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Fast Product Optimization with Uniform Design, Application in Cosmetic

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Abstract:
Design of Experiment is one useful way to optimize formula performance in cosmetic. Traditional screening design starts with fewer levels for each factor, less than 4, which is efficient to identify key factors but not enough to find the appropriate factor range neither the candidate formula. If one seeks to optimize directly, too many factors have to be considered, which increased dramatically the number of experiments.

Research scientists have strong needs to conduct small experiment but aiming at finding candidate formula, when there is limited information on how factors affect the formula performance, and also limited information on the appropriate dosage for key factors. A particular example is to fast track the product market within short time.

Uniform design (UD) was proposed by Professor Fang Kai-Tai and Professor Wang Yuan in 1980. A uniform design seeks design points that are uniformly scattered in the exploration domain, but much more homogeneous distributed, with potentially as many levels for each factor as the number of experiments. UD has been successfully applied in various fields, including chemical, pharmaceutics, quality engineering, natural sciences, etc., but seems less applied in cosmetic. UD has potential to answer lab's fast tracking needs within short time thanks to its many levels but fewer trials. (1, 2, 3)

One UD case study in cosmetic is shared in this paper. In this case study 6 factors have been investigated with no clear information on factor's effect neither target dosage range. This study is composed of 12 experiments with 6 factors, each with 12 levels. This design, which combined screening and optimization objectives together, allowed to identify one target candidate.

Compared to space filling and other screening or optimization designs used internally, UD shows real benefit to find quick answer with fewer trials. More than 70% lab resources have been saved in this case study.

Keywords:
uniform design; fast track; hair color; cosmetic; DoE

1. Introduction:

Having a quick option to cover grey hair, easy to use and not spreading everywhere during application, with long lasting performance is highly appreciated by consumers. Product benchmark 1 is performing well in Japan market. It is a perfect mix of color performance (gradual coloration, quick coloration process), packing (easy to use, appropriate viscosity) and claim (melanin precursor). Lab wants to propose a fast track answer to this product.

Several internal benches (bench 2/ 3/ 4) have been developed, but none of them can give similar or higher color uptake results compared to benchmark 1. Design of Experiment has been proposed for the feasibility study, to check whether higher color update results can be achieved, viscosity is also evaluated but as second optimization criterial (scientist has rich expertise on viscosity optimization).

With many challenges on factor setting, lab capability and time constraint in this feasibility study, uniform design (UN) has been selected as one possible solution.

2. Methodology:

Challenges have been listed here, and Plan C with UN has been selected.

Wide factor range (ingredient dose):

- new dye system has to be studies, as one key ingredient (factor) has to be replaced due to patent restriction,
- for the new system, lab does not have much information on the appropriate factor range. Factors have to be explored from a wide range, from 0 to 1% which is the highest allowed range based on safety regulation
- typical screening DoE with 2 or 3 levels, can help answer which factor is key, but cannot answer the “appropriate range”, also has limitation to find good candidate during the screening DoE
- first “screening” to select key factors, and then “optimization” to find appropriate range and candidate, two experiments, more time needed

Time constraint:

- need to provide candidate within a short time, approx. 2 weeks.
- Ideally 1 week to find candidate, 1 week to validate this candidate (repeat the formulation and evaluation process to confirm the performance).

Lab capability:

- maximum 20 trials per week

	Plan A	Plan B	Plan C
DoE	1st step: Screening DoE 2nd step: Optimization DoE	1st step: Optimization DoE with all 6 factors	1st step: optimization with all 6 factors
Estimated trials	**22 trials**	**34 trials**	**12 trials**
	1st step 12 trials (6 factors) (2 levels screening + Plackett Burman)	1st step 34 trials (6 factors) (RMS model & 2 centers)	1st step 12 trials (UN + 6 factors + 12 levels for each factor)
	2nd step 10 trials (e.g, 2 factors selected) (CCD & 2 centers)		
Validation	1 trial	1 trial	1 trial
Note	RMS: Response surface,	CCD: central composite design	

Factors and evaluation:

Factors	Min %	Max %
B1:M17	0	1
B2:MP5	0	1
M70	0	1
M55	0	1
M16	0	1
M74	0	1
CONSTRAINT	B1:M17 and B2:MP5 have same functionality. Lab will use one of them in the formula. Here both have been studied, to pick up the most efficient one.	

