CHAPTER 40

RESPONSE SURFACE METHODOLOGY FOR THE OPTIMIZATION OF EXTRACTION PROCESSES

Eldho Varghese
ICAR-Central Marine Fisheries Research

ABSTRACT

RSM involves setting up experiments, determining a model that fits the data, and finding optimal settings for experimental factors. The text also introduces response surface designs, factorial designs, and mixture designs for experimentation and optimization. The stages of implementing RSM, including fixing objectives, screening, regression modeling, experimentation, model building, optimization, and verification, are detailed. The text concludes with case studies illustrating the application of RSM in food processing and mixture design for dark chocolate production. Additionally, information on constructing response surface designs using software and an overview of the stages of RSM implementation are provided.

Keywords: Response Surface Methodology (RSM), Optimization, Experimental Design, Factorial Designs, Mixture Designs

INTRODUCTION

In any product and process optimization, the use of the traditional OFAT approach examines only one parameter at a time while keeping other parameters constant and does not estimate interaction which results in inadequate optimization. On the other hand, however, factorial designs allow us to identify both the significant factors and important interactions among the factors in fewer test than OFAT, it fails to predict the best factor level settings to meet the desired goal (minimum/maximum/desired responses) in the experimental region. The limitations of classical method are eliminated by optimizing all the affecting variables collectively using response surface methodology (RSM) introduced by Box and Wilson (1951). Response Surface Methodology (RSM) isused to examine the functional relationship between one or more response variables and a set of experimental variables or factors. These methods are often employed after one has identified a “vital few” controllable factors and the factor settings that optimize the response are to be found. Designs of this type are usually chosen when a curvature in the response surface is suspected. RSM is thus a set of techniques that includes (i) Setting upan experiment (designing an experiment) that will yield adequate and reliable estimates of theresponse of interest, (ii) Determining a model that best fits the data collected from the design chosen by conducting appropriate tests of hypotheses concerning the model's parameters and

(iii) Determining the optimal settings of the experimental factors that produce the maximum (orminimum) value of the response. RSM finds a wide range of applications in developing, improving, and optimizing processes inseveral research field viz., agricultural experiments, food science and technology, life science, fisheries, biochemistry, analytical chemistry and engineering etc.,

Example 1: Food processing studies are being carried out to add value to agricultural produce. The main goal of these studies is to find the best mix of values for numerous parameters that areessential for the product. To be more specific, suppose you're conducting an experiment on osmotic

dehydration of banana slices to find the best combination of sugar solution concentration, solution to sample ratio, and osmosis temperature. The following are the levels ofthe various factors:

	Factors	**Levels**
1.	Concentration of sugar solution	40%, 50%, 60%, 70% and 80%
2.	Solution to sample ratio	1:1, 3:1, 5:1, 7:1 and 9:1
3.	Temperature of osmosis	25^0C, 35^0C, 45^0C, 55^0C and 65^0C

In this situation, response surface designs for 3 factors each at five equispaced levels can be used.

Example 2: In the fish culture experiment, the optimization of fish culture condition is required to produce larvae of Genetically Improved Farmed Tilapia (GIFT). Thus, for instance to optimize the culture conditions at different levels of salinity and temperature, the response surface methodology using two factors Central Composite Design is suitable.

Example 3: In analytical chemistry, the enzyme Anthocyanins (ACNs) is emerged as promising nutraceutical ingredients for developing functional foods and dietary supplements. To enhancethe concentration of anthocyanins, optimization of enzyme-assisted processing with subject tofollowing factors level is needed:

	Factors	Levels
1.	Enzyme Concentration (%)	0.05, 0.15 and 0.25
2.	Temperature (˚C)	50, 60 and 70
3.	Time (minutes)	30, 60 and 90

This can be achieved by using response surface methodology with the use of a three-level Box-Behnken design.

