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Mixture DOE Done Right

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November 14-17, 2022

Mixture Design for Optimal Formulations (DL)

Find the sweet spot and optimize your formulations by mastering mixture designs in this 1-week (4 half-day sessions) instructor-led online course. 10:00am - 1:30pm (USA Central Time)

Agenda

- ➢ **What is a Mixture Experiment?**
- ➢ Types of Mixture Designs
- ➢ Tips and Tricks
- ➢ Conclusion

What is a Mixture Experiment?

- A typical non-mixture experiment looks something like this:
  - Suppose we are baking a cake
  - We can vary (1) **time** and (2) **temperature** in the oven:

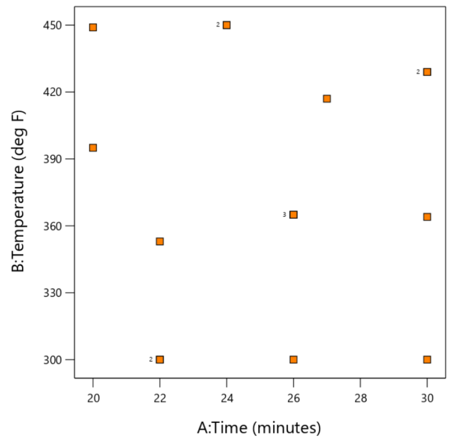
    time: 20 to 30 minutes

    temperature: 300°F to 450°F
  - The **response** we are measuring is moisture content of the cake.
  - In this experiment, both of our factors can be set independently. That is, if we set time to 25 minutes, temperature can take any value between 300F and 450F.
  - This is a typical **response surface method** experiment (RSM).

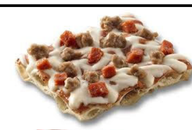
What is a Mixture Experiment?

An example response surface DOE would look something like this:

Run	Factor 1 A:Time minutes	Factor 2 B:Temperature deg F	Response 1 Moisture
1	20	395	
2	27	417	
3	24	450	
4	26	365	
5	30	364	
6	30	429	
7	30	429	
8	24	450	
9	26	365	
10	26	300	
11	22	300	
12	20	449	
13	22	300	
14	26	365	
15	22	353	
16	30	300	



What is a Mixture Experiment?



- Now consider this experiment:
  - Suppose we are deciding what cheese to put on a pizza.
  - We can blend three cheeses to make up the blend (A) **mozzarella** (B) **provolone** and (C) **white cheddar**.
  - We try various combinations of the three cheeses. Each pizza that we cook will be topped with a total of 6 ounces of cheese.

    mozzarella: 0 to 6 ounces
    provolone: 0 to 6 ounces
    white cheddar: 0 to 6 ounces

  - **Notice: mozzarella + provolone + white cheddar** = 6 ounces

What is a Mixture Experiment?

- The responses we measure will be:
  1. **appearance**
  2. **taste**
  3. **texture** (soft & oozy **versus** hard & chewy)
  4. **cost**
- In this situation the components of the cheese blend **cannot** be set independently of one another. For example, if we put 2 ounces of mozzarella cheese into the blend, we must put a total of 4 ounces of the other two cheeses into the blend.
- This is a typical **mixture experiment**.

CRITICAL!

mozzarella + **provolone** + **white cheddar** = 6 ounces

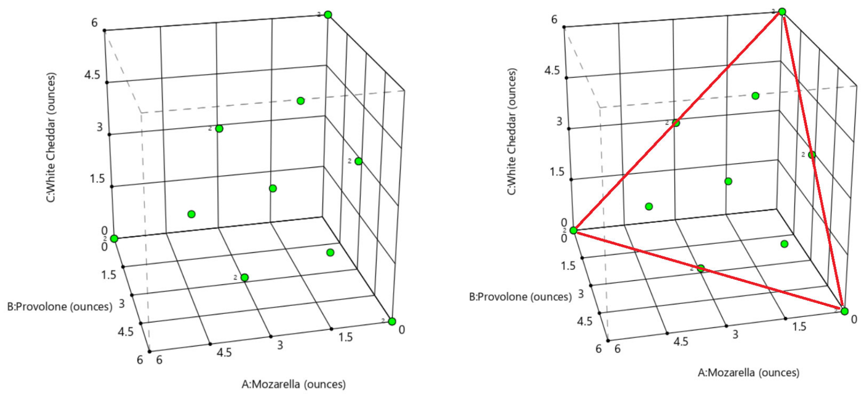
What is a Mixture Experiment?

