Response Surface Methodology: Central Composite Designs

BIOE 498/598 PJ

Spring 2021

Last time: The method of steepest ascent

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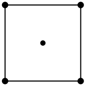

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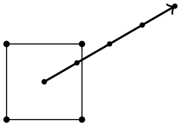

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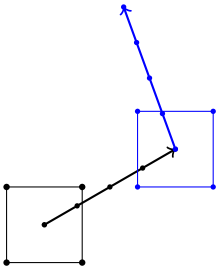

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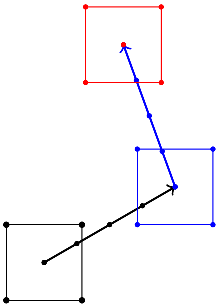

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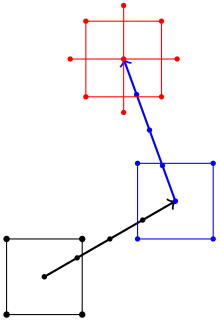
- **Today**: Fitting a model to a curved response surface.



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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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- Usually we don't know f, so we approximate it with a simpler function.
- **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:

$$f(x_1,x_2) \approx \underbrace{f|_0}_{\beta_0} + \underbrace{\left.\frac{\partial f}{\partial x_1}\right|_0}_{\beta_1} x_1 + \underbrace{\left.\frac{\partial f}{\partial x_2}\right|_0}_{\beta_2} x_2 + \underbrace{\left.\frac{1}{2}\frac{\partial^2 f}{\partial x_1^2}\right|_0}_{\beta_{11}} x_1^2 + \underbrace{\left.\frac{1}{2}\frac{\partial^2 f}{\partial x_2^2}\right|_0}_{\beta_{22}} x_2^2 + \underbrace{\left.\frac{1}{2}\frac{\partial^2 f}{\partial x_1 \partial x_2}\right|_0}_{\beta_{12}} x_1 x_2$$

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- The function f and its derivatives are unknown, so we fit the parameters β with a linear model.
- In general we will have k factors and the quadratic approximation will be

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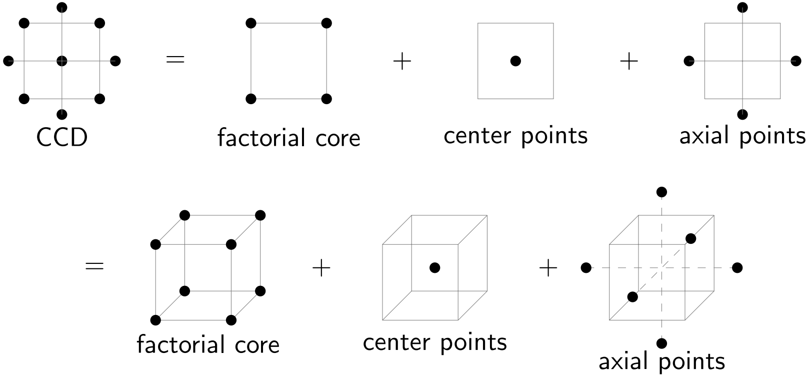
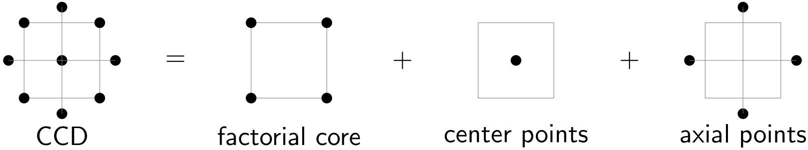


Parts of the CCD



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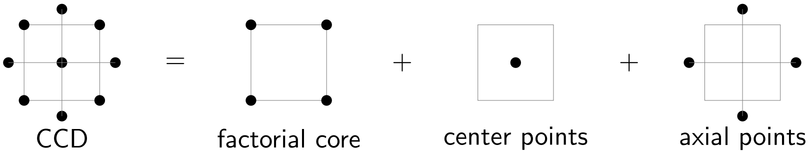

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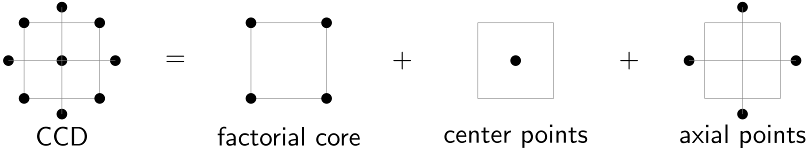

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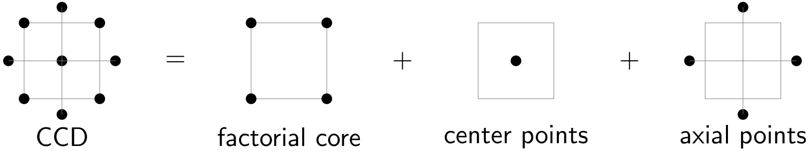