RESPONSE SURFACE MODEL

Response Surface Designs (RSDs) are extensively used in experiments to determine the relationship between the response and a set of experimental factors (quantitative and/or qualitative) and to find the factor levels combination that renders the optimum responses (Khuri and Cornell,1996 and Myers et al., 2016). RSD shave broad applications in developing, improving, and optimizing processes in diversified fields of sciences. Several books are available in order to understand general philosophy of the theory vide Myers (1971), Khuri and Cornell (1996), Khuri (2006), Box and Draper (2007) and Myers et al. (2016). Also, many review papers on Response Surface Methodology (RSM) concept (Hill and Hunter,1966; Mead and Pike,1975; Myers et al. 1989; Myers et al. 2004 and Khuri and Mukhopadhyay, 2010; Hemavathi et al., 2022) are available

Let there be v independent input/ experimental variables/ factors denoted by x_1, x_2,……..x_v and a response variable y and there are N observations. The response is a function of input factors, i.e.,

$$Yu= f(x_{1u}, x_{2u}, x_{3u},\ldots\ldots,x_{vu}) + e_u \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(1)$$

where u=1,2,…,N, x_{iu} is the level of the i^{th} (i =1, 2, …….,v) factor in the u^{th} treatment combination, y_u denotes the response obtained from uth treatment combination. The function f describes the form in which the response and the input variables are related and u_e is the random error associated with the u^{th} observation that is independently and normally distributed with mean zero and common variance σ^2

In practice, the form of f is not known and it is therefore approximated, within the experimental region, by a polynomial of suitable degree in variables. Polynomials which adequately represent the true dose-response relationship are called response surface models and the designs that allow the fitting of response surfaces and provide a measure for testing their adequacy are called response surface designs.

A response surface model can be represented in matrix notation as,

$\beta Y = e X +$,

where $Y = (y_1 y_2 \ldots y_N)'$ is an N×1 vector of observations, X is a N × (p+1) matrix of independent variables, $\beta = (\beta_0\, \beta_1 \ldots \beta_p)'$ is a (p+1) × 1 vector of parameters. $e = (e_1\, e_2 \ldots e_N)'$ is N×1 vector of random errors distributed as $\sigma N\,(I0,)'_N$. The Least squares estimator of β is

$\beta\hat{} = (X'X)^{-1}X'Y$

With, $DB(\hat{})=X(X')^{-1}\,\sigma^2$

An estimate of σ^2 can be obtained as

$\sigma^2 = (\beta Y - YX)(X\beta) / N\text{-}P$

In many response surface problems, the experimenter is interested in predicting the response Y or estimating the mean response at a particular point in the variable space. The variance of the prediction is also of interest, because this is a direct measure of the likely error associated with the point estimate produced by the model. The variance of the estimate of the mean response at

$$Var[\hat{y}(x_0)]=s2x_0'(X'X)^{-1}x_0$$

The point x_0 is given by. If the variance is same for all points x_0 that

are at the same distance from the centre of the design, the design property is called rotatability.

EXPERIMENTAL DESIGNS FOR OPTIMIZATION TRIALS

Response surface designs

Response surface designs are experimental designs used in statistical modeling and optimizationto study the relationship between input variables (factors) and the output response of a system or process. These designs are particularly useful when the relationship between the factors and theresponse is complex and cannot be easily represented by a simple linear model. Response surface designs aim to efficiently explore the design space and identify optimal conditions for the desired response.

Factorial designs are widely used in experiments involving several factors where it is necessary to investigate the joint effects (main effects and interactions) of the factors on a response variable. A very important special case of the factorial design is that where each of the v factors of interest has only two levels. Because each replicate of such design has exactly

2^v experimental trials or runs, these designs are usually called 2^v factorial designs. The class of 2^v factorial designs are very important in response surface work. Specifically, they find applications in three areas:

1. The 2^v design (or a fraction of it) is useful at the start of a response surface study where screening experiments should be performed to identify the important process or system variables.

2. A 2^v design is often used to fit a first-order response surface model and to generate the factor effect estimates.

3. A 2^v design is a basic building block used to create other higher order response surface designs. For example, augmenting a 2^vdesign with axial runs, a central composite design isobtained which is one of the most important designs for fitting second- order responsesurface models.

