

TMA4267 Linear statistical models

Spring 2026

Thea Bjørnland

2 level factorial designs

- Aim: What affects our response Y , and by how much?
- Procedure:
 - Select k factors
 - Select **two** levels for each factor
 - "High" and "low" level
 - One experimental run: measure Y at all 2^k factor level combinations
 - Repeat if necessary

Example 1



Process Biochemistry 40 (2005) 779–788

PROCESS
BIOCHEMISTRY

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Biosorption of chromium using factorial experimental design

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Received 10 October 2003; accepted 5 February 2004

<https://doi.org/10.1016/j.procbio.2004.02.024>

2^3 full factorial design, duplicated

Wikipedia:

Biosorption can be defined as the ability of biological materials to accumulate heavy metals from wastewater through metabolically mediated or physico-chemical pathways of uptake.^[2] Though using biomass in environmental cleanup has been in practice for a while, scientists and engineers are hoping this phenomenon will provide an economical alternative for removing toxic heavy metals from [industrial wastewater](#) and aid in [environmental remediation](#).

Example 1: Biosorption of chromium using factorial experimental design

- Aim: Removal of Cr^{3+} (and Cr^{6+})
- Design: 2^3 factorial design
- Factors:
 - T : temperature (29 and 55 degrees celcius)
 - C : metal concentration (10 and 1200 mg/L)
 - pH : pH (2.0 and 6.0)
- Response: Efficiency of chromium removal after 6h exposition time

We first consider one experimental run, no interaction effects

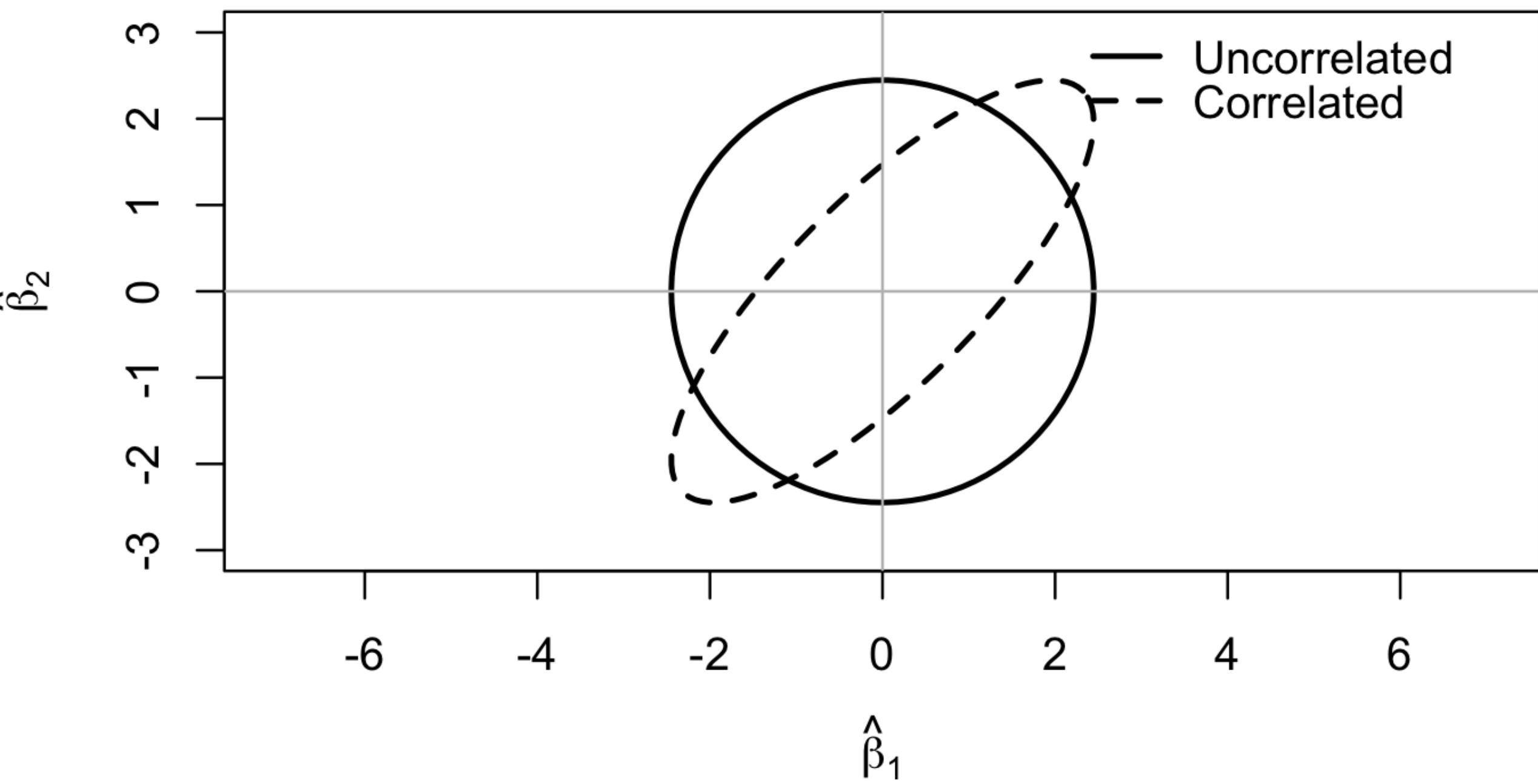
Design matrix, one experimental run ($2^3 = 8$ trials)