- A typical mixture DOE would look something like this:

Run	Component 1 A:Mozarella ounces	Component 2 B:Provolone ounces	Component 3 C:White Cheddar ounces	Response 1 appearance	Response 2 taste	Response 3 texture	Response 4 cost
1	0	3	3				
2	4	1	1				
3	3	0	3				
4	0	6	0				
5	2	2	2				
6	1	1	4				
7	6	0	0				
8	1	4	1				
9	0	0	6				
10	3	0	3				
11	3	3	0				
12	0	6	0				
13	3	3	0				
14	0	3	3				
15	6	0	0				
16	0	0	6				

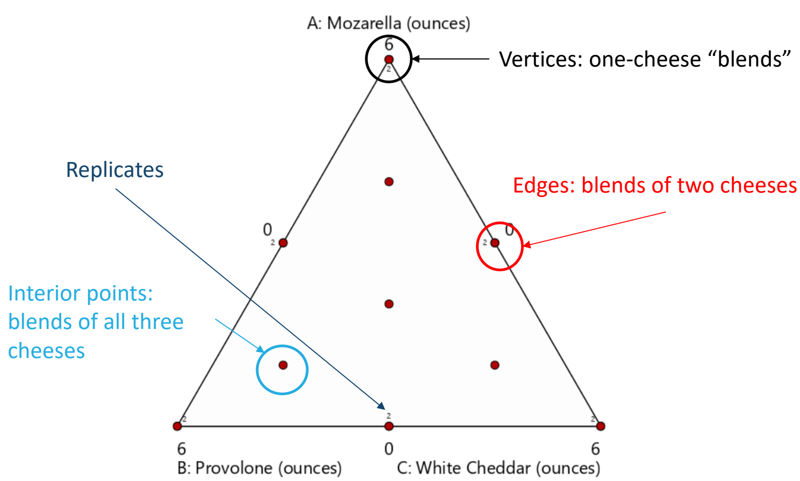
- Note that the **sum of the three cheeses = 6** in each run!

What is a Mixture Experiment?



Mixture DOE Done Right 9

What is a Mixture Experiment?



Mixture DOE Done Right 10

Identifying a Mixture Experiment

- Blending experiments should usually be set up as a mixture DOE, but not always.
  - If you are varying concentration or amounts of the components, rather than varying the weight %, volume %, or proportion of total, you may have a response surface experiment.
- The key to verifying whether you need a mixture design is to determine if any of the columns in the design plan **add up to a fixed total** in each run of the experiment.
- Part of an experiment may be a mixture (e.g. a cake formulation) and you may have non-mixture factors as well (e.g. temperature of the oven). This is called a **mixture-process combined design**.

Agenda

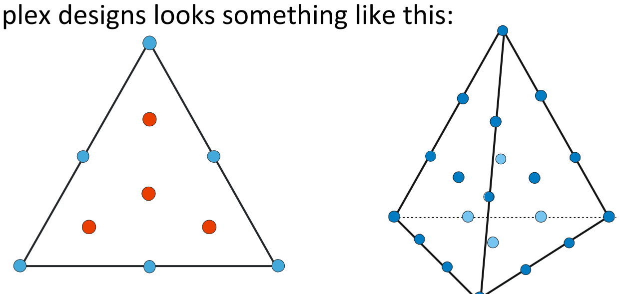
- What is a Mixture Experiment?
- **Types of Mixture Designs**
- Tips and Tricks
- Conclusion

Types of Mixture Designs

- There are two basic categories of mixture DOEs:
  - **Simplex**-based designs (canned)
  - **Optimal** computer-generated designs
- In practice, most of the designs I use are optimal designs due to their flexibility.

