Strategies for Mixture-Design Space Augmentation

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Outline

Design of Experiments

- **Design of experiments (DOE)** is a systematic series of tests, in which purposeful changes are made to input factors, so that causes for significant changes in the output responses may be identified.
- **Examples:**
  1. Three characteristics (e.g. size, color, position) of an online banner ad are varied, and the click-through rate is measured.
  2. Several features of a stent are varied, and the burst pressure of the stent is measured.
  3. Three olive oils are mixed together in various proportions. It's thought that some blend of the three oils has better sensory characteristics than any of the individual oils.
  4. The proportions of ingredients in a cake batter are varied, and the cakes are baked at different temperatures.

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The Basics

- In a typical experiment, we assume n observed responses $\boldsymbol{y} = (y_1, \ldots, y_n)$ are a function of k factors $(x_1, \ldots, x_k)$ that are intentionally changed:

$$\boldsymbol{y} = f(x_1, ..., x_k)$$

- f is unknown, but we commonly use a linear model as an approximation:

$$\boldsymbol{y} = \boldsymbol{X}\beta + \boldsymbol{\varepsilon}, \quad \boldsymbol{\varepsilon} \sim \mathrm{N}_n(0, \sigma^2 \boldsymbol{I})$$

where $\boldsymbol{X}$ is an $n \times p$ model matrix, β is a $p \times 1$ vector of parameters, $\boldsymbol{\varepsilon}$ is an $n \times 1$ vector of errors, and σ^2 is the error variance.

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Mixture Designs

- In many experimental settings, $\boldsymbol{y}$ is expected to be affected by the magnitudes of the factor levels:
  - **Example:** Baking a pie at
    - 350°F for 30 minutes
    - 700°F for 60 minutes

    where $\boldsymbol{y}$ is the taste rating of the pie.
- In other experimental settings, ingredients are mixed together and $\boldsymbol{y}$ is only thought to depend on their proportions:
  - **Example:** Preparing lemonade with
    - 1 cup sugar water + 1 lemon
    - 2 cups sugar water + 2 lemons

    where $\boldsymbol{y}$ is the taste rating of the lemonade.

Mixture Designs

- In a mixture experiment, q components $(x_1, ..., x_q)$ are blended together. The dependence of $\boldsymbol{y}$ on the proportions of the components introduces an equality constraint:

  $$x_1 + x_2 + \cdots + x_q = \mathbf{T}$$

  Without loss of generality, we say $\mathbf{T} = 1$ and so all $0 \leq x_j \leq 1$.

- In most cases, it does not make sense for some $x_j \approx 0$ or $x_j \approx 1$, so the component ranges may need be constrained:

  $$0 < L_j \leq x_j \leq U_j < 1, \quad \text{for some } j$$

  This is a critical step!

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Mixture Designs

- Constraints involving multiple components may also be necessary.
  - **Example:** Two oils can each comprise $0 - 20$ volume % of a mixture, but together must comprise a minimum of 10% of the mixture.
- The equality constraint makes one component redundant, since

$$x_q = 1 - (x_1 + \cdots + x_{q-1})$$

  and so the components cannot vary independently of one another.
- The standard linear model must be re-parameterized to account for the loss of dimension (e.g. Scheffe, Slack, Cox).
- This complicates the design, analysis, and interpretation of the model.

Other Issues

- More complicated constraints:
  - Ratio constraints
  - Group constraints
- All of the above defines the **mixture design space**
- How is this space chosen?
  - Previous experimental information
  - Subject-matter knowledge
  - Range-finding experiments
- Straightforward in response surface designs (usually), but much more difficult in mixture DOE due to the equality constraint.
- This space is almost never chosen perfectly the first time around!

Applications

Mixture experiments are useful in a large number of industries:

- Food and beverage
- Pharmaceutical
- Paints and coatings
- Production of materials (e.g. plastics)
- Oil and gas
- ... and so on

Design Build Considerations

- There are few existing off-the-shelf designs for mixture experiments.
- Building the design via "eye-balling" and intuition can result in a number of problems:
  - Non-estimable model terms
  - Poor coverage of the design space
  - Designs that are too small (not enough precision) or too large (inefficient)
- Designs with multicomponent constraints are even more challenging.
- **Solution**: Build using optimal design algorithms.