(Intercept)	Tmp	Conc	pH	Removal efficiency (%) ^a
1	1	1	1	75.2
1	1	1	-1	11.4
1	1	-1	1	62.7
1	1	-1	-1	82.9
1	-1	1	1	99.5
1	-1	1	-1	2.5
1	-1	-1	1	62.3
1	-1	-1	-1	73.4



y

Confidence Ellipses for Estimators



Example 1: Biosorption of chromium using factorial experimental design

Table 2

Experimental factorial design results for Cr^{3+}

Factor			Species		
T	C	pH	Cr^{3+}		
			Removal efficiency (%) ^a	Average (%)	
1	1	1	75.2	74.8	75.0
1	1	−1	11.4	5.4	8.4
1	−1	1	62.7	56.4	59.6
1	−1	−1	82.9	83.5	83.2
−1	1	1	99.5	99.5	99.5
−1	1	−1	2.5	17.3	9.9
−1	−1	1	62.3	68.9	65.6
−1	−1	−1	73.4	74.2	73.8

^a Experiments in duplicate.

Call:

```
lm.default(formula = y ~ Tmp + Conc + pH, data = data)
```

Residuals:

Min	1Q	Median	3Q	Max
-32.99	-21.52	-2.15	19.97	32.92

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)	
(Intercept)	59.369	7.075	8.392	2.3e-06	***
Tmp	-2.831	7.075	-0.400	0.6960	
Conc	-11.169	7.075	-1.579	0.1404	
pH	15.544	7.075	2.197	0.0484	*