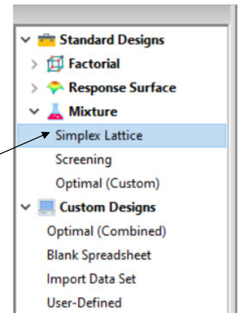
Simplex-Based Designs

- Simplex designs are **canned** and straightforward.
- In order to use a simplex design, one of the following conditions must hold true:
  - All the components have ranges 0 to 100%.
  - All the components must have the same range.
- Simplex designs looks something like this:



Simplex-Based Designs

- Simplex designs are incredibly restrictive and limited purpose.
- It **rarely** makes sense for all components to go from 0% to 100% of the mixture (100% yeast in a bread dough formulation?)
- It's also somewhat rare that all the components have the same range.
- **Do not** force all your components to have the same range so you can use a simplex design!!
- A better option is an **optimal computer-generated** design.



Simplex designs in our software.

Optimal Design

- Suppose you have the following set of constraints:

Single component

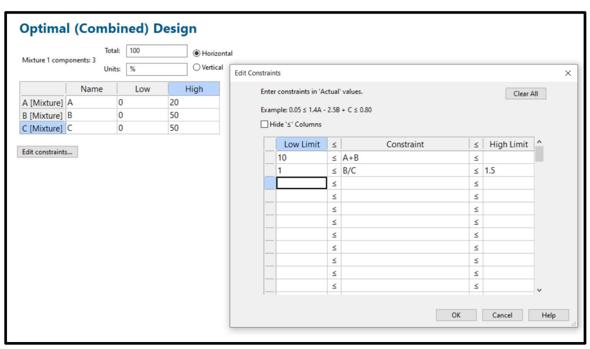
- 0% ≤ **A** ≤ 20%
- 0% ≤ **B** ≤ 50%
- 0% ≤ **C** ≤ 50%

Multicomponent

- **A** + **B** ≥ 10%
- 1 < **B**/**C** < 1.5

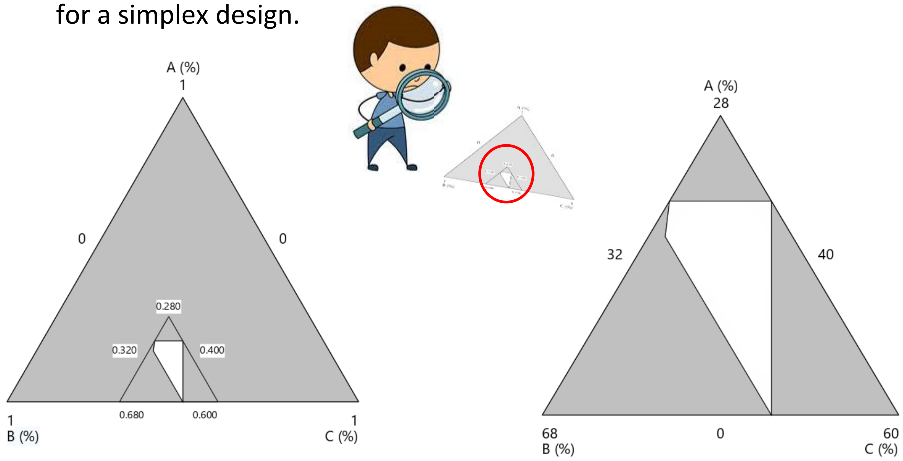
Equality constraint

- **A** + **B** + **C** = 100%



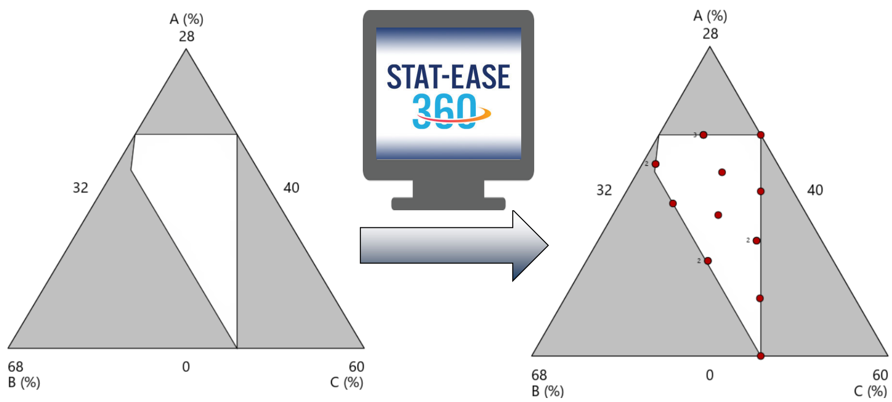
Optimal Design

- This is what the experimental design space looks like. Not a great fit for a simplex design.



