Analysis of the Ranitidine Experiment

- Model:

LME

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

$$+\beta_{11} x_1^2 + \beta_{22} x_2^2 + \beta_{33} x_3^2 + \varepsilon$$

2fi

$(x_i)^2$ not $x_{i,2}$

QME

- Run 7 in Table 2 is dropped due to a blockage occurred in the seperation

faulty.

Table 8: Least Squares Estimates, Standard Errors, t Statistics and p-values, Ranitidine Experiment (Run 7 Dropped)

might not remove insignificant effects in the study of $\hat{y}$.

Effect	Estimate	Standard Error	t	p-value
intercept	2.1850	0.5785	3.78	0.00
β_1	1.1169	0.4242	2.63	0.03
β_2	0.7926	0.4242	1.87	0.09
β_3	0.0101	0.4262	0.02	0.98
β_{11}	2.7061	0.3788	7.14	0.00
β_{22}	−0.0460	0.3786	−0.12	0.91
β_{33}	−0.1295	0.3850	−0.34	0.74
β_{12}	1.4667	0.5890	2.49	0.03
β_{13}	−0.1918	0.5890	−0.33	0.75
β_{23}	0.2028	0.5890	0.34	0.74

- only effects involving factors pH and voltage are important

Analysis of the Ranitidine Experiment

- Fitted response surface:

$$\hat{y} = 2.0373 + \underbrace{1.1543}_{\hat{\beta}_1} x_1 + \underbrace{0.7552}_{\hat{\beta}_2} x_2 + \underbrace{2.7103}_{\hat{\beta}_{11}} x_1^2 + \underbrace{1.530}_{\hat{\beta}_{12}} x_1 x_2$$

- Contour plot

eigenvalues
(2.91, -0.20)
eigenvectors

$$\begin{bmatrix} -0.97 & -0.25 \\ -0.25 & 0.97 \end{bmatrix}$$

stationary pt.
(-0.49, 0.99)

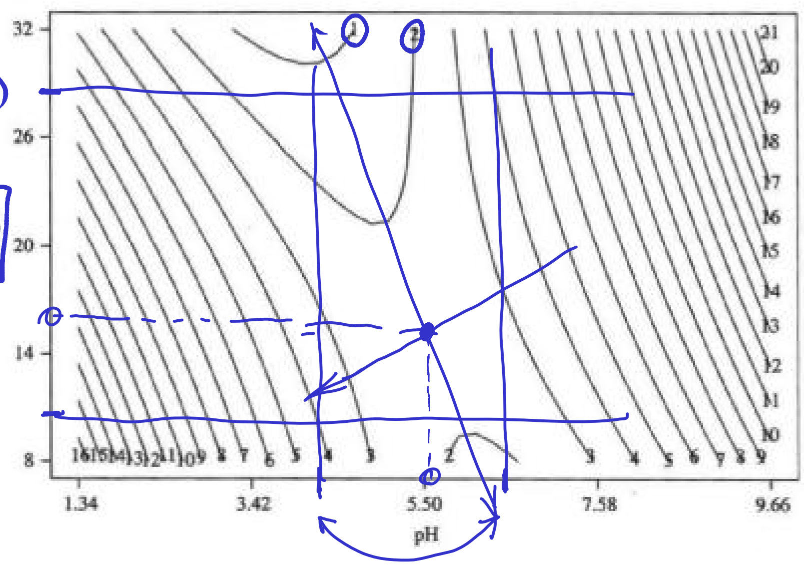


Figure 8: Estimated Response Surface, Ranitidine Experiment (Run 7 Dropped)

Analysis of the Ranitide Experiment

- A follow-up experiment in pH and voltage
  - Range of pH (A) was narrowed with levels (4.19, 4.50, 5.25, 6.00, 6.31)
  - Levels of voltage (B) were (11.5, 14.0, 20.0, 26.0, 28.5)
  - The coded values are $(-1.41, -1, 0, 1, +1.41)$

-1 +1 -1 +1

Table 9: Design Matrix and Response Data, Final Second-Order Ranitidine Experiment

Run order	Factor A	Factor B	ln CEF
2	1	−1	6.248
7	1	1	3.252
11	−1	−1	2.390
12	−1	1	2.066
3	−1.41	0	2.100
8	1.41	0	9.445
9	0	1.41	1.781
1	0	−1.41	6.943
4	0	0	2.034
5	0	0	2.009
6	0	0	2.022
10	0	0	1.925
13	0	0	2.113

Analysis of Final Ranitidine Experiment

- Model: $y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_{12} x_1 x_2 + \beta_{11} x_1^2 + \beta_{22} x_2^2 + \varepsilon$
- Analysis result:

cf. results in Table 8.