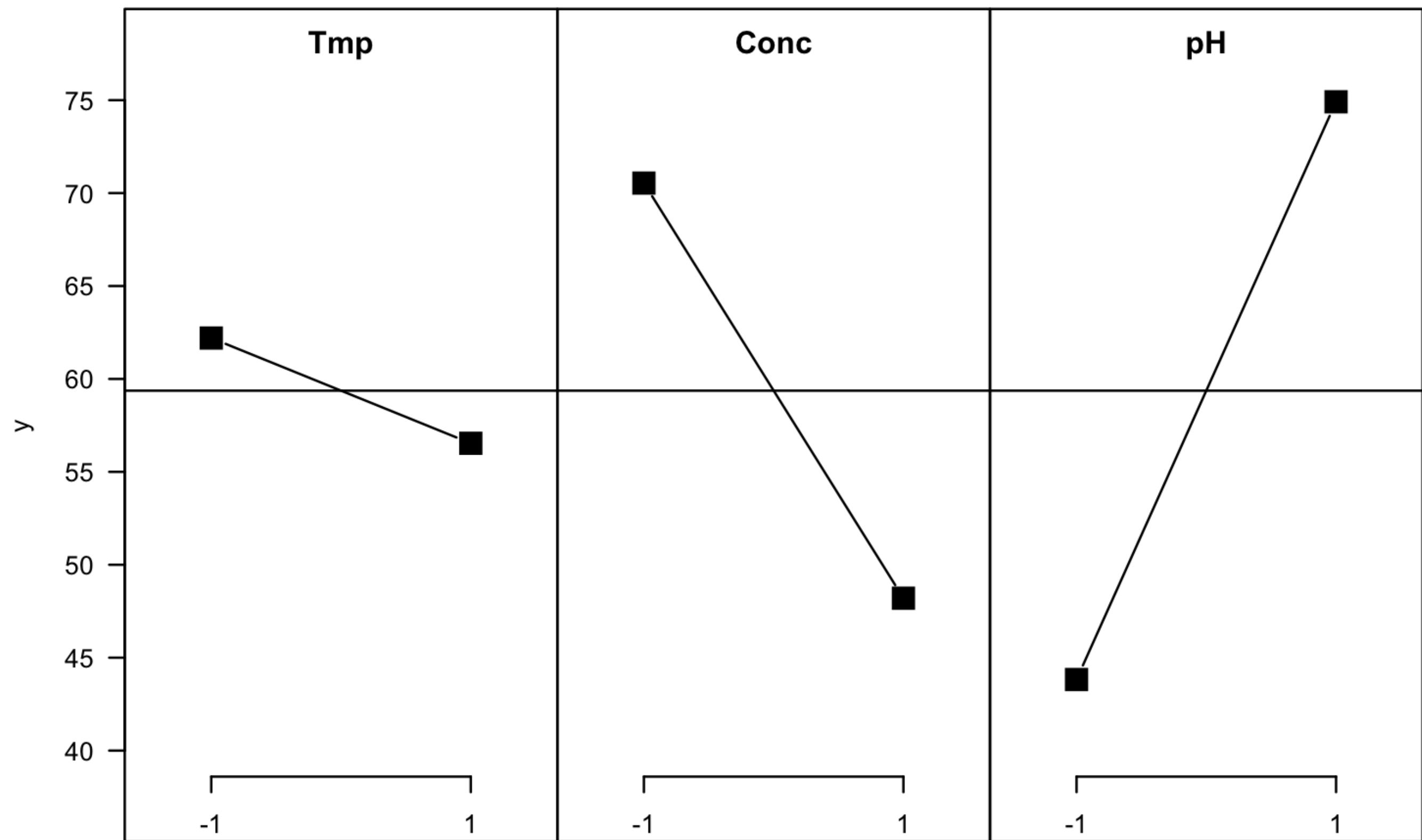
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 28.3 on 12 degrees of freedom

Multiple R-squared: 0.384, Adjusted R-squared: 0.23

F-statistic: 2.493 on 3 and 12 DF, p-value: 0.1098

Main effects plot for y



Design matrix

Main effects

Interaction effects

Run 1:

Run 2:

(Intercept)	Tmp	Conc	pH	Tmp:Conc	Tmp:pH	Conc:pH	Tmp:Conc:pH
1	1	1	1	1	1	1	1
1	1	1	-1	1	-1	-1	-1
1	1	-1	1	-1	1	-1	-1
1	1	-1	-1	-1	-1	1	1
1	-1	1	1	-1	-1	1	-1
1	-1	1	-1	-1	1	-1	1
1	-1	-1	1	1	-1	-1	1
1	-1	-1	-1	1	1	1	-1
1	1	1	1	1	1	1	1
1	1	1	-1	1	-1	-1	-1
1	1	-1	1	-1	1	-1	-1
1	1	-1	-1	-1	-1	1	1
1	-1	1	1	-1	-1	1	-1
1	-1	1	-1	-1	1	-1	1
1	-1	-1	1	1	-1	-1	1
1	-1	-1	-1	1	1	1	-1