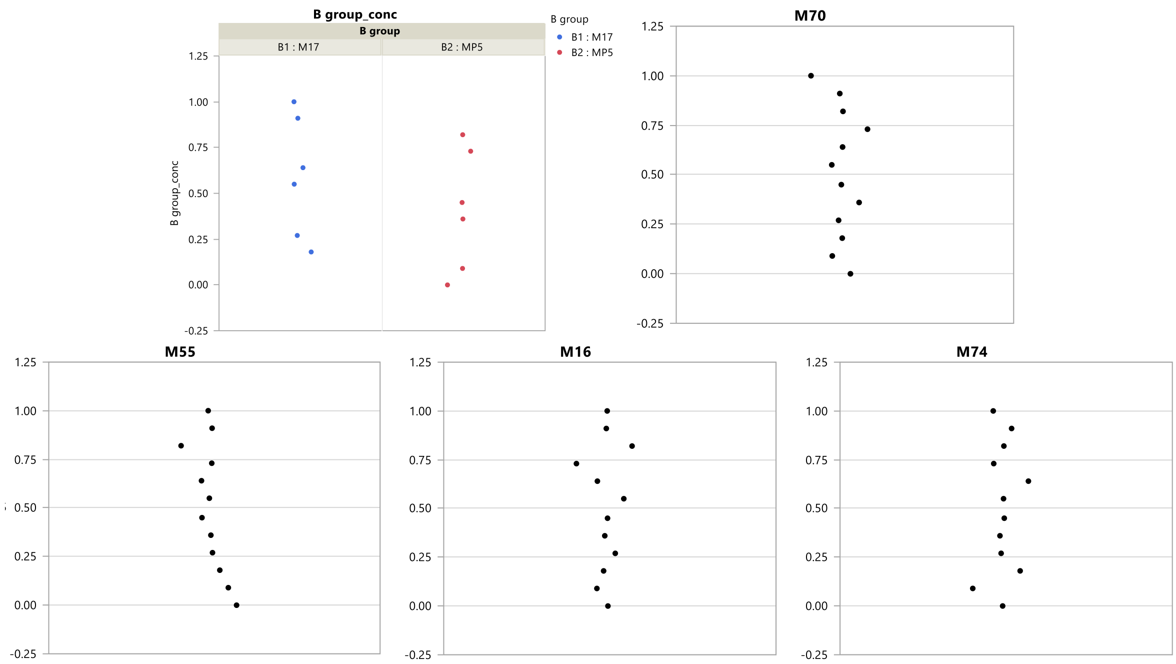
Performance evaluation:

- Color uptake has been measured, ⊿E*ab(D65) (⊿E)
- Viscosity,
- pH

Experiment Plan:
For each factor, the 12 levels are equally distributed within [0, 1] percentage.
For B1:M17, B2:MP5, 6 levels are selected from above 12.

	Run ID	B1:M17	B2:MP5	M70	M55	M16	M74	Base	MP6	DHI	MP51	QS	Total	⊿E*ab(D65)	vis (M2)	pH
12 DoE Trials	1	0	0.82	0.55	0.64	0.09	1	75	2	0.25	2.5	17.15	100	32.99	18.9	9.52
	2	0	0	0.09	0.45	0.64	0.73	75	2	0.25	2.5	18.34	100	51.49	27.2	9.75
	3	1	0	0.91	0.55	0.36	0.27	75	2	0.25	2.5	17.16	100	50.98	18.6	9.73
	4	0	0.09	0.27	1	0.18	0.36	75	2	0.25	2.5	18.35	100	55.21	16	9.77
	5	0.55	0	0	0.18	0.27	0.91	75	2	0.25	2.5	18.34	100	49.95	50	9.67
	6	0.91	0	0.73	0	0.82	0.64	75	2	0.25	2.5	17.15	100	45.03	25.2	9.67
	7	0.27	0	0.64	0.91	0.45	0.82	75	2	0.25	2.5	17.16	100	29.35	18.6	9.53
	8	0	0.45	1	0.82	0.73	0.09	75	2	0.25	2.5	17.16	100	53.33	24.7	9.76
	9	0.64	0	0.18	0.73	1	0.55	75	2	0.25	2.5	17.15	100	28.73	25.4	9.46
	10	0.18	0	0.45	0.36	0.91	0	75	2	0.25	2.5	18.35	100	55.61	32.6	9.97
	11	0	0.36	0.82	0.27	0	0.45	75	2	0.25	2.5	18.35	100	57.61	14.5	10.02
	12	0	0.73	0.36	0.09	0.55	0.18	75	2	0.25	2.5	18.34	100	55.89	33.2	9.95
internal benches	bench 1	na	na	na	na	na	na	na	na	na	na	na	na	52.64	165	10.2
	bench 2	na	na	na	na	na	na	na	na	na	na	na	na	38.77	75.3	8.4
	bench 3	0	0	0	0.25	0	0.25	75	2	0.25	2.5	19.75	100	47.84	na	na
	bench 4	0	0	0	0	0	0	75	2	0.25	2.5	20.25	100	35.33	na	na