Table 10: Least Squares Estimates, Standard Errors, t Statistics and p-values, Final Second-Order Ranitidine Experiment

Effect	Estimate	Standard Error	t	p-value
intercept	2.0244	0.5524	3.66	0.0080
β_1	1.9308	0.4374	4.41	0.0031
β_2	−1.3288	0.4374	−3.04	0.0189
β_{12}	−0.6680	0.6176	−1.08	0.3153
β_{11}	1.4838	0.4703	3.15	0.0160
β_{22}	0.7743	0.4703	1.65	0.1437

not removed in the following analysis.

Analysis of the Ranitidine Experiment

- Fittied model:

$$\hat{y} = 2.0244 + 1.9308x_1 - 1.3288x_2 - 0.6680x_1x_2 + 1.4838x_1^2 + 0.7743x_2^2$$
$$= \hat{\beta}_0 + \mathbf{x}^T\mathbf{b} + \mathbf{x}^T\mathbf{B}\mathbf{x},$$

where
$$\mathbf{b} = (1.9308, -1.3288)^T$$

$1/2$

and
$$\mathbf{B} = \begin{bmatrix} 1.4838 & -0.3340 \\ -0.3340 & 0.7743 \end{bmatrix}.$$

- The stationary point is $\mathbf{x}_s = -\frac{1}{2}\mathbf{B}^{-1}\mathbf{b} = (-0.5067, 0.6395)^T$, which yields $y_s = 1.1104$
- The eigen-decomposition of $\mathbf{B}$ yields eigenvalues

$$\Lambda = diag(1.6163, 0.6418), \geq 0.$$

and eigenvectors
$$\mathbf{P} = \begin{bmatrix} -0.9295 & -0.3687 \\ 0.3687 & -0.9295 \end{bmatrix}.$$

Analysis of the Ranitidine Experiment

- Since both λ_1 and λ_2 are positive, $y_s = 1.1104$ is the minimum value which is achieved at $\mathbf{x}_s$ (pH of 4.87 and voltage of 23.84).

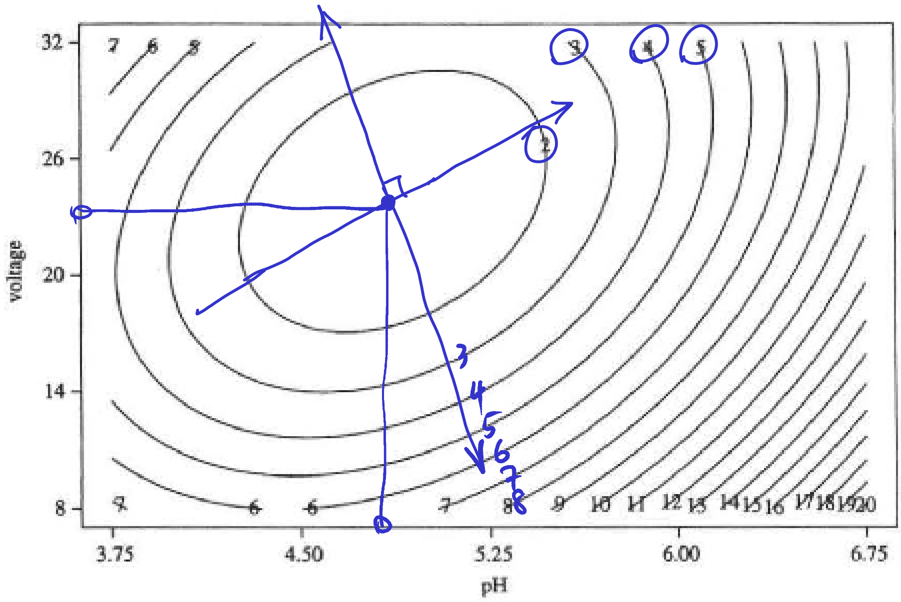
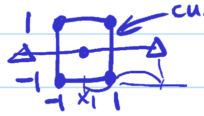


Figure 9: Estimated Response Surface, Final Second-Order Ranitidine Experiment

v Reading: textbook, 10.5



Central Composite Designs

most famous 2nd-order design

- The k input factors in coded form are denoted by $\mathbf{x} = (x_1, \ldots, x_k)$.
- A second-order model has $1 + k + k + \binom{k}{2} = \frac{(k+1)(k+2)}{2}$ parameters

make the 2nd-order model identifiable

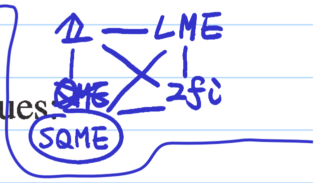
- A central composite design consists of the following three parts:
  1. n_f *cube points* (or *corner points*) with $x_i = -1$ or 1 for $i = 1, \ldots, k$. They form the *factorial portion* of the design.