Call:

```
lm.default(formula = y ~ Tmp * Conc * pH, data = data)
```

Residuals:

Min	1Q	Median	3Q	Max
-7.40	-1.05	0.00	1.05	7.40

Coefficients:

	Estimate	Std. Error	t value	Pr(> t)	
(Intercept)	59.3687	1.1515	51.557	2.22e-11	***
Tmp	-2.8313	1.1515	-2.459	0.03940	*
Conc	-11.1688	1.1515	-9.699	1.07e-05	***
pH	15.5437	1.1515	13.499	8.70e-07	***
Tmp:Conc	-3.6688	1.1515	-3.186	0.01288	*
Tmp:pH	-4.8063	1.1515	-4.174	0.00311	**
Conc:pH	23.5063	1.1515	20.413	3.47e-08	***
Tmp:Conc:pH	-0.9438	1.1515	-0.820	0.43619	

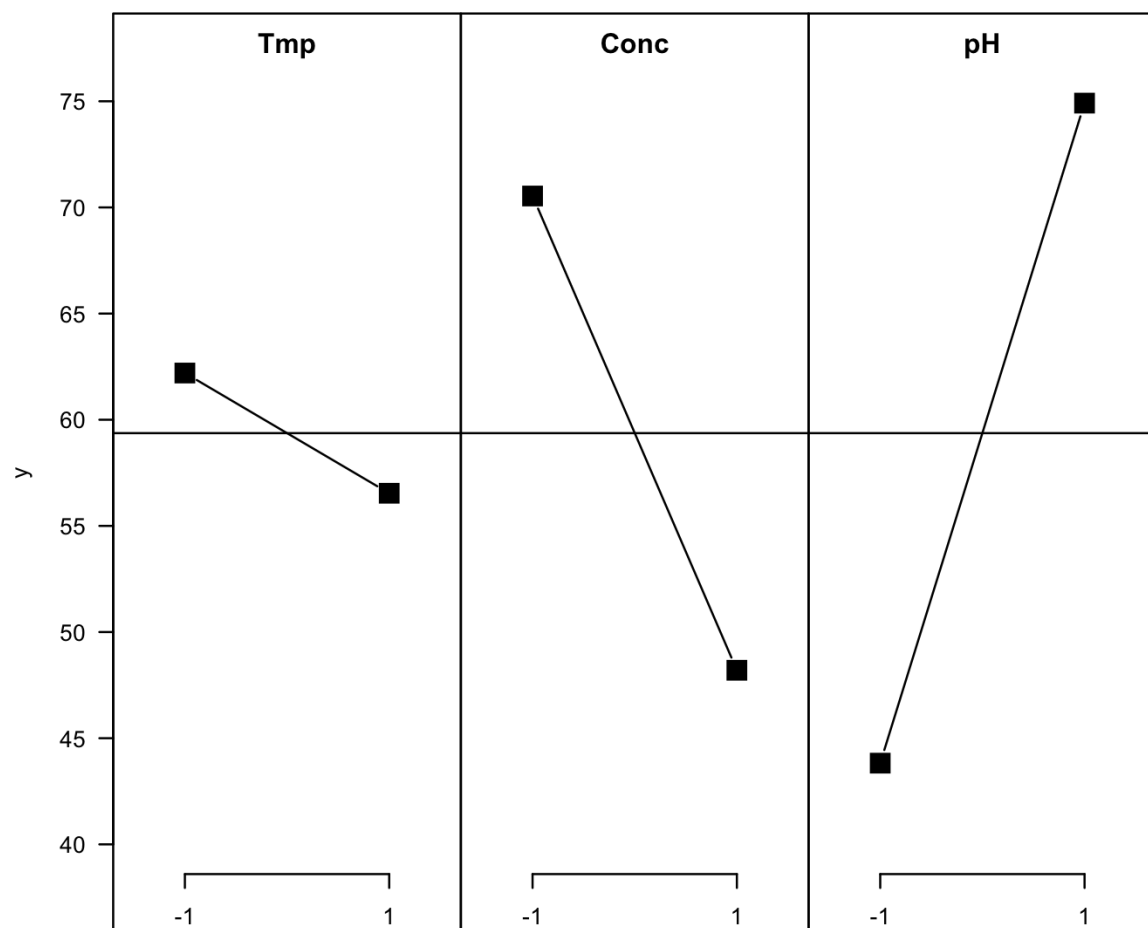
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 4.606 on 8 degrees of freedom