Central composite design (CCD) is one of the most popular class of second-order designs. It wasintroduced by Box and Wilson (1951). Much of the motivation of the CCD evolves from its usein sequential experimentation. It involves the use of a two-level factorial or fraction (resolutionV) combined with the following 2v axial or star points and some central points. The designinvolves, F factorial points, 2v axial points and nc center runs. The total number of runs is F +2v+ n_c. The factorial points represent a variance optimal design for a first order model or a firstorder plus two-factor interaction type model. Center runs clearly provide information about theexistence of curvature in the system. If curvature is found in the system, the additional of axialpoints allow for efficient estimation of the pure quadratic terms.

For fitting second order response surfaces, Box and Behnken (1960) devised a series of efficient three-level designs. This design class is based on the construction of BIB designs. In many RSM circumstances, the research is too large to allow all runs to be done in the same way. As a result, second-order designs that promote blocking—that is, the inclusion of block effects—are crucialand intriguing to examine. It is critical that the design points be assigned to blocks in such a way that the impact on the model coefficients is minimized. The property sought is orthogonal blocking, which implies that the block effects in the model are orthogonal to the model coefficients.

DESIGNS FOR MIXTURE EXPERIMENTS

When all of the factors are quantitative, it's natural to consider of the response as a function of the levels factors, and data from quantitative factorial experiments can be used to fit the response surface to the desired region. To deal with such issues, response surface designs are developed.

The levels of components are independent in response surface designs, and the number of inputs (levels) is fixed by the experimenter to get the best response region. In another sort of experiment known as mixture experiments, the response is determined by the proportions of theinput ingredients employed, i.e. researchers are interested to evaluate the performance of various mixtures generated by mixing two or more substances in mixture experiments. The percentage orfraction of a component in the mixture refers to the amount of that component in relation to the over all amount of the mixture. As a result, the sum of proportions of the mixing components equals one.

Designs for mixture experiments have been widely employed in agricultural and industrial research. Split fertilizer application, inter cropping experiments where the goal is to find the bestcrop mixtures; sensory evaluation experiments for agricultural and animal products; fertilizer, insecticides/pesticides mixtures for optimum response; feeding trials in animal /fish nutritional experiments; in construction concrete, the hardness or compression strength of the mixture is of interest; in railway flares, the illumination and duration of the illumination of the flares are the interesting properties; in fruit punch the fruitiness flavor of the punch is the property of interest; and in cake formulation, the property of interest is the fluffiness of the cake or the layered appearance are just a few examples of situations where these designs could be beneficial. The property of the final product depends on the percentage or proportions of the ingredients mixed. From experimental view point, such a study is of interest in order (i) to determine some combination of the mixture ingredients that would be best in some sense, or (ii) to have a better understanding of the effects of the ingredients on the response. Mixture experiments can be used in with unrestricted region, with restricted region having upper and/or lower bounds, with process variable(s).

STAGES OF IMPLEMENTATION OF RESPONSE SURFACE METHODOLOGY (RSM)

1. Fixing the objective of the study.
2. Screening phase/Screening Experiment in which significant independent variables areselected with the help of first order response surface design such as 2v factorial designs (FD), fractional replicates of the 2v factorial designs (FFD), Simplex designs, Plackett-Burman designs (PB), Definitive screening designs (DSD) and custom design.

3. Regression modelling: Form the regression equation using the effect term that showsstatistical significance on response. If the response is well modelled by a linear term of independent variables, then the approximating function is a first-order model. If the model shows a significant lack of fit (from ANOVA), then the first-order model will be inadequate; hence a polynomial of a higher degree (second order design) must be used. For screening experiment first order model is used.

4. Experimentation using response surface design: Select the appropriate second order rotatable design according to the selected experimental matrix (based on the number of factors selected, the level, and the number of runs). The most commonly used second order response surface designs are (i) 3vfactorial design, (ii) Box Behnken design (BBD) and (iii) Central (face) Composite design (CCD/FFCD).