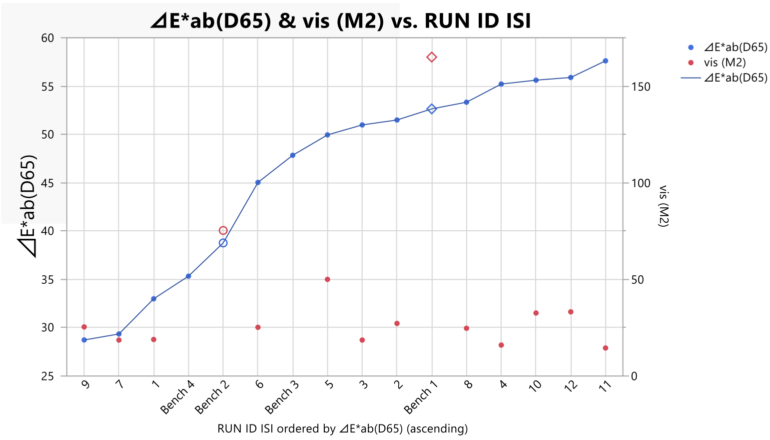
Level distribution for each factor



3. Result:

Results have been visualized in below graph. Blue point indicates color uptake results, the higher, the better; red points indicates the viscosity results, similar as benchmark 1 is better. Bench 2/ 3/ 4 are internal benches.

Several candidates (Run 8/ 4/ 10/ 12/ 11) have been found in this UN, with similar or higher color update results (⊿E*ab(D65)) than benchmark 1. The viscosity is lower compared to benchmark 1, but lab has technical solution to improve it.



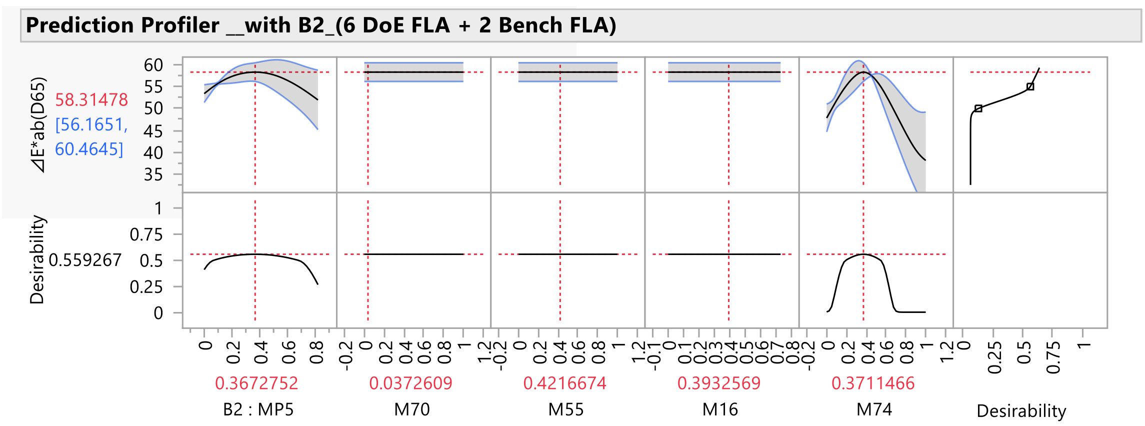
Color uptake understanding, ⊿E*ab(D65) (⊿E))