Optimal Design

These designs are typically built algorithmically.

- Mixture component and process factor lows and highs.
- Constraints involving multiple components or process factors.
- A target model that the design should support.

An optimality criterion (i.e. design scoring method) must also be chosen:

- **D**: Minimize volume of the joint confidence ellipsoid around the model coefficients:

$$D(\boldsymbol{X}) = |(\boldsymbol{X}^T \boldsymbol{V}^{-1} \boldsymbol{X})^{-1}|$$

- **I**: Minimize the average prediction variance:

$$I(\boldsymbol{X}) = E[Var(\hat{y})]$$

For the remainder of the talk, we only use **I**-optimality.

Some Variations

- Combined mixture-process designs
- Split-plot designs
  - Hard to change factors/components
- Mixture-amount experiments
  - Fertilizer: composition and amount
  - Tablet coating: formulation and amount
- Double-mixture experiments
  - Separate frosting and filling formulation
  - Two mixtures

The Mixture DOE Sequence

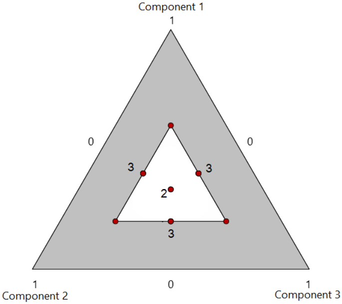
1. Select q components $\mathbf{x_1}, \ldots, \mathbf{x_q}$ and define their ranges
2. Choose a design $\mathcal{D}$ and evaluate it
3. Perform the experiment
4. Analyze data and fit model $\mathbf{f}$ $\rightarrow$ Fix problems
5. Optimize the process
6. Confirm $\rightarrow$ **Finish!**
7. Continue Experimentation?

Motivating Example

- Suppose we have a three-component mixture with component ranges

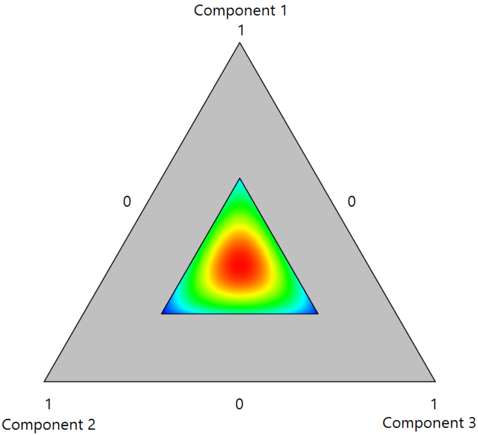
$$0.2 \leq \mathbf{x_1} \leq 0.6$$
$$0.2 \leq \mathbf{x_2} \leq 0.6$$
$$0.2 \leq \mathbf{x_3} \leq 0.6$$
$$\mathbf{x_1} + \mathbf{x_2} + \mathbf{x_3} = 1$$

- We build a 14-run **I**-optimal mixture design.



Potential Results

- What we hope happens:

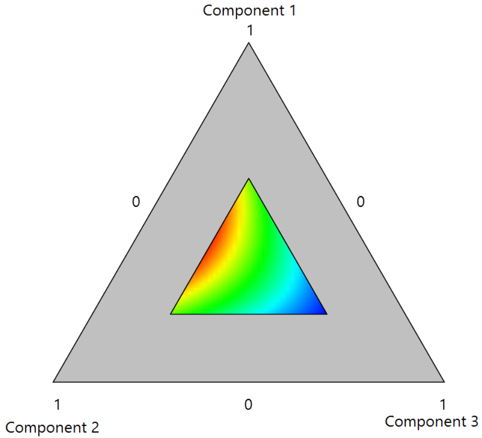


Why is this good?

- The optimum lies neatly in the middle of the space.
- Low prediction error and uncertainty.
- Large operating window for production.
- Useful for Quality by Design (QBD) applications.
- Should perform some confirmation runs.

Potential Results

- What usually happens:



Why is this bad?

