Response Surface Methodology: Central Composite Designs

BIOE 498/598 PJ

Spring 2022

Last time: The method of steepest ascent

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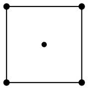

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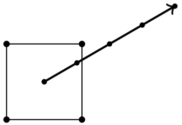

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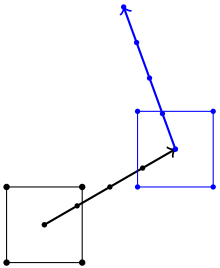

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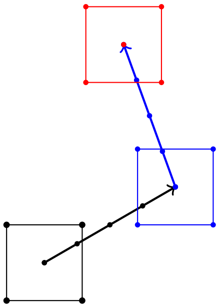

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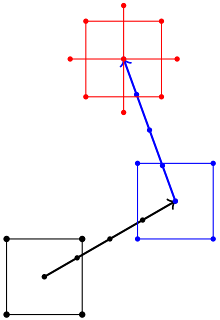
- **Today**: Fitting a model to a curved response surface.



When is a first order model not good enough?

- The FF designs used for process improvement are usually augmented by **center points** — repeated runs at the design center $(0, 0)$.
- Center points serve two purposes:
  1. Estimate the *pure error* via the standard deviation of the repeated runs.
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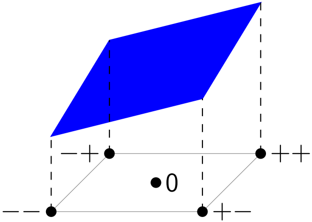

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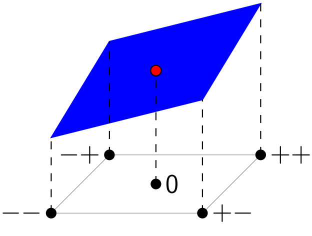

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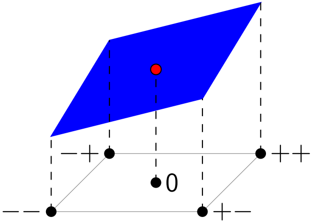

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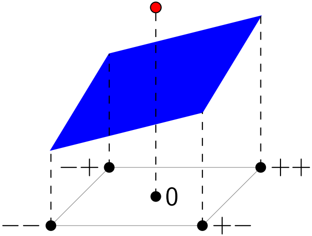

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4. $$F_{\text{curve}} = \frac{SS_{\text{curve}}/\text{DF}(SS_{\text{curve}})}{SS_{\text{error}}/\text{DF}(SS_{\text{error}})}$$

Example: Testing for curvature (Myers 2009)

temp	time	yield
$-$	$-$	39.3
$-$	$+$	40.0
$+$	$-$	40.9
$+$	$+$	41.5
0	0	40.3
0	0	40.5
0	0	40.7
0	0	40.2
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Example: Testing for curvature (Myers 2009)

1. $\bar{y}_{\text{fact}} = (39.3 + 40.0 + 40.9 + 41.5)/4 = 40.425$
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`pf(0.0605, 1, 4, lower.tail=FALSE)` $\rightarrow p < 0.818$.

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5. Switch to a **curved** model and *Response Surface Methodology* (RSM).

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$$y = 20 + 3.6x_1 - 1.8x_2 - 0.6x_1x_2$$

Set $x_2 = 0$, then $y \to \infty$ as $x_1 \to \infty$.

Nonlinear response surfaces

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- **We are not claiming that f is a particular shape.** Rather, we claim that an approximation is "good enough" over our domain of interest.

Approximating f with a general quadratic

Let's find the second-order Taylor series of $f(x_1, x_2)$ centered at zero:

$$f(x_1, x_2) \approx \; f|_0 \; + \; \left.\frac{\partial f}{\partial x_1}\right|_0 x_1 + \; \left.\frac{\partial f}{\partial x_2}\right|_0 x_2 + \; \frac{1}{2}\left.\frac{\partial^2 f}{\partial x_1^2}\right|_0 x_1^2 + \; \frac{1}{2}\left.\frac{\partial^2 f}{\partial x_2^2}\right|_0 x_2^2 + \; \frac{1}{2}\left.\frac{\partial^2 f}{\partial x_1 \partial x_2}\right|_0 x_1 x_2$$

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$$y = \beta_0 + \sum_{i=1}^{k} \beta_i x_i + \sum_{i=1}^{k} \beta_{ii} x_i^2 + \sum_{j=1}^{k} \sum_{i=1}^{j-1} \beta_{ij} x_i x_j.$$

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- This model has $1 + 2k + k(k-1)/2$ parameters, so RSM designs must have at least this many runs.

