

# Sequential Experiments: Introduction

BIOE 498/598

# Sequential Experimentation

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- ▶ Design experiments
- ▶ Collect data
- ▶ Fit and analyze a model
- ▶ Interpret

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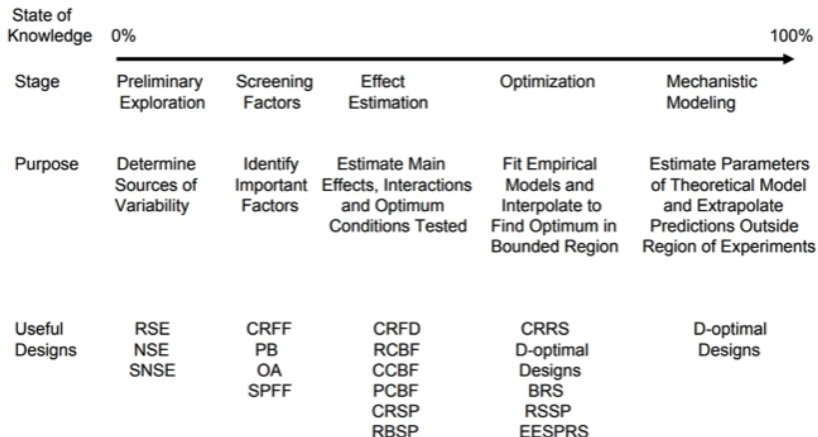
The exception was RSM, which allowed two blocks of experiments and included an optimization that presumably led to additional experiments.

RSM is one example of strategies for increasing knowledge by **sequential experimentation**.

# Why sequential experimentation?

There is an inherent tradeoff between the breath and width of our experimental designs. This tradeoff is described by the *knowledge line*.

Figure 13.1 *The State of Knowledge Line*



# Stage 1: Preliminary Exploration

- ▶ What factors could possibly matter for my system?
- ▶ Overlaps with needs assessment from design.
- ▶ We did not cover this stage.

## Stage 2: Screening Factors

- ▶ What factors actually matter?
- ▶ Resolution III fractional factorial designs.
- ▶ Estimate main effects only; interactions are usually confounded.

## Stage 3: Effect Estimation

- ▶ How much do the factors affect the response?
- ▶ Full factorial, resolution IV and V fractional designs.
- ▶ Often the last stage for science, the beginning stage for engineering.

## Stage 4: Optimization

- ▶ What are the optimal operating conditions?
- ▶ RSM
- ▶ All factors must be important since designs are expensive.



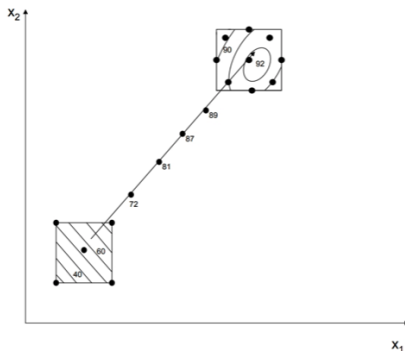
## Stage 5: Mechanistic modeling

- ▶ A mechanistic model contains only important factors and allows effect estimation and optimization.
- ▶ Experiments are only needed to fit parameter values.
- ▶ Often the best at extrapolating beyond the region of experimentation.

## Early sequential experiments: Box & Wilson (1951)

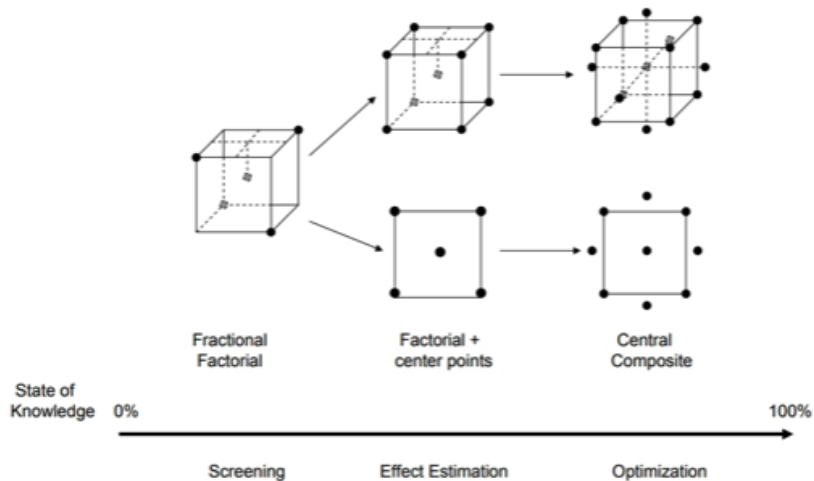
- ▶ A full/fractional design identified the direction of steepest ascent for process improvement.
- ▶ Experiments were run one-at-a-time in this direction until improvement stopped.
- ▶ An RSM-like procedure was run at the endpoint to assess the curvature and declare a maximum.

Figure 13.2 *The Method of Steepest Ascent*



# RSM with a CCD allows sequential experimentation

Figure 13.3 *Blocked Response Surface*



# Online learning

Process improvement is often at odds with the goals of production.

The goals of production are:

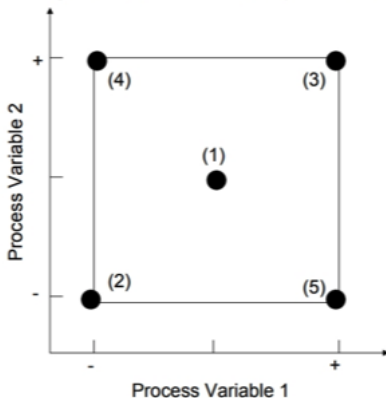
- ▶ Quality products
- ▶ High output
- ▶ Low costs
- ▶ Low variability

Our experimental designs require runs with multiple changes and large perturbations. This strategy cannot be implemented online.

## How do we balance learning with production?

In 1957 Box invented Evolutionary Operation (EVOP) to learn from an active production line.

Figure 13.6 A  $2^2$  Plan for EVOP



## EVOP example: $2^2$ full factorial

- ▶ Rotate the production through cycles of five runs:
  - ▶  $y_{00}$  is the current operating conditions
  - ▶  $y_{--}, y_{++}, y_{-+}, y_{+-}$
- ▶ After every cycle, estimate the effects:
  - ▶  $\beta_1 = \text{mean}(y_{+.}) - \text{mean}(y_{-.})$
  - ▶  $\beta_2 = \text{mean}(y_{.+}) - \text{mean}(y_{.-})$
  - ▶  $\beta_{12} = [\text{mean}(y_{++}) - \text{mean}(y_{--})] - [\text{mean}(y_{+-}) - \text{mean}(y_{-+})]$
- ▶ Test for significant effects using  $\text{s.e.} = 2\sigma/\sqrt{4r}$  where  $r$  is the cycle number.

Since  $r$  increases over time, any truly nonzero effect will become significant over time *regardless of the effect size*. These data can be used to modify the process.

## Next steps: Reinforcement Learning

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Examples of RL systems:

- ▶ Computer chess
- ▶ Chatbots
- ▶ Self-driving cars
- ▶ Humans