     ← 2-level factorial design.
  2. n_c *center points* with $x_i = 0$ for $i = 1, \ldots, k$.
  3. $2k$ *star points* (or *axial points*) of the form $(0, \cdots, x_i, \cdots, 0)$ with $x_i = \alpha$ or $-\alpha$ for $i = 1, \ldots, k$.

     ← one-factor-at-a-time expt.
  - For the ranitidine experiment, the cube points are the 2^3 design, $n_c = 6$ and $\alpha = 1.66$.
  - $N = n_f + 2k + 1 \geq \frac{(k+1)(k+2)}{2} \Rightarrow n_f \geq \frac{k(k-1)}{2}$
- The central composite design can be used in a *single* experiment or in a *sequential* experiment.

LME: cube pts, axial pts
2fi's: cube pts
QME: cube pts, center pts, axial pts

Central Composite Designs



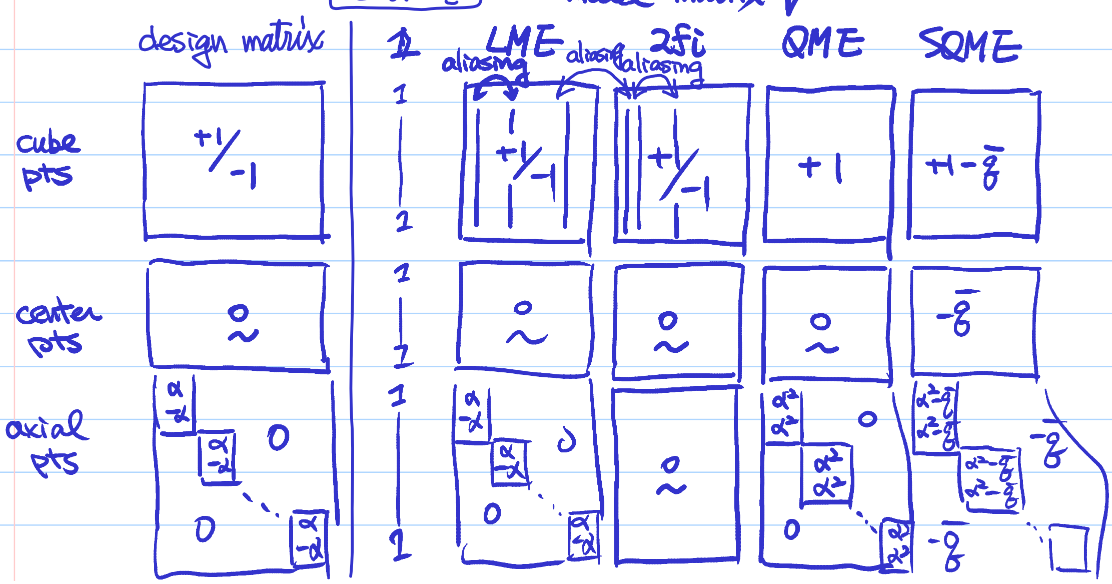
- In choosing a central composite design, there are three issues:
  1. choosing the factorial portion of the design,

     ← use what 2-level factorial design?
  2. determining the number of center points,

     ← n_c = ?
  3. determining the α value for the star points.

     ← α = ?

average: $\frac{n_f + 2\alpha^2}{N_c = n_f + 2k + n_c} = \bar{q}$



Central Composite Designs - Cube Points

cube +center

aliasing
LME↔LME
QME↔QME
LME↔2fi's

- Function of the three parts in fitting a second-order model:
  - cube points: estimating linear main effects and interactions
  - center points: estimating overall quadratic main effects and $\hat{\sigma}$ (replicates)
  - star points: estimating and dealiasing linear and quadratic main effects

why? LNp.3-38.