The Central Composite Design (CCD)

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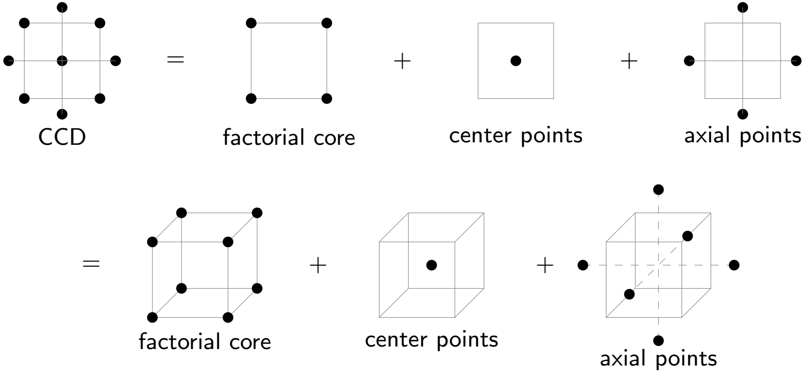
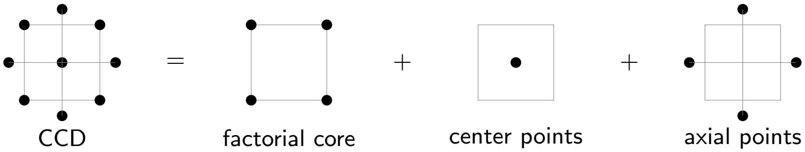


Parts of the CCD



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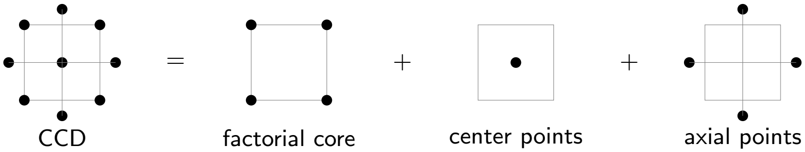

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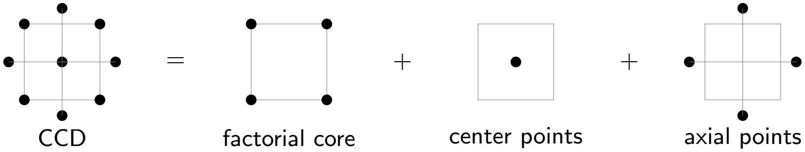

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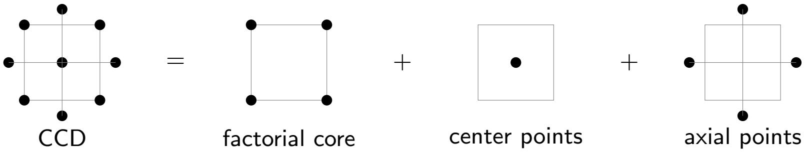

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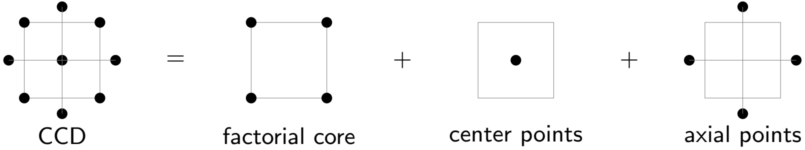

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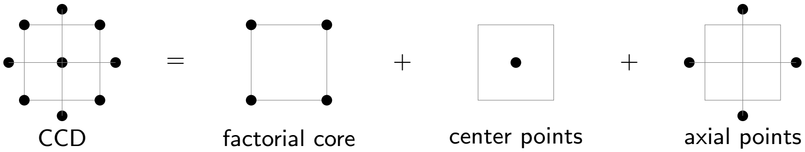

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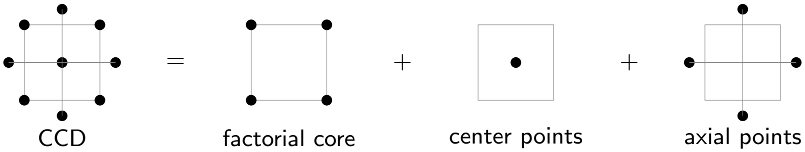
Parts of the CCD