5. Model building and validation: The adequacy of the fitted model is evaluated based onseveral mathematic–statistical criteria such as prediction error sum of squares (PRESS) residuals, the lack-of-fittest, residual analysis, coefficient of determination (R^2) etc. Sometimes high value of R^2 is not an indicative of the accuracy of the model, in such casethe best measure is absolute average deviation (AAD). Once the fitted model is found tobe adequate the required optimization technique can be applied. If the model shows significant lack of fit, then go for further higher order model.

6. Optimization of response using graphical (response surface plot and contour plot) and numerical approach. In case of multi-response optimization desirability function approach is used.

7. Verification of results: To verify the desired optimum conduct confirmatory trial.

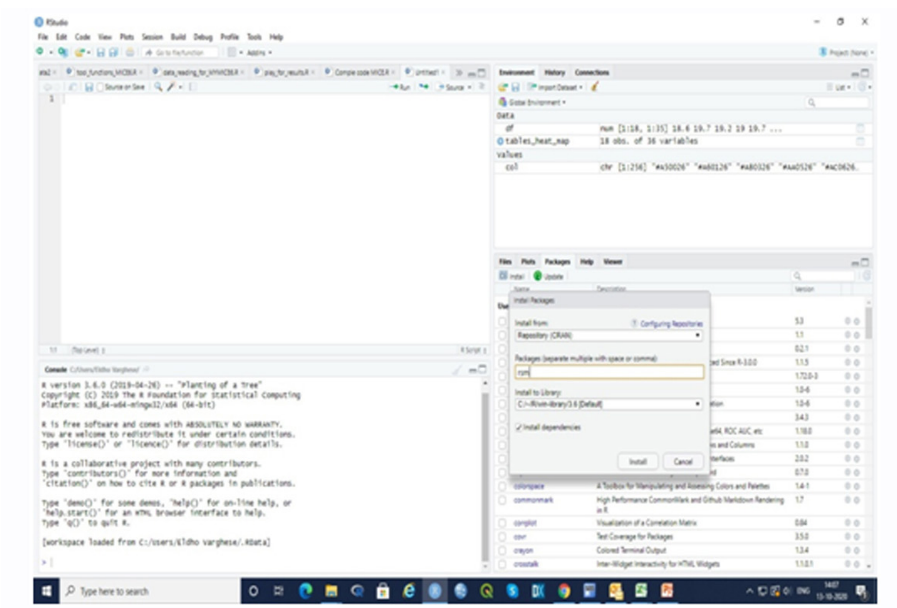
5. RESPONSE SURFACE METHODOLOGY USING SOFTWARE

Construction of response surface design

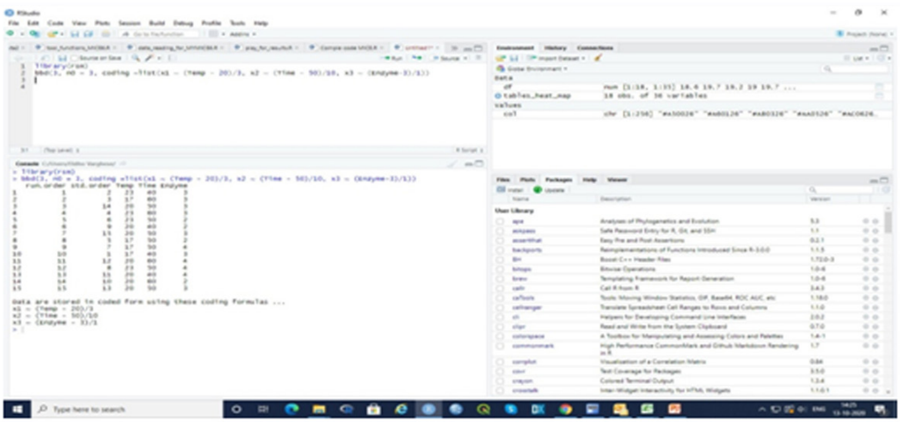
There are R packages available for the generation of response surface and mixture designs and also for the analysis.