- **Theorem**. In any central composite design whose factorial portion is a 2^{k-p} design that does not use any main effect as a defining relation, the following parameters in (2) are estimable: β_0, β_i, β_{ii}, $i = 1, \ldots, k$, and one β_{ij} selected from each set of aliased effects for $i < j$. It is not possible to estimate more than one β_{ij} from each set of aliased effects.

regular

# of aliased sets $= 2^{k-p}$

The reason why resolution V design for cube pts is usually recommended

word of length 2 → I=AB ⇒ A=B, AC=BC
3 → I=ABC ⇒ A=BC.
4 → I=ABCD ⇒ AB=CD ← cannot be dealiased.
5 → I=ABCDE ⇒ no aliasing ...

Central Composite Designs - Cube Points

- It is interesting to note that
  - even defining words of length two (for $k = 2$ case) are allowed and
  - words of length four are worse than words of length three.

only consider identifiability

- Any resolution III design whose defining relation does not contain words of length four is said to have **resolution** III*.
- *Any central composite design whose factorial portion has resolution III* is a second-order design.*

regular 2^{k-p} designs

why? LNp.3-45

- For the estimability of the parameters in the second-order model, one can only use the cube and star points of the central composite design if $\alpha \neq \sqrt{k}$. Such a design is referred to as a *composite design* and its run size is $n_f + 2k$.
  - the smallest designs without center points in the Table 11 for k= 2, 3, 5, 6 and 7 have the minimal run size and are saturated.

Central Composite Designs - Cube Points

Table 11: Central Composite Designs for $2 \le k \le 7$

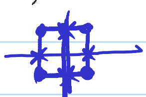
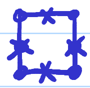
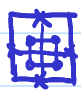
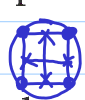
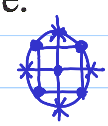
k	$(k+1)(k+2)/2$	N ($N-1$)	n_f ($k(k-1)/2$)	Factorial Portion (cube points)
2	6	7	2	$2^{2-1}(\mathbf{I}=AB)$
2	6	9	4	2^2
3	10	11	4	$2^{3-1}_{III}(\mathbf{I}=ABC)$
3	10	15	8	2^3
4	15	17	8	$2^{4-1}_{III}(\mathbf{I}=ABD)$ ~~MA 2^{4-1}_{IV} (I=ABCD)~~
*4	15	20	11	11×4 submatrix of 12−run PB design
4 ✓	15	25	16	2^4
*5	21	22	11	11×5 submatrix of 12−run PB design
*5	21	23	12	12×5 submatrix of 12−run PB design
5 ✓	21	27	16 (10)	$2^{5-1}_{V}(\mathbf{I}=ABCDE)$ ~~2^5~~
6	28	29	16	$2^{6-2}_{III^*}(\mathbf{I}=ABE=CDF=ABCDEF)$ ~~2^{6-2}_{IV} MA~~
*7	36	37	22	22×7 submatrix given in Table 10A.2 (textbook)
*7	36	38	23	23×7 submatrix given in Table 10A.3 (textbook)
7 ✓	36	47	32	$2^{7-2}_{III^*}(\mathbf{I}=ABCDF=DEG)$ ~~MA 2^{7-2}_{IV}~~

small composite design (use OA, non-regular design, as the cube pts)

15 → 25 (+10); 21 → 27 (+6); 36 → 47 (+11)

24-run PB design

Central Composite Designs - Axial Points

- The efficiency of the parameter estimates is increased by pushing the axial points toward the extreme ← of the expt'al region.
- In general, α should be chosen between 1 and $\sqrt{k}$ and rarely outside this range.
  levels of cube pts = 1; length of cube pts. $(0,\cdots 0,\sqrt{k},0\cdots 0) \to \| \| = \sqrt{k}$
  
- For α=1, the axial points are placed at the center of the faces of the cube.
  - The design is therefore called the *face center cube*.
  - They are the only central composite designs that require three levels.
  - They are effective designs if the design region is a cube.
    $\alpha=1$   $\alpha>1$.
- For $\alpha=\sqrt{k}$, the axial points and cube points lie on the same sphere.
  - The design is often referred to as a *spherical design*.
    $\alpha=1$   $\alpha=\sqrt{k}$
  - They are effective designs if the design region is spherical.
  - For large k, this choice should be taken with caution.
    ∵ axial pts might be far away from the center
- In general the choice of α depends on the geometric nature of and the practical constraints on the design region.