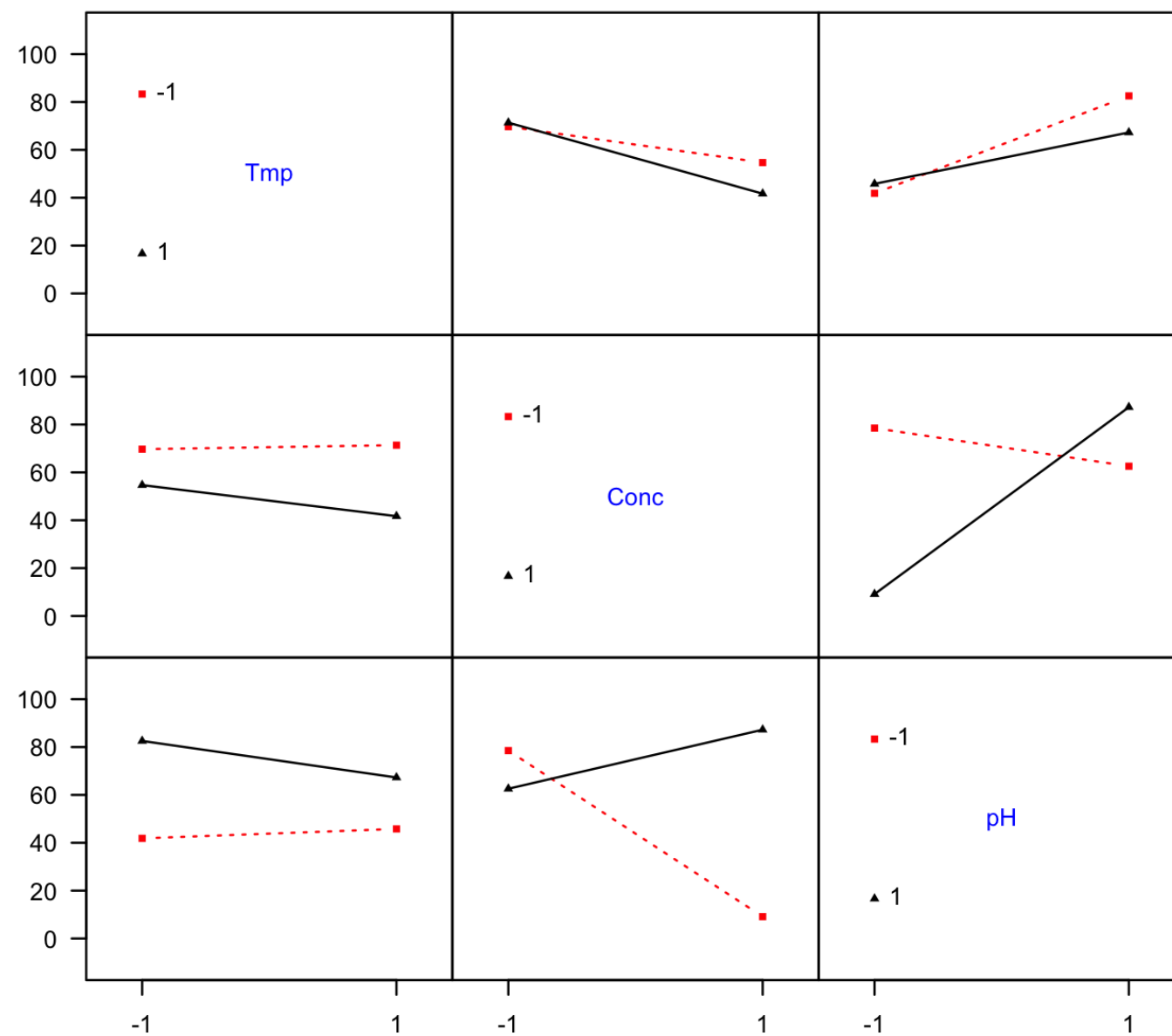
Multiple R-squared: 0.9891, Adjusted R-squared: 0.9796

