0.500
x_1	0.513	0.500
t	0.230	0.186
x_1x_1	12.048	11.999
x_1x_1	12.348	11.999
x_1x_1	12.440	11.999
$x_1x_2x_3$	609.102	593.897

Similar conclusions can be drawn from the Color Map on Correlations, as shown in figure 6b which clearly shows an aliasing between several effects and the covariate time effect. On the other hand, the time robustness of the design from question 2.1 is clear from figure 6a



(a) Time robust design

(b) Randomized design

Figure 6: Color Map on Correlations of time robust designs

The Fraction of Design Space plot shown in Figure 7 gives the variance of prediction for a given percentage of the design space. The upper blue line is for the randomly ordered design, while the lower red line is for the time trend robust design constructed for question 2.1. We can see the time trend robust design outperforms the randomly ordered design, as the prediction variance is larger than the randomly ordered design at all fractions of the design space.

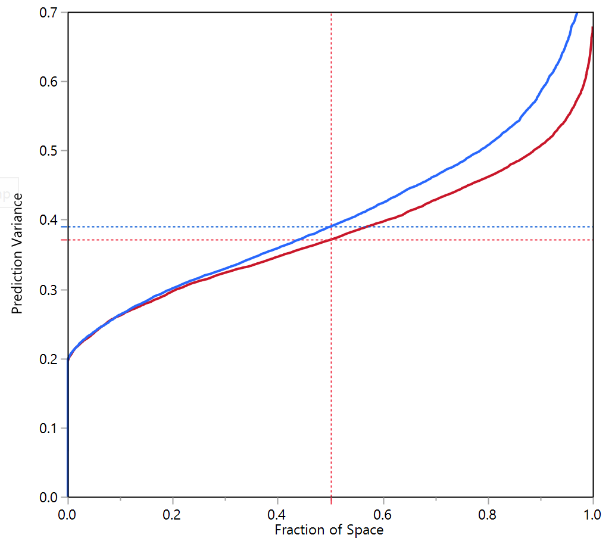


Figure 7: Fraction of design space plots for a D-optimal design including (lower) and a D-optimal design ignoring the time trend (upper)

All comparisons show that the model with a randomised order will have a worse prediction variance. This was to be expected, as when we remove the orthogonal nature of the design with a linear time trend, we will start detecting correlations between the time trend covariate factor and the main and interaction effects. This in turns introduces bias to the model and increases the errors we see in our parameter estimates, and hence reduces our ability to accurately predict the model.

The design generated without taking the covariate into account has a trend robustness factor of 0.973. Let us now define a Relative trend robustness as

$$\begin{aligned} \text{Relative trend robustness} &= \frac{\text{Trend robustness of design with } t}{\text{Trend robustness of design without } t} \\ &= \frac{1}{0.973} \\ &= 1.02 \end{aligned} \tag{10}$$

Which tells us that the trend robust design is slightly better than the design that does not take the covariate into account.

Question 2.4

When choosing what the worst order to perform the experimental runs in is, we look for a design that has similar runs at adjacent times. Doing this requires removing the perfect symmetry in the design and replacing it with something as asymmetrical as possible to maximise correlation between studies instead of minimising it. By doing this we are maximising the effect the time trend has on the model. Of course this only makes sense if the time trend is linear (which we are assuming).

To do so, we need to come up with some kind of metric to quantify the similarity between the design points. The metric we propose is a quantification of the relative distance $\mathcal{D}$ between the design points given their coördinates in the simplex. Let us first define the design point vector α_i as vectors with q elements, being the proportion of every component in the mixture. Thus for a design with n design points we find n design point vectors as

$$\alpha_i = [x_{1\,i} \quad x_{2\,i} \;\ldots\; x_{q\,i}] \quad \text{and} \quad \| \alpha_i \| = 1 \qquad \text{for each } i = 1, \ldots n \tag{11}$$

Using this definition, we find $\mathcal{D}_{i,j}$ as the length of the difference vector of two design point vectors α_i and α_j.

$$\mathcal{D}_{i,j} = \| \alpha_i - \alpha_j \| \qquad \text{for } i, j = 1, \ldots, n \text{ and } i \neq j \tag{12}$$

The worst possible design would be that design that minimizes the following sum of relative distances

$$\text{worst design} = \min \left(\sum_{i=1}^{n-1} \mathcal{D}_{i,i+1} \right) \tag{13}$$

As example, assume we want to calculate the relative distance between two design points on two different vertices. We find that

$$\alpha_1 = [\,1 \quad 0 \quad 0\,] \qquad \alpha_2 = [\,0 \quad 1 \quad 0\,]$$

and thus

$$\begin{aligned} \alpha_{1-2} &= \alpha_1 - \alpha_2 \\ &= [\,1 \quad -1 \quad 0\,] \end{aligned}$$

which yields

$$\begin{aligned} \mathcal{D}_{1,2} &= \| \alpha_{1-2} \| \\ &= 2 \end{aligned}$$

Table 11 is the worst design we could create using this metric. The final column is the value of the metric $\mathcal{D}_{i,i+1}$ for $i = 1, \ldots, 13$. The Trend robustness factor for this model is 0.593, meaning that the relative trend robustness of this design compared to the trend robust design from question 2.1 is a staggering 1.69.

Table 11: Worst design for $q = 3$ and $n = 14$, assuming a time trend (t)

x_1	x_2	x_3	t	$\mathcal{D}_{i,i+1}$
1.00	0.00	0.00	−1.00	0.00
1.00	0.00	0.00	−0.85	0.50
0.50	0.50	0.00	−0.69	0.00
0.50	0.50	0.00	−0.54	0.50
0.00	1.00	0.00	−0.38	0.00
0.00	1.00	0.00	−0.23	0.50
0.00	0.50	0.50	−0.08	0.00
0.00	0.50	0.50	0.08	0.50
0.00	0.00	1.00	0.23	0.00
0.00	0.00	1.00	0.38	0.50
0.50	0.00	0.50	0.54	0.00
0.50	0.00	0.50	0.69	0.17
0.33	0.33	0.33	0.85	0.00
0.33	0.33	0.33	1.00	