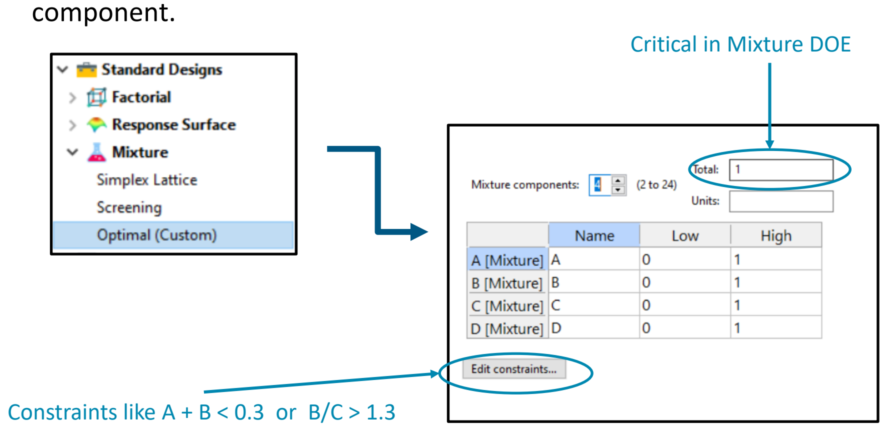
Optimal Design

- Here's what an **optimal computer-generated** design looks like for this complicated design space.



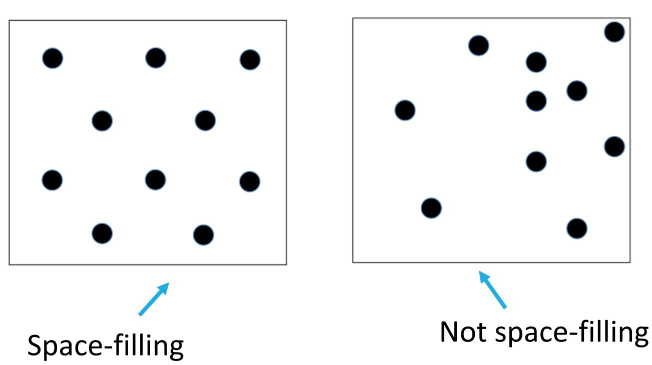
Optimal Design

Optimal designs are straightforward to build. First choose components, set their bounds, and add any constraints involving more than 1 component.



Space-Filling Designs

- **Space-Filling Designs** are another category of mixture designs. They aim to “fill” a design space – evenly distribute points, leave no large gaps, etc.

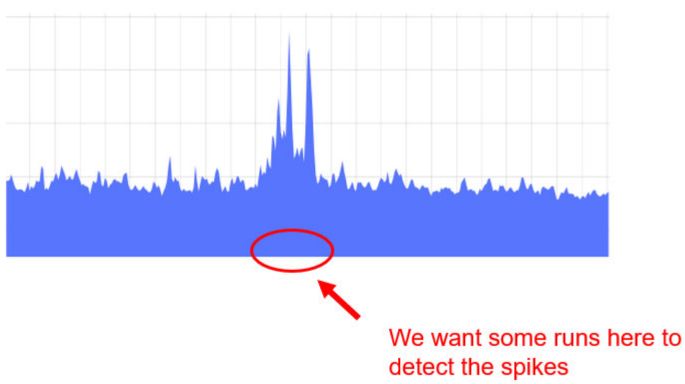


Space-Filling Designs

Space-Filling Designs (SFDs) can be used in a wide variety of cases:

- They are especially useful in **computer experiments** where the response of interest is generated by a simulation rather than a physical experiment. These responses are deterministic with no error, so it makes no sense to do replicates. A space-filling design will give maximum information in this case.
- SFDs can be used in **exploratory studies**, where there is much uncertainty about the design space. SFDs include more unique points than other optimal designs, giving you more information about a new experimental design space.
- If you expect a sharp **peak** in your response, a SFD has a better chance of catching that peak since there are more unique design points that are nicely spread apart.