F-statistic: 103.9 on 7 and 8 DF, p-value: 3.217e-07

Main effects plot for y



Interaction plot matrix for y



Example 1: Biosorption of chromium using factorial experimental design

Table 3
Statistical parameters for 2^3 design

Factor	Species			
	Cr^{3+}			
	Coefficient	Standard error	Effect	
Average	59.4	1.15	59.4	
T	-2.8	1.15	-5.6	
C	-11.2	1.15	-22.3	
pH	15.5	1.15	31.1	
TC	-3.7	1.15	-7.3	
TpH	-4.8	1.15	-9.6	
CpH	23.5	1.15	47.0	
$TCpH$	-0.94	1.15	-1.9	

Example 1: Biosorption of chromium using factorial experimental design

Table 4
Analysis of variance — full model fitting for Cr^{3+}

Factor	Statistics				
	Sum of squares	Degrees of freedom	Mean square (MS)	F_o	P -value
T	128.26	1	128.26	6.0	0.039397
C	1,995.86	1	1,995.86	94.1	0.000011
pH	3,865.73	1	3,865.73	182.2	0.000001
TC	215.36	1	215.36	10.1	0.012880
T pH	369.60	1	369.60	17.4	0.003106
C pH	8,840.70	1	8,840.70	416.7	0.000000
TC pH	14.25	1	14.25	0.7	0.436193
Error	169.73	8	21.22		
Total	15,599.47	15			

$F_o = \text{MS}_{\text{FACTOR}}/\text{MS}_{\text{ERROR}}$; $R^2 = 0.9891$; $R^2 \text{ adj.} = 0.9796$.

Blocking

What if the experiment had to be done in two different labs?

	(Intercept)	Tmp	Conc	pH	Tmp:Conc	Tmp:pH	Conc:pH	Tmp:Conc:pH
LAB 1:	1	1	1	1	1	1	1	1
	1	1	1	-1	1	-1	-1	-1
	1	1	-1	1	-1	1	-1	-1
	1	1	-1	-1	-1	-1	1	1
	1	-1	1	1	-1	-1	1	-1
	1	-1	1	-1	-1	1	-1	1
	1	-1	-1	1	1	-1	-1	1
	1	-1	-1	-1	1	1	1	-1
.....								
LAB 2:	1	1	1	1	1	1	1	1
	1	1	1	-1	1	-1	-1	-1
	1	1	-1	1	-1	1	-1	-1
	1	1	-1	-1	-1	-1	1	1
	1	-1	1	1	-1	-1	1	-1
	1	-1	1	-1	-1	1	-1	1
	1	-1	-1	1	1	-1	-1	1
	1	-1	-1	-1	1	1	1	-1

Blocking

What if the experiment had to be done in two different labs?

