TMA4267 Linear statistical models

25. march 2025

Thea Bjørnland

Last Thursday and today

Three scientific publications (2004, 2005, 2012)
illustrating the use of 2-level factorial experiments,
and motivating the theory that we cover in TMA4267

ELSEVIER
Process Biochemistry 40 (2005) 779–788
PROCESS BIOCHEMISTRY
www.elsevier.com/locate/procbio

Biosorption of chromium using factorial experimental design

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Received 10 October 2003; accepted 5 February 2004

2^3 duplicated (n = 16)

ELSEVIER
Journal of Hazardous Materials B135 (2006) 165–170
Journal of Hazardous Materials
www.elsevier.com/locate/jhazmat

Phosphate removal from water by fly ash: Factorial experimental design

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2^3 (n = 8)

Repetition

Example: 2^3 full factorial design

$$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_{12} x_1 x_2 + \beta_{13} x_1 x_3 + \beta_{23} x_2 x_3 + \beta_{123} x_1 x_2 x_3 + \varepsilon$$

The length of β is 8, if we do one run we have 8 observations.
To test for significance of effects we discussed 'sacrificing' some interactions, for example:

$$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_{12} x_1 x_2 + \beta_{123} x_1 x_2 x_3 + \varepsilon$$

If the experiment has to be **blocked**, we also took advantage of interactions, for example using AB and AC as blocking factors. Then, no main effect is confounded by the block effect, but all of the two-factor interactions are (AB*AC = BC)

Today: fractional factorial designs

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Assume now that we can only afford to do 4 experiments, which?

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

Example 3

Research Article

Statistics in Medicine

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

Application of fractional factorial designs to study drug combinations

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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: ABCDE = F

Table II. Factors and levels for the initial two-level antiviral drug experiment.

	Levels (ng/mL)	
Factor	Low (−1)	High (+1)
A = interferon alpha	3.12	50
B = interferon beta	3.12	50
C = interferon gamma	3.12	50
D = ribavirin	1560	2.5e4
E = acyclovir	312	5e3
F = 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)

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.

Effect aliasing is a consequence of using a fractional factorial design. A related concept is resolution, which captures the amount of aliasing. This half-fraction design has resolution VI, which allows the estimation of all main effects and two-factor interactions under the assumption that fourth-order and higher interactions are negligible. In general, the higher the resolution of a fractional factorial design, the less restrictive is the assumption regarding which interactions are negligible to obtain a unique interpretation of the data.

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.

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

	Factor						
Run	*A*	*B*	*C*	*D*	*E*	*F*	readout
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

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AE	–0.009	0.002	0.3
AF	0.005	0.001	0.1
BC	[illegible]	[illegible]	[illegible]
BD	[illegible]	[illegible]	[illegible]
BE	[illegible]	[illegible]	[illegible]
BF	[illegible]	[illegible]	[illegible]
CD	[illegible]	[illegible]	[illegible]
CE	[illegible]	[illegible]	[illegible]
CF	[illegible]	[illegible]	[illegible]
DE	[illegible]	[illegible]	[illegible]
DF	0.014	0.006	0.7
EF	–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.

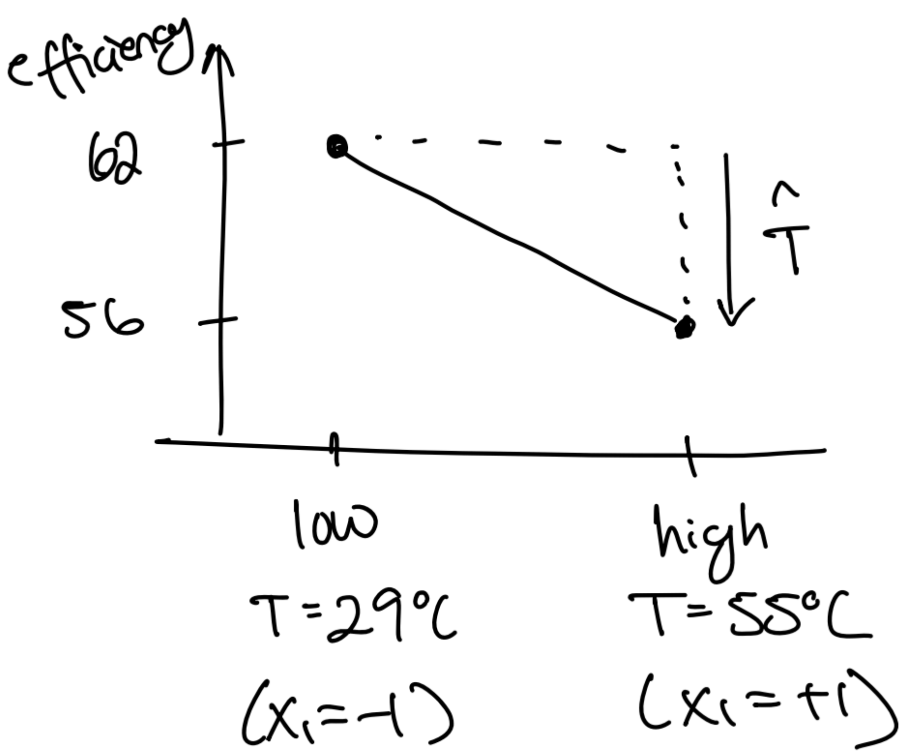
Example 3: Application of fractional factorial designs to study drug combinations