Space-Filling Designs



Space-Filling Designs

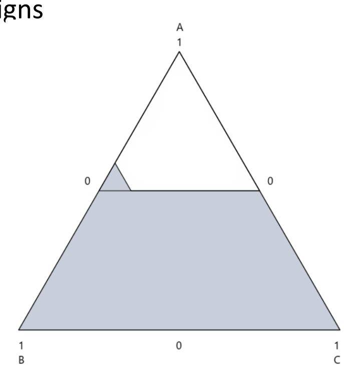
Demo: Space-Filling Designs vs. Optimal designs

We'll look at a three-component example:

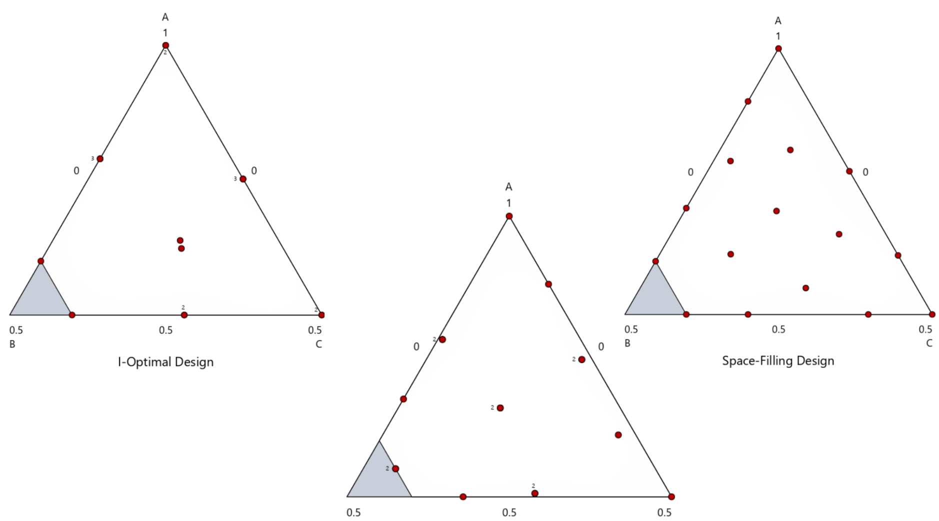
- $0.5 \le A \le 1$
- $0 \le B \le 0.4$
- $0 \le C \le 0.5$

Three different designs will be compared:

- Space-filling design
- Modified I-optimal design
- I-optimal design



Space-Filling Designs

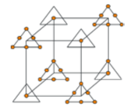


I-Optimal Design

Modified I-Optimal Design

Space-Filling Design

Mixture-Process Designs



- In some experiments, a formulation may be processed under various conditions. For example, a cake batter formulation could be baked at several different temperatures.
- Historically, this type of experiment would be done in two stages:
  - **Step 1**: find the optimal formulation under the "middle" setting of the process parameters.
  - **Step 2:** take the formulation from the previous step and tweak the process parameters to try to improve the results.
- There is a better way to do this type of experiment: use a mixture-process design.

Mixture-Process Designs

- One disadvantage of the two-stage approach in the previous slide is that the ideal mixture often depends on the process parameters and vice versa. Essentially, the mixture interacts with the process parameters.
- A mixture-process design models the effects of the mixture, the effects of the process parameters, and the interaction between the two, giving you a complete picture of what's going on.
- Mixture-process designs are almost always built as computer-generated optimal designs.

Other Designs

Some other designs to be aware of:

- **Double mixture designs**

  Two separate mixtures are part of the experiment. For example, a cake batter formulation + a frosting formulation. The two mixtures may depend on one another.

- **Split-plot (restricted randomization) designs**

  Formulations must be prepared in batches, or several independent formulations must be processed at the same time (e.g. in an oven). Full randomization not possible or feasible.

- **Mixture of mixtures design**

  Several mixtures are blended together to form a final mixture.

Agenda

- What is a Mixture Experiment?
- Types of Mixture Designs
- **Tips and Tricks**
- Conclusion

Tips and Tricks

Here are a few **tips and tricks** to help you get started with mixture experiments.