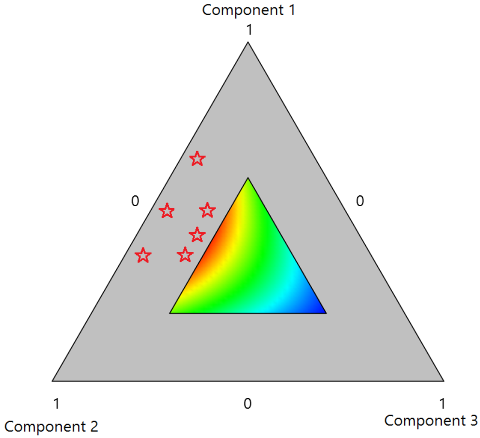
- The solution is on the edge of the design space.
- Process is not fully optimized.
- Little operating space for production.
- High prediction error and uncertainty.

Where to go from here?

- Accept results and move on?
  - Cannot do more experiments
  - Optimum may actually be "good enough"
- Throw away data and start over?
  - Inefficient, especially if the optimum is close to the design space
  - Less information, more error and uncertainty

Where to go from here?

- Extrapolate?
  - Prediction accuracy and precision falls off quickly.
  - Model trend not guaranteed to hold outside of design space.
  - Confirmation runs are critical in this situation.



Design Space Augmentation

- Many experimenters are completely unaware of **design space augmentation**.
- The idea behind design space augmentation (expansion) is to perform a follow-up experiment near the optimum found in the original design space, without throwing away the original data.
- **Assumption:** The original design space can be expanded to "capture" the optimum. The true optimum is reasonably close to the original space.
- Little to no research is available on this topic, especially in the context of mixture experiments.

Design Space Augmentation

- Typically done in an ad-hoc, “intuitive” manner, if at all.
- “Augmentation” is typically studied in the context of adding runs to support fitting of a higher-order model, fixing problems, testing new hypotheses, adding new factors/components etc:
  - **Example:** Factorial design $\rightarrow$ central composite design
  - **Example:** Quadratic $\rightarrow$ mixture special cubic model
- May not always work (disjoint region)
- May require several iterations

Common Strategy

1. Start with a design $\mathcal{D}_{\text{base}}$ over design space $\mathcal{R}_{\text{base}}$, with n_{base} runs.
2. Perform experiment and decide whether to expand the design space.
3. **Key:** Re-define the component limits for some (or all) of the mixture components $\leftarrow$ **Difficult!**.
4. The new portion of the design space is $\mathcal{R}_{\text{aug}}$. The full region is $\mathcal{R} = \mathcal{R}_{\text{base}} \cup \mathcal{R}_{\text{aug}}$.
5. This is difficult in mixtures due to the equality constraint. Adding more of one component means you must add less of another component.

Common Strategy

6. Fill $\mathcal{R}$ with a follow-up design $\mathcal{D}_{\text{aug}}$ with n_{aug} runs.
7. The full design is $\mathcal{D} = \mathcal{D}_{\text{base}} \cup \mathcal{D}_{\text{aug}}$.
8. Choose $\mathcal{D}_{\text{aug}}$ such that

   $$\mathcal{D}_{\text{aug}} = \text{argmin}_{\mathcal{D}*}\ g(\mathcal{D}* \cup \mathcal{D}_{\text{base}})$$

   where g is an optimality criterion.
9. In mixture designs, the I optimal criterion is typically used, which measures the average prediction variance throughout the design space.
10. Perform the additional runs and optimize.

Simple Example

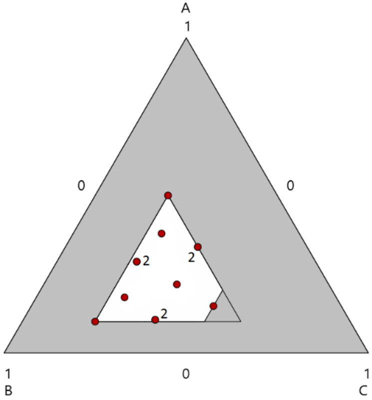
- Here is a simple illustration (based on a real example) which demonstrates the methodology.
- Suppose we have a three component mixture.
- For the sake of brevity, label the components $\mathbf{A}, \mathbf{B}, \mathbf{C}$.
- The component ranges are:

$$0.1 \leq \mathbf{A} \leq 0.5$$
$$0.3 \leq \mathbf{B} \leq 0.7$$
$$0.2 \leq \mathbf{C} \leq 0.5$$

- These component ranges produce a non-simplex (non-triangular) design space, so a 12-run **I**-optimal design was created.