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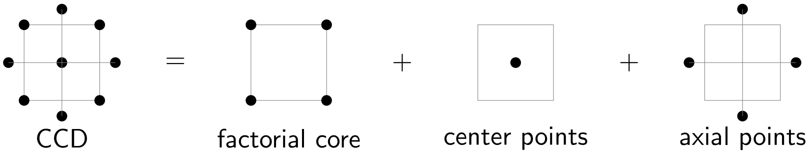

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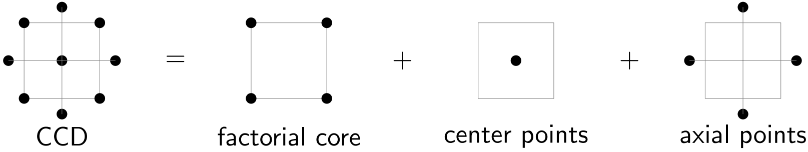

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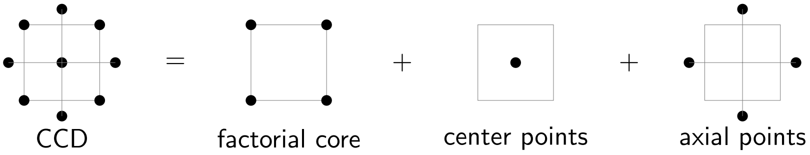

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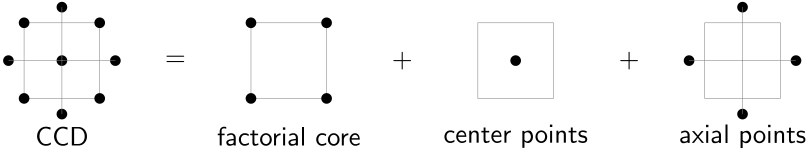

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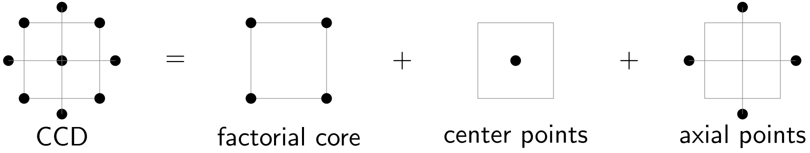

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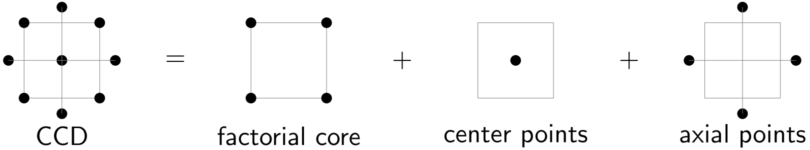

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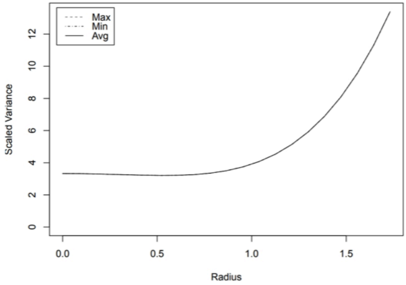

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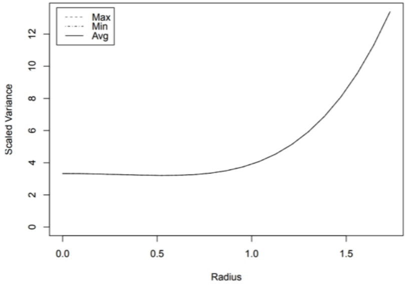

- Choosing the correct number of center points in a CCD ensures uniform precision.

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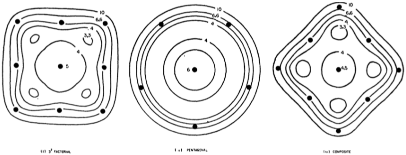

FIG. 2. Variance contours for some 2 dimensional designs

Image from Box and Hunter 1957.

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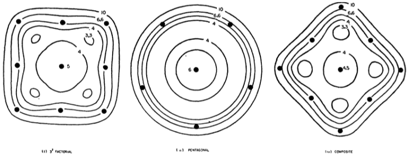

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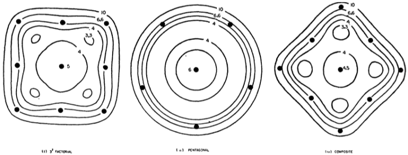

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- A CCD with F factorial points is rotatable when $\alpha = \sqrt[4]{F}$.

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!

Coding the CCD

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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$$F = 2^3 = 8 \Rightarrow \alpha = \sqrt[4]{8} = 1.68$$

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