	(Intercept)	Tmp	Conc	pH	Tmp:Conc	Tmp:pH	Conc:pH	Tmp:Conc:pH
LAB 1 ???	1	1	1	1	1	1	1	1
	1	1	1	-1	1	-1	-1	-1
	1	1	-1	1	-1	1	-1	-1
	1	1	-1	-1	-1	-1	1	1
.....								
LAB 2 ???	1	-1	1	1	-1	-1	1	-1
	1	-1	1	-1	-1	1	-1	1
	1	-1	-1	1	1	-1	-1	1
	1	-1	-1	-1	1	1	1	-1

Blocking

What if the experiment had to be done in two different labs?

(Intercept)	Tmp	Conc	pH	Tmp:Conc	Tmp:pH	Conc:pH	Tmp:Conc:pH
1	1	1	1	1	1	1	1
1	1	1	-1	1	-1	-1	-1
1	1	-1	1	-1	1	-1	-1
1	1	-1	-1	-1	-1	1	1
1	-1	1	1	-1	-1	1	-1
1	-1	1	-1	-1	1	-1	1
1	-1	-1	1	1	-1	-1	1
1	-1	-1	-1	1	1	1	-1

Choose 3-factor interaction
to be confounded (aliased)
with lab

Example 3

Statistics
in Medicine

Research Article

Received 19 April 2012,

Accepted 11 June 2012

Published online 1 August 2012 in Wiley Online Library

(wileyonlinelibrary.com) DOI: 10.1002/sim.5526

Application of fractional factorial designs to study drug combinations

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Weng Kee Wong^c and Chih-Ming Ho^b

<https://doi.org/10.1002/sim.5526>

2^{6-1} fractional factorial design

Example 3: Application of fractional factorial designs to study drug combinations

- Response ('readout'): the percentage of GFP-positive* cells after combinatorial drug treatments
- Factors: 6 drugs for HSV-1 (low and high dosage)
- 2^{6-1} fractional factorial design
- Defining relation: ABCDEF = 1

Table II. Factors and levels for the initial two-level antiviral drug experiment.		
Factor	Levels (ng/mL)	
	Low (−1)	High (+1)
<i>A</i> = interferon alpha	3.12	50
<i>B</i> = interferon beta	3.12	50
<i>C</i> = interferon gamma	3.12	50
<i>D</i> = ribavirin	1560	2.5e4
<i>E</i> = acyclovir	312	5e3
<i>F</i> = tumor necrosis factor alpha	0.31	5

*GPF-positive means cells carry green fluorescent protein (GFP) gene, which occurs when infected with HSV-1 virus (Herpes simplex virus type 1)

Table I. Design and data for the initial two-level experiment: a 2^{6-1} design.

Run	Factor						readout
	<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>	<i>E</i>	<i>F</i>	
1	−1	−1	−1	−1	−1	−1	31.6
2	−1	−1	−1	−1	1	1	32.6
3	−1	−1	−1	1	−1	1	13.4
4	−1	−1	−1	1	1	−1	13.2
5	−1	−1	1	−1	−1	1	27.5
6	−1	−1	1	−1	1	−1	32.5
7	−1	−1	1	1	−1	−1	11.6
8	−1	−1	1	1	1	1	20.8
9	−1	1	−1	−1	−1	1	37.2
10	−1	1	−1	−1	1	−1	51.6
11	−1	1	−1	1	−1	−1	14.1
12	−1	1	−1	1	1	1	19.9
13	−1	1	1	−1	−1	−1	27.3
14	−1	1	1	−1	1	1	40.2
15	−1	1	1	1	−1	1	19.3
16	−1	1	1	1	1	−1	23.3
17	1	−1	−1	−1	−1	1	31.2
18	1	−1	−1	−1	1	−1	32.6
19	1	−1	−1	1	−1	−1	14.2
20	1	−1	−1	1	1	1	22.4
21	1	−1	1	−1	−1	−1	32.7
22	1	−1	1	−1	1	1	41.0
23	1	−1	1	1	−1	1	20.1
24	1	−1	1	1	1	−1	18.7
25	1	1	−1	−1	−1	−1	29.6
26	1	1	−1	−1	1	1	42.3
27	1	1	−1	1	−1	1	18.5
28	1	1	−1	1	1	−1	20.0
29	1	1	1	−1	−1	1	30.9
30	1	1	1	−1	1	−1	34.3
31	1	1	1	1	−1	−1	19.4
32	1	1	1	1	1	1	23.4
33	0	0	0	0	0	0	16.8
34	0	0	0	0	0	0	17.5
35	0	0	0	0	0	0	16.2