1. Don't use factorial designs.
2. Don't convert to ratios so that you can use factorial or response surface designs.
3. Spend a lot of time choosing the components and the ranges.
4. Experiment iteratively, especially in new problems.
5. Master building optimal designs.
6. If possible, analyze mixture-process experiments as a single experiment, rather than as two separate experiments.
7. Use KCV models for mixture-process designs if possible to save runs.
8. Fully randomize a mixture experiment. If it's not possible, use a split-plot design!

Mixture DOE Done Right 29

Tips and Tricks

Tip 1: Don't use factorial designs

- We often have a situation like this one:
  - Components **A**, **B**, **C** go from 0 to 10%
  - Component **D** is a "filler" to bring the total up to 100%
- Textbooks will often suggest ignoring **D** and performing a 2^3 factorial design on components **A**, **B**, and **C**.
- This approach has two major issues:
  - The design is poor (only looks at extremes of factor ranges).
  - The resulting factorial model is misleading if component **D** actually has an active effect.

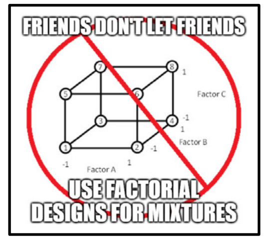
Mixture DOE Done Right 30

Tips and Tricks

Tip 1: Don't use factorial designs

4-component I-optimal design

Run	Component 1 A:A	Component 2 B:B	Component 3 C:C	Component 4 D:D
1	3.6	10	10	76.4
2	0	10	0	90
3	5.6	0.2	5.6	88.6
4	10	3.8	10	76.2
5	0.3	5.5	5.5	88.7
6	5.5	5.3	0	89.2
7	10	10	3.8	76.2
8	10	0	0	90
9	0	0	0	100
10	0	0	10	90



Factorial design ignoring **D**

Factor 1 A:A	Factor 2 B:B	Factor 3 C:C	Response 1 R1
10	10	10	
0	10	10	
10	10	0	
0	10	0	
10	0	10	
0	0	10	
10	0	0	
0	0	0	

Tips and Tricks

Tip 2: Don't use ratios so that you can use factorial or response surface designs.

- To avoid using Mixture DOE, and to overcome the limitations of factorial designs in the previous tip, experimenters will often convert their mixture to problem to a ratio problem.
- Suppose you have three components **A**, **B**, and **C**. A two-factor response surface design can be created, taking the two factors to be **A**/**C** and **B**/**C**.
- In my experience, this is usually a **bad** idea. This approach produces poor designs in the original mixture space, is tedious (requires lots of converting between % and ratios), and once again produces models that may be misleading.

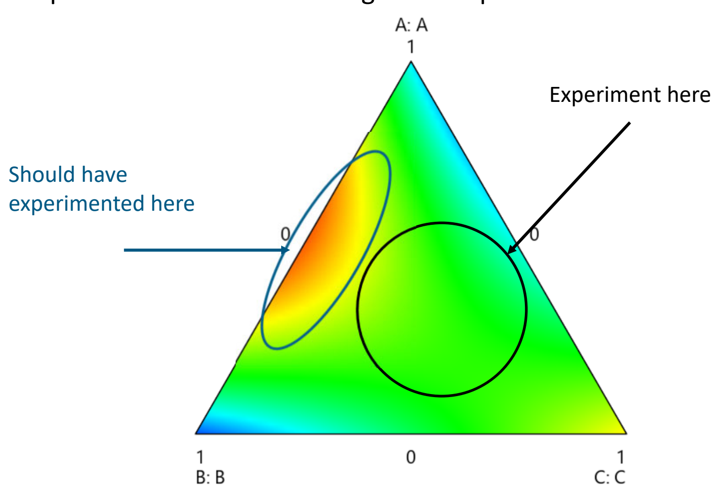
Tips and Tricks

Tip 3: Spend a lot of time choosing the components and the ranges

- The first step in any mixture experiment is choosing what components to blend, and what the upper/lower bounds of each component will be.
- In experience this step is **critical**. Most "failures" (of an experiment to produce results) are due to choosing the wrong mixture components and/or the wrong bounds.
- Components and their bounds are usually chosen using subject-matter knowledge, historical data, and guessing.
- Choosing bounds is tricky with mixtures because of the equality constraint.