12 DoE trials (6 trials with B2:MP5 (B2), 6 with B1:M17) have been conducted. To better study the B2's effect on ⊿E, 6 trials with B2 (Run 1/ 2/ 4/ 8/ 11/ 12) and additional 2 benches (bench 3, bench 4) without both B1 and B2 are selected for following statistical analysis <u>(Gaussian Process).</u>

<u>Prediction profiler for ⊿E</u>

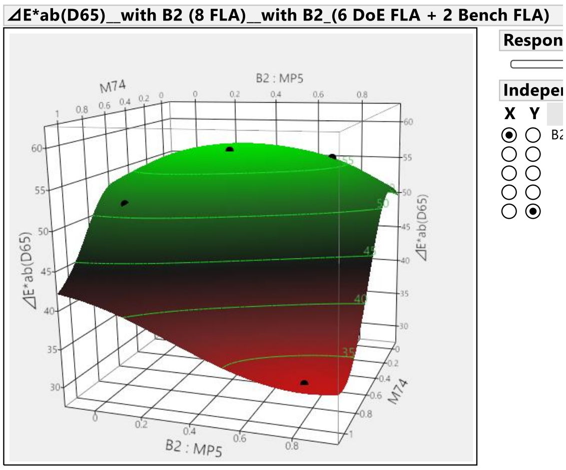
The prediction profiler gives overall review on factors' influence on ⊿E. Factor B2 and M74 show big effect on ⊿E compared to others. The flat line indicates playing on these factors will not affect the response much, thus less important for ⊿E.

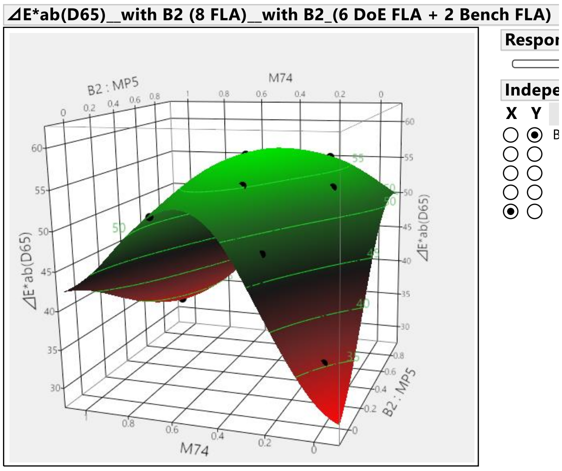
The desirability function approach transforms an estimated response into a scale-free value, called desirability (4, 5, 6), desirability setting as Maximize (Low: 50, Middle: 55, High: 100).



Surface profiler for ⊿E

The surface plot with green and red color provides more details on how B2 and M74 influence the ⊿E. Green color for higher ⊿E value, and red color for lower ⊿E value. The points on same counter line with same predicted ⊿E results. For B2 (when M74 at 1), negative effect, increasing B2 concentration (conc.) ⊿E decreased; for B2 (when M74 at 0), positive effect, increasing B2 conc. ⊿E increased.