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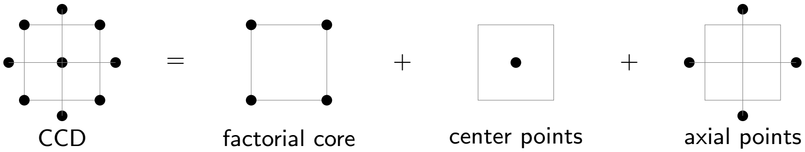

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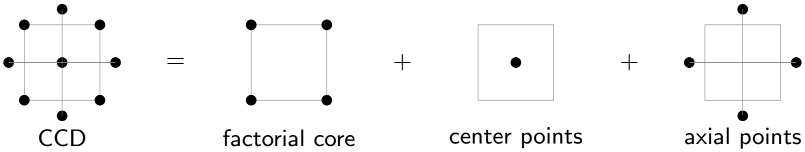

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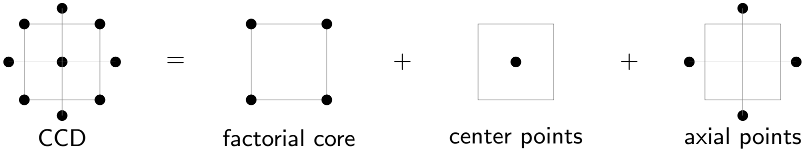

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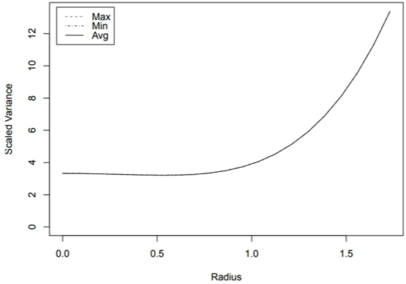

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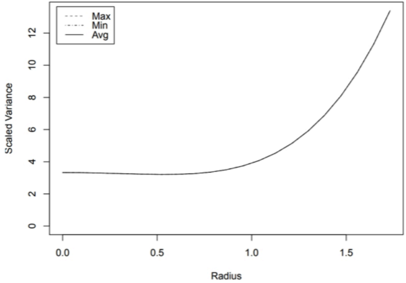

- Choosing the correct number of center points in a CCD ensures uniform precision.

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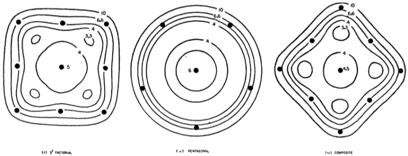

FIG. 2. Variance contours for some 2 dimensional designs

Image from Box and Hunter 1957.

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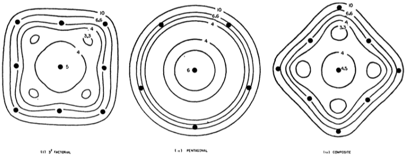

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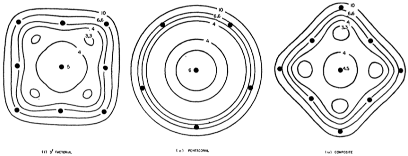

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- Designs where the variance only depends on the radius are called **rotatable designs**.
- A CCD with F factorial points is rotatable when $\alpha = \sqrt[4]{F}$.

Rotatable, uniform precision CCDs

factors (k)	2	3	4	5	$5-1$	6
factorial points	4	8	16	32	16	64
axial points	4	6	8	10	10	12
center points	5	6	7	10	6	15
axial distance (α)	1.414	1.682	2.000	2.378	2.000	2.828

factors (k)	$6-1$	7	$7-1$	8	$8-1$	$8-2$
factorial points	32	128	64	256	128	64
axial points	12	14	14	16	16	16
center points	9	21	14	28	20	13
axial distance (α)	2.378	3.364	2.828	4.000	3.364	2.828

Factor levels in a CCD

Each factor in the CCD will be set at five levels:

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Unlike a 2-level design, the coded units in a CCD have meaning!

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Let's say we're designing a combination screening of three drugs. The absolute widest concentration range we can use for drug A is $[-3.2, 1.0]$ on a $\log_{10}$-μM scale. What are the five levels assuming a full-factorial CCD?

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code:	$-\alpha$	-1	0	1	α
$\log_{10}$-μM:	-3.2	-2.4	-1.1	0.2	1.0