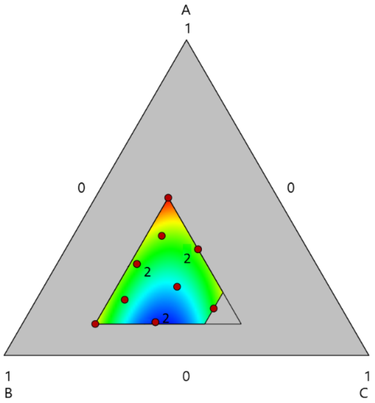
Simple Example

The design used in the experiment was



Simple Example

The 12-run experiment was performed, and the following plots of the model fit were obtained. **Not good!**



Simple Example

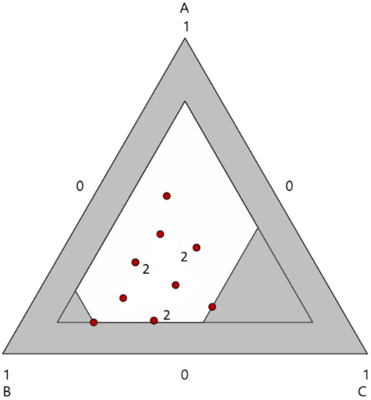
- The maximum predicted response at the vertex fell short of the experimental goals.
- The design space was augmented, leaving in the original data. The component ranges were changed to:

$$0.1 \leq \mathbf{A} \leq 0.8$$
$$0.1 \leq \mathbf{B} \leq 0.7$$
$$0.1 \leq \mathbf{C} \leq 0.5$$

- This allowed the experimenters to continue working towards their goal without having to throw away data.

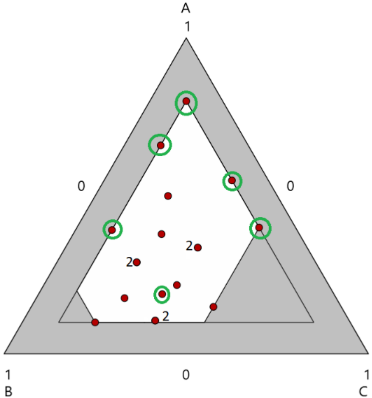
Simple Example

The design space with the added runs looks like:



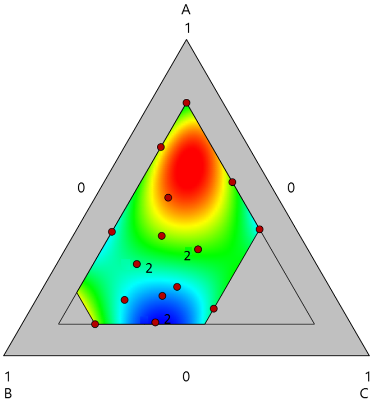
Simple Example

- Afterwards, 6 runs and 1 space-filling point were added in a second block.
- The points were chosen to minimize the I-optimality score over the entire (expanded) design space.



Simple Example

- The experimenters performed the 7 follow-up runs.
- After data analysis, the following results were obtained.



Sunscreen Example

Design space augmentation is easy to visualize with only three components. Here is a slightly more complicated example.