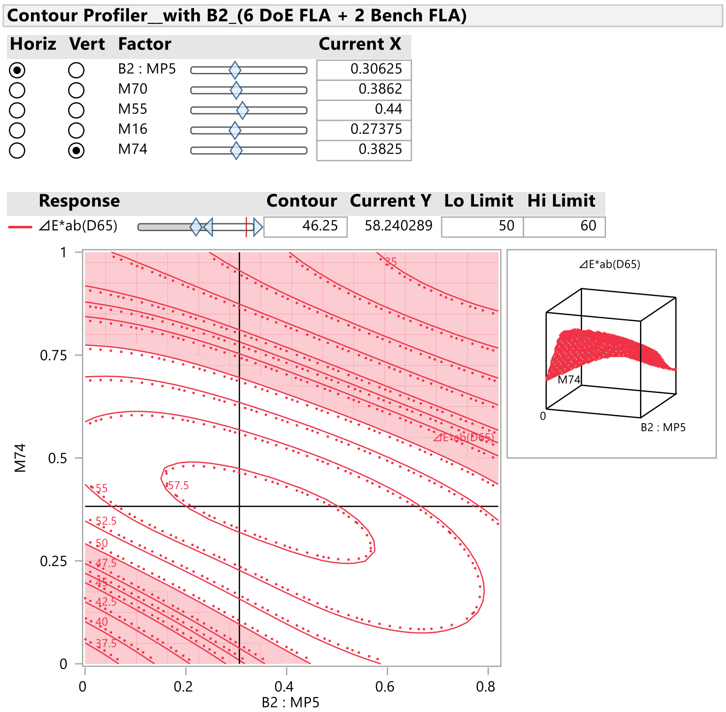




Contour profiler for ⊿E

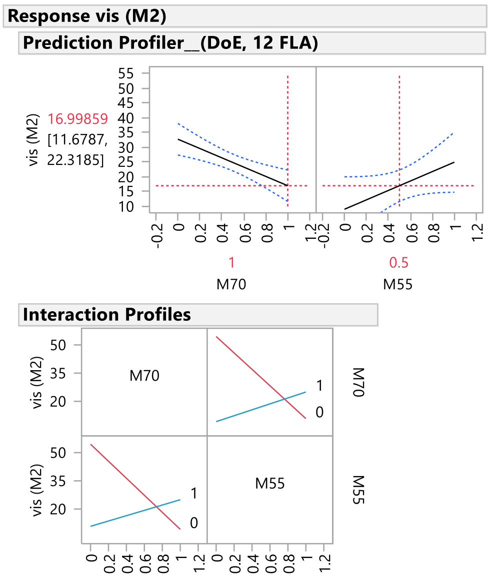
The counter profiler is the 2-dimension projection of the surface plot. Points on the same counter line will generate same predicted ⊿E results.

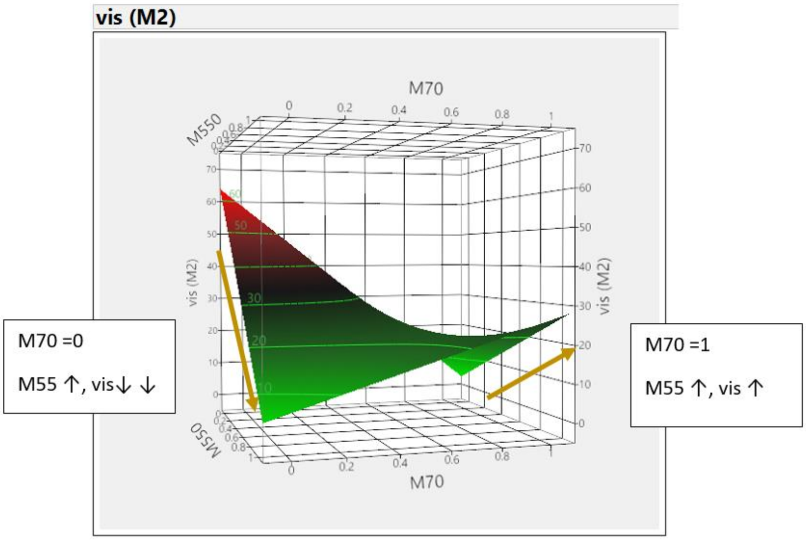
The white area is target formulation space, with predicted ⊿E between 50 and 60.



<u>Viscosity understanding (vis(M2))</u>

All 12 DoE trials are used for following analysis on viscosity. And interaction between M70 and M55 has been explored and visualized. When M70 at low conc. as 0%, increasing M55 the viscosity decreased; when M70 at high conc. as 1%, increasing M55, viscosity increased.





4. Discussion and Conclusion:

Compared to space filling and other screening or optimization designs used internally, UD shows real benefit to find quick answer with fewer trials. More than 70% lab resources have been saved in this case study.

UN can be one solution to answer fast track needs. When fewer factors are important for the performance, UN also allowed to construct mathematical modelling for better quantify factors' effect on product performance.

References:

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