Some snap shots have been provided below

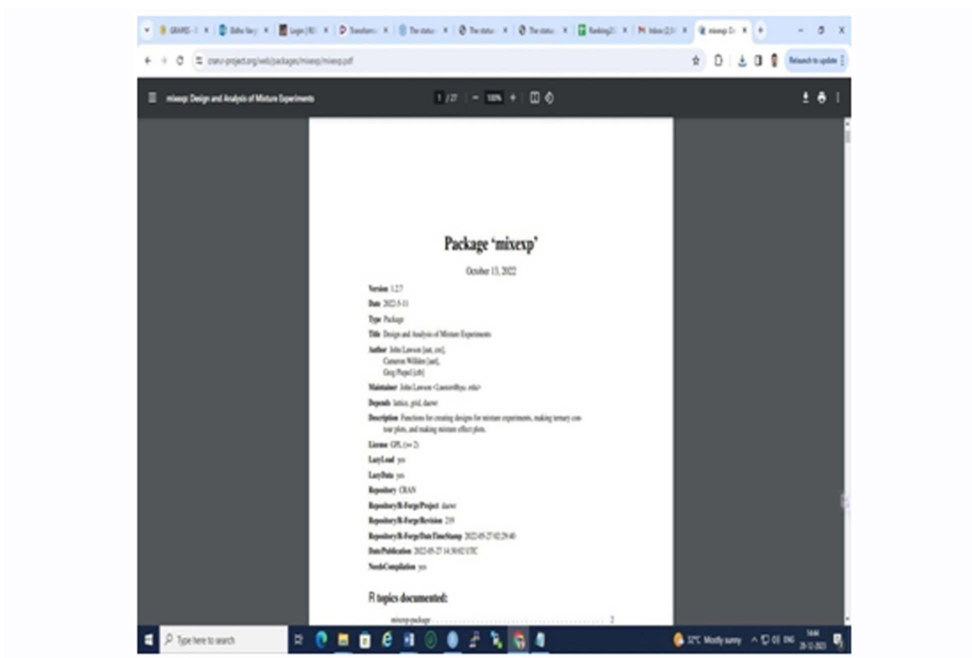
To install the package named “rsm”



Generation of Box-Behnken design



Another package named “mixexp” is available for the for generating mixture designs

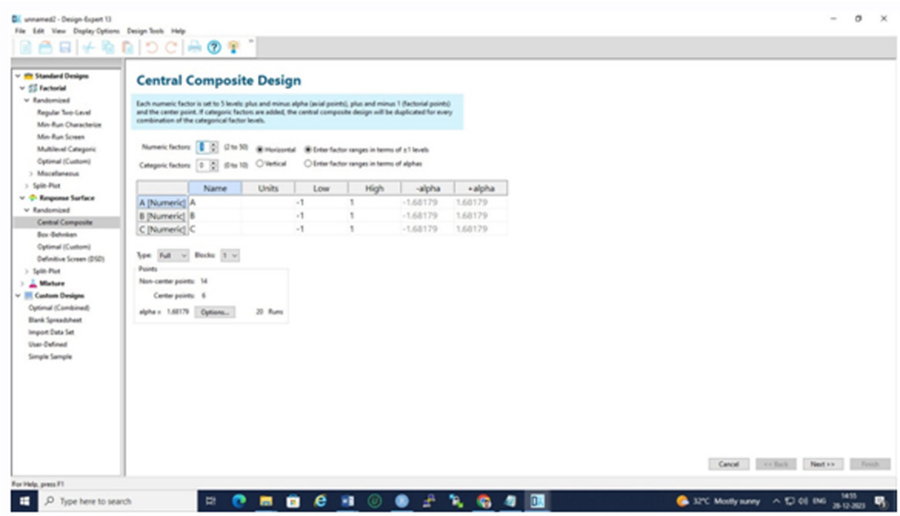


Generation of Response surface design and fitting of model using Design Expert Software