- "A follow-up experiment using a **blocked three-level fractional factorial design** indicates that tumor necrosis factor alpha has little effect and that HSV-1 infection can be suppressed effectively by using the right combination of the other five antiviral drugs"

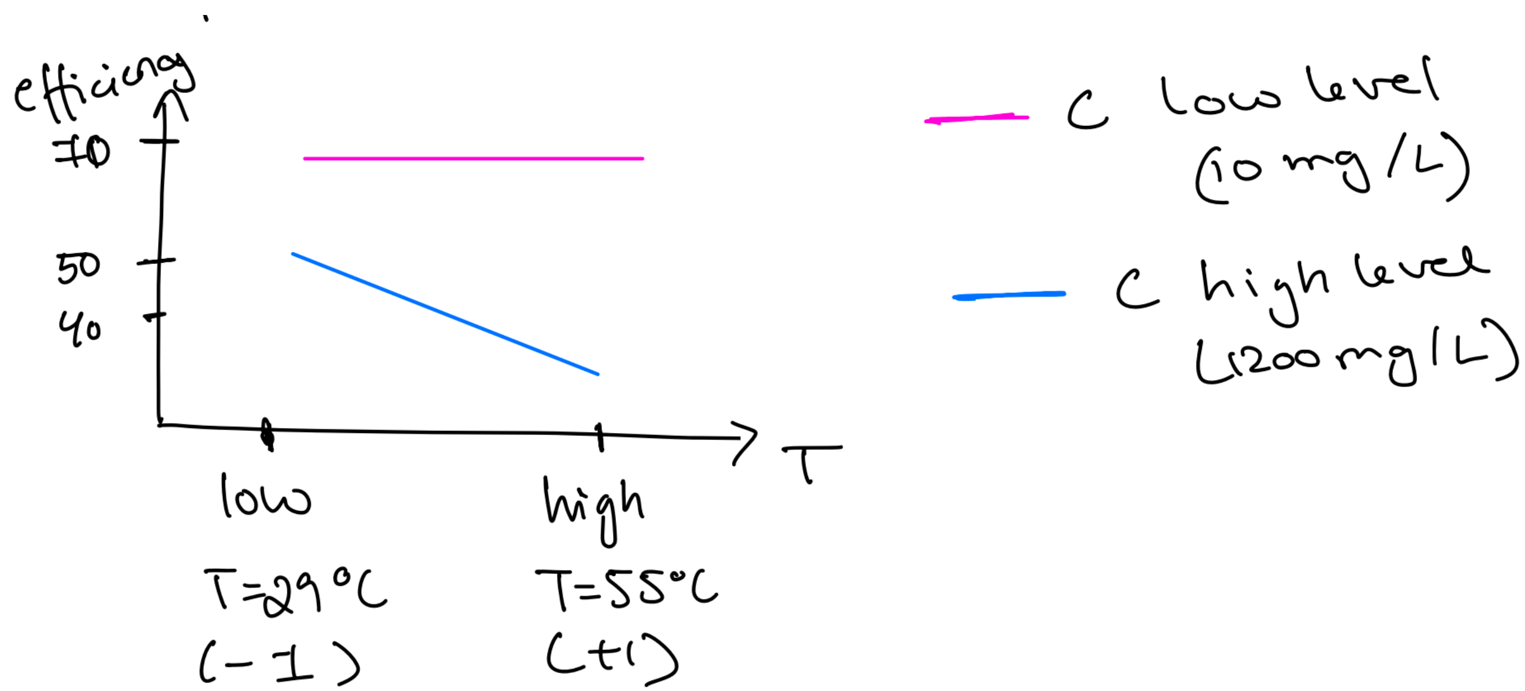
Presentation of results

Some R code for plotting

Main effects:



Interaction effects:



Presentation of results

Some R code for plotting

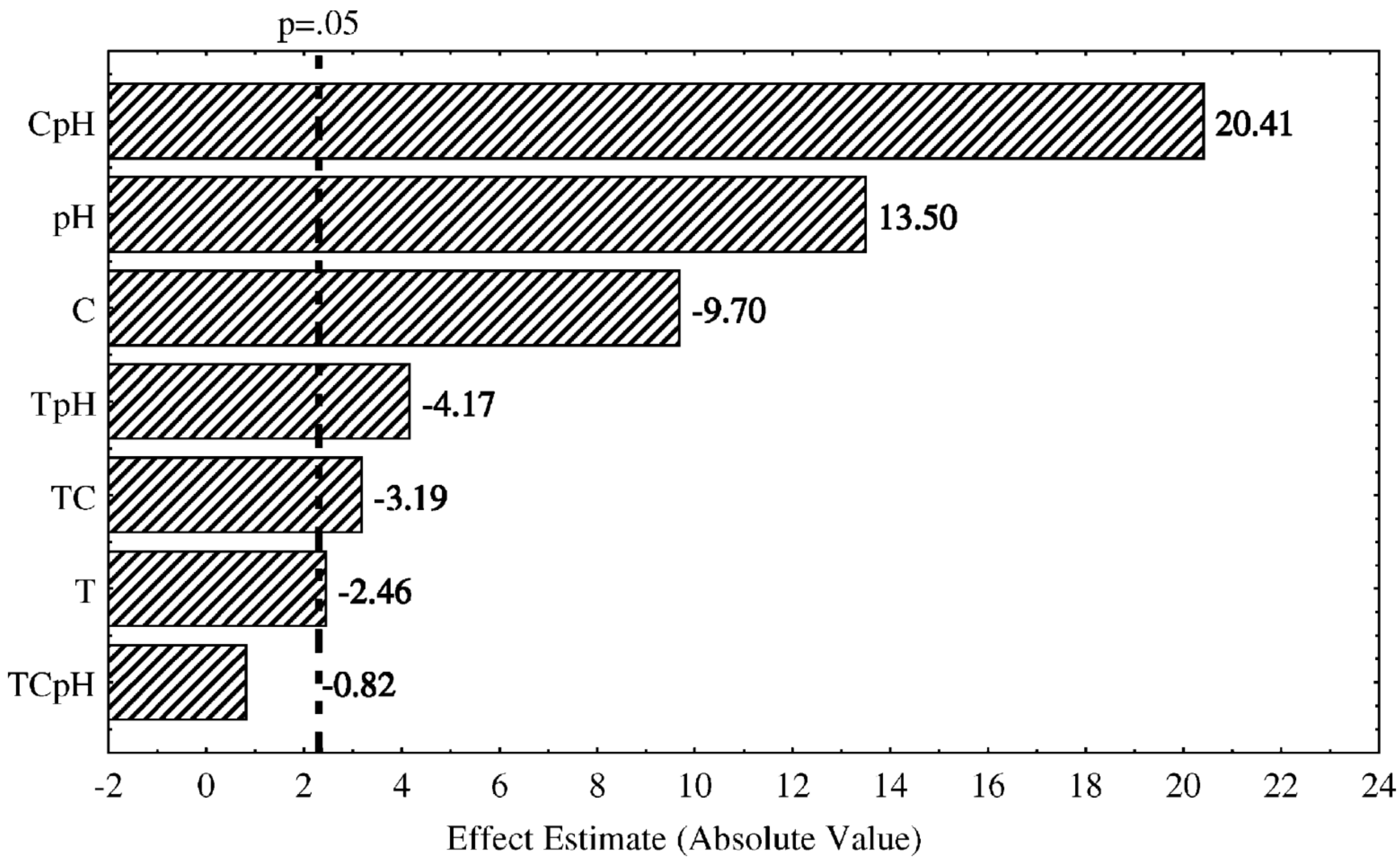


Fig. 1. Pareto chart of effects on the removal efficiency of Cr^{3+}.

NB: Thursday 27th

Use the lecture time (and room) to work on your project and ask questions.

Also use the exercise class.