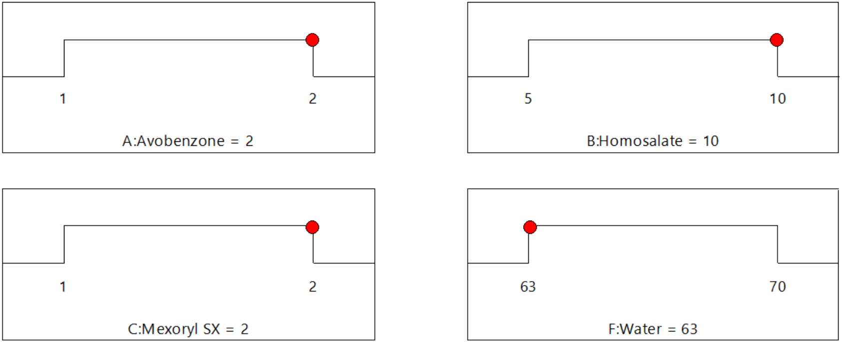
- Four components are blended together in an attempt to create an SPF 70 sunscreen.
- The component ranges are:

$$1 \leq \mathbf{A} \leq 2$$
$$5 \leq \mathbf{B} \leq 10$$
$$1 \leq \mathbf{C} \leq 2$$
$$63 \leq \mathbf{F} \leq 70$$

  where $\mathbf{A} + \mathbf{B} + \mathbf{C} + \mathbf{F} = 77$ wt%. Components **D**, **E**, and **G** were held fixed in each sunscreen blend.
- The experimenters built a 20-run **I**-optimal design.

Sunscreen Example

Optimization shows that the highest predicted SPF is ≈ 50, which falls short of our target of 70. Looking at the components shows that this maximum occurs at:



Sunscreen Example

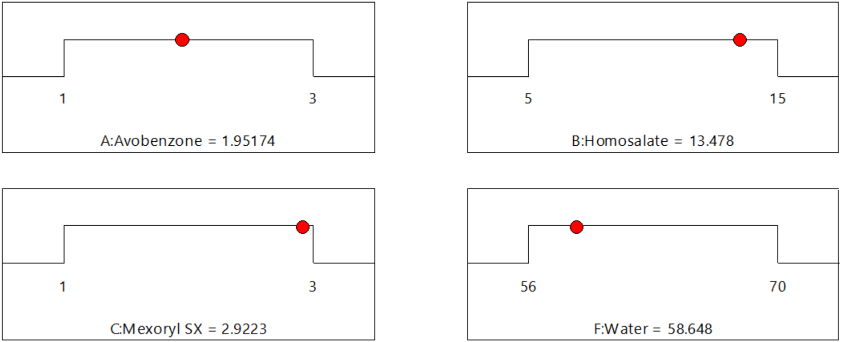
- The formulators changed the component limits:

$$1 \le \mathbf{A} \le 2 \rightarrow 3$$
$$5 \le \mathbf{B} \le 10 \rightarrow 15$$
$$1 \le \mathbf{C} \le 2 \rightarrow 3$$
$$0 \leftarrow 63 \le F \le 70$$

- 7 follow-up runs were added in a second block. The 7 runs were chosen in a way that minimized the average prediction variance over all 27 runs, according to the strategy.

Sunscreen Example

Optimization now shows that we can achieve our desired SPF of 70:



What Next?

The proposed strategy works well, but:

- By finding the optimal design for the combined design region $\mathcal{R}$, the algorithm may place points in the original region $\mathcal{R}_{\text{base}}$ if it improves the criterion - not ideal!
- By only building the “best” design for the new region $\mathcal{R}_{\text{aug}}$, you will likely be performing too many runs at the edge between $\mathcal{R}_{\text{base}}$ and $\mathcal{R}_{\text{aug}}$.

Proposal

- A proposed restricted criterion for selecting the follow-up runs:

$$\mathcal{D}_{\text{aug}} = \text{argmin}_{\mathcal{D}* \in \mathcal{R}_{\text{aug}}} g(\mathcal{D}* \cup \mathcal{D}_{\text{base}})$$

- Advantages:
  - This criterion uses all the available data from the first experiment.
  - All follow-up runs are forced to be in the new region.
  - **Unresolved Issue:** Blocking may require that at least one follow-up run be contained in the old region.
  - **Disadvantage:** Somewhat complicated to implement.

Other Issues

- This is an interesting problem that often arises in practice, with few known solutions. Some other related problems are:
  - Shrinking the design space?
  - Selection of runs and evaluation of follow-up design.
  - Extensions to split-plot, strip-plot, and combined designs.
  - Generalization to all constrained design spaces (e.g. RSM).

The End

Thanks for listening!

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