Tips and Tricks

Tip 3: Spend a lot of time choosing the components and the ranges



Tips and Tricks

Tip 4: Consider an **iterative** approach

- Design of experiments is often presented as a **one-shot** approach
  - ✓Build the experiment according to your run budget
  - ✓Perform the experiment
  - ✓Analyze data, optimize, and go home
- This is often wasteful in my experience.

Mixture DOE Done Right 35

Tips and Tricks

Tip 4: Consider an **iterative** approach

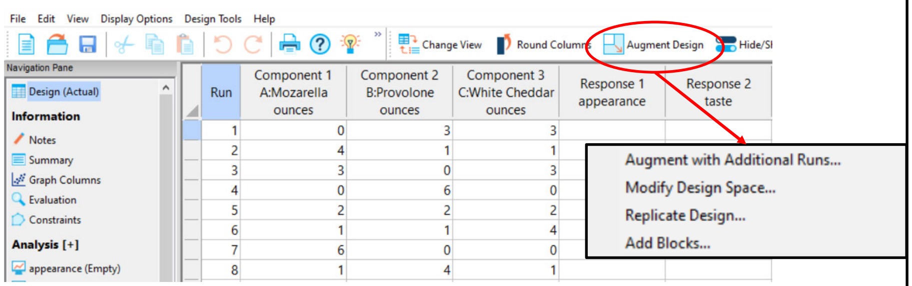
- Instead of depleting your entire run budget on the first pass of the experiment, use a **fraction** of the runs and leave some behind.
- After analyzing the data, you can choose what to do with the remaining runs:
  - **Expand** the mixture space and put the remaining runs in the new area to better optimize the process.
  - **Shrink** the mixture space and put the remaining runs in a smaller area where greater precision is desired.
  - Use the runs to estimate **higher-order models**.
  - Maintain the original design space and use the remaining runs to fill large gaps.

Mixture DOE Done Right 36

Tips and Tricks

Tip 4: Consider an **iterative** approach

- This is very easy to do in Design-Expert and Stat-Ease® 360:



- Webinar on sequential experimentation:
  www.youtube.com/watch?v=xiX1VxRPU5k

Tips and Tricks

Tip 5: Master building optimal computer-generated designs.

- Most of the designs you'll build will be optimal computer-generated designs. Even in situations where a canned simplex design can be used, an optimal design may have better properties.
- Learning the ins and outs of these designs will pay huge dividends going forward.
- Building and analyzing and optimal mixture design:
  www.youtube.com/watch?v=FTKMUNalToU
- Using optimal designs (advanced):
  www.youtube.com/watch?v=ZPgzc9bH5NA

Tips and Tricks

A few more tips:

6. If possible, analyze mixture-process experiments as a single experiment, rather than as two separate experiments.
7. Use KCV models for mixture-process designs if possible to save runs.
8. Fully randomize a mixture experiment. If it's not possible, use a split-plot design!

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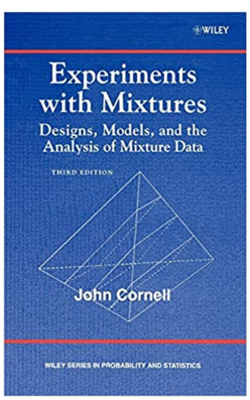
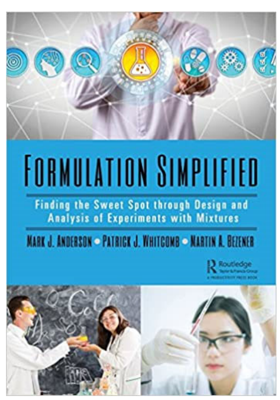
Conclusion

- Mixture DOE is a **very powerful** tool that unfortunately does not receive much attention.
- Design-Expert and Stat-Ease® 360 software contains all the **latest and greatest** tools for building and analyzing mixture experiments.
- The key to recognizing a mixture experiment is determining if there is an **equality constraint**.
- If you enjoyed this presentation and found it useful, consider taking our 4-day distance-learning workshop that dives into more detail on all the topics I discussed, including software use.

Mixture DOE Done Right 41

Resources





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Thanks for listening!

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