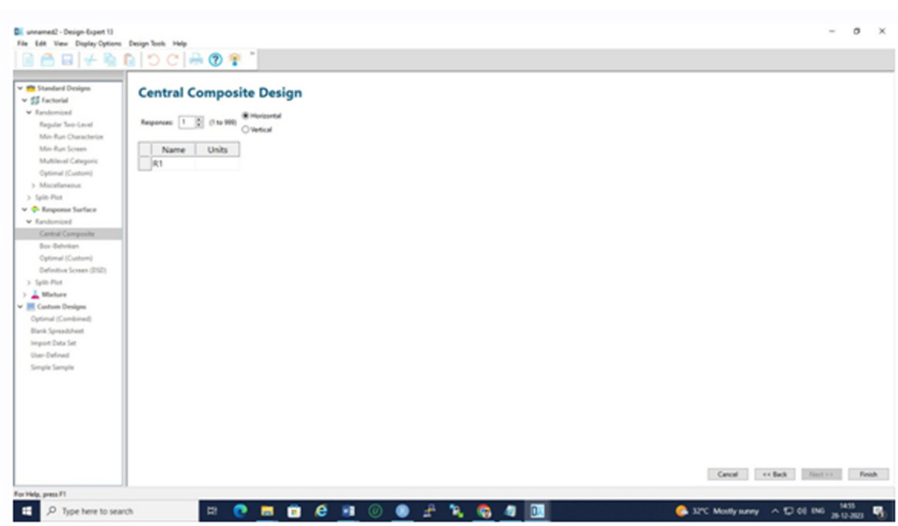
(i) Construction of CCD

Go to main menu and click Central Composite under response surface tab

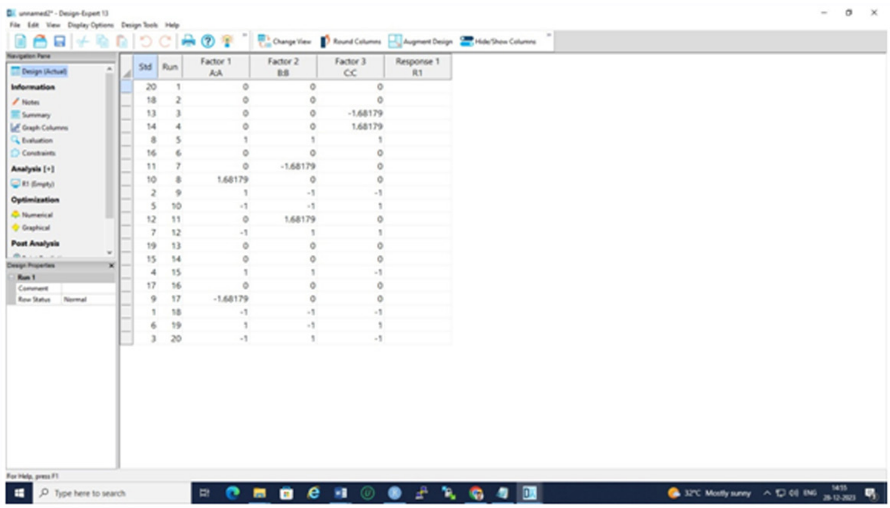
Enter the number of factors and continue



Select the number of response variables and continue

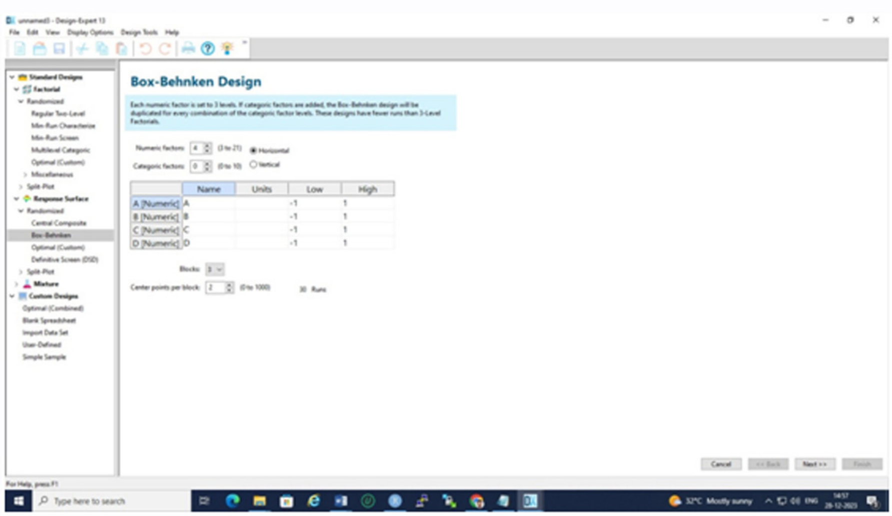


Layout of the design as follows:

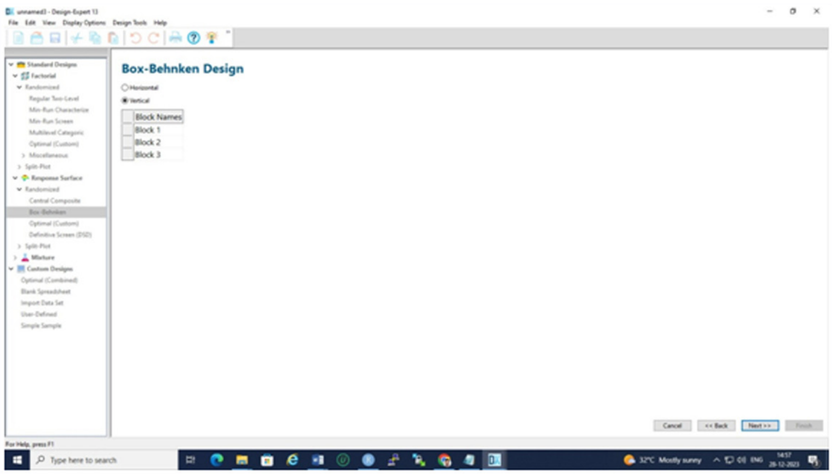


(ii) Construction of Box-Behnken Design

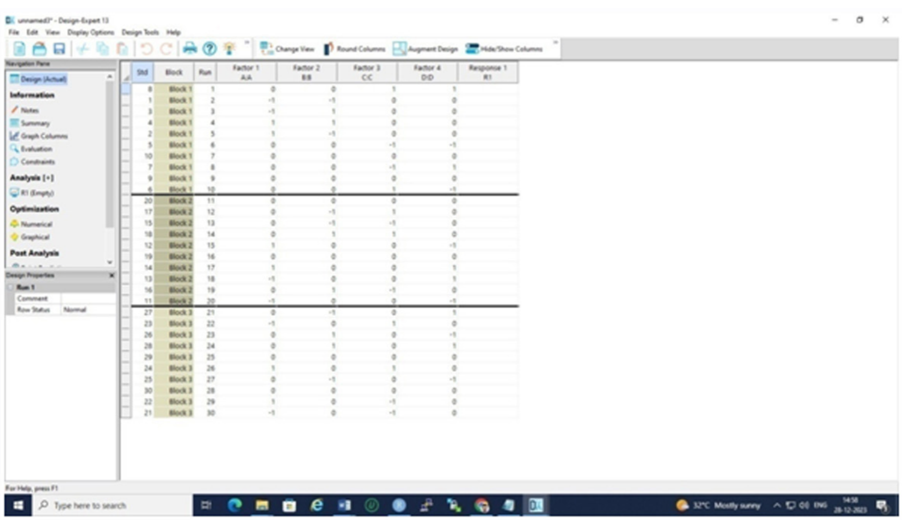
Go to main menu and click Box-behnken under response surface tabEnter the number of factors and number of blocks and then continue



Give the block labels (If required)