NB: 3 'center runs', not in our curriculum,
but useful for estimating variance

Example 3: Application of fractional factorial designs to study drug combinations

2.4. Analysis and results

As explained in Section 2.2, our design can estimate all six main effects, all 15 two-factor interactions, and 10 pairs of aliased three-factor interactions, assuming that four-factor and higher interactions are negligible.

Table III. Estimates for the initial two-level experiment.			
Effect	Estimates	Sum sq.	% Sum sq.
A	0.017	0.009	1
B	0.03	0.029	3.1
C	0.008	0.002	0.2
D	−0.141	0.636	68
E	0.046	0.068	7.3
F	0.024	0.018	1.9
AB	−0.022	0.015	1.6
AC	0.005	0.001	0.1
AD	0.019	0.011	1.2
AE	−0.009	0.002	0.3
AF	0.005	0.001	0.1
BC	−0.009	0.003	0.3
BD	0.008	0.002	0.2
BE	0.008	0.002	0.2
BF	−0.008	0.002	0.2
CD	0.024	0.018	1.9
CE	0.002	0	0
CF	0.003	0	0
DE	0.001	0	0
DF	0.014	0.006	0.7
EF	−0.001	0	0
ABC + DEF	−0.002	0	0
ABD + CEF	0.002	0	0
ABE + CDF	−0.006	0.001	0.1
ABF + CDE	−0.001	0	0
ACD + BEF	−0.017	0.009	0.9
ACE + BDF	−0.015	0.007	0.8
ACF + BDE	−0.012	0.004	0.5
ADE + BCF	−0.004	0	0
ADF + BCE	−0.009	0.002	0.2
AEF + BCD	0.014	0.007	0.7
Residuals	—	0.077	8.3
Total	—	0.935	100

Example 3: Application of fractional factorial designs to study drug combinations

Table III. Estimates for the initial two-level experiment.

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<i>A</i>	0.017	0.009	1
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<i>F</i>	0.024	0.018	1.9
<i>AB</i>	−0.022	0.015	1.6
<i>AC</i>	0.005	0.001	0.1
<i>AD</i>	0.019	0.011	1.2
<i>AE</i>	−0.009	0.002	0.3
<i>AF</i>	0.005	0.001	0.1
<i>BC</i>	0.000	0.002	0.2
<i>BD</i>	0.000	0.002	0.2
<i>BE</i>	0.000	0.002	0.2
<i>BF</i>	0.000	0.002	0.2
<i>CD</i>	0.000	0.002	0.2
<i>CE</i>	0.000	0.002	0.2
<i>CF</i>	0.000	0.002	0.2
<i>DE</i>	0.000	0.002	0.2
<i>DF</i>	0.014	0.006	0.7
<i>EF</i>	−0.001	0	0

Table III suggests that the effects of drugs *D* and *E* are the largest. The linear effect of drug *D* is the most significant with an estimate of three times the estimate of the next most significant drug, *E*, showing that drug *D* is very significant and important relative to the other drugs. Together, drugs *D* and *E* account for 75.3% of the total sum of squares in the data. Overall, the six main effects contribute 81.5% of the sum of squares, the 15 two-factor interactions contribute 6.8%, the 10 pairs of three-factor interactions contribute 3.2%, and the residuals account for 8.3%. In this antiviral experiment, the main effects dominate the system, and drug *D* alone accounts for 68.0% of the total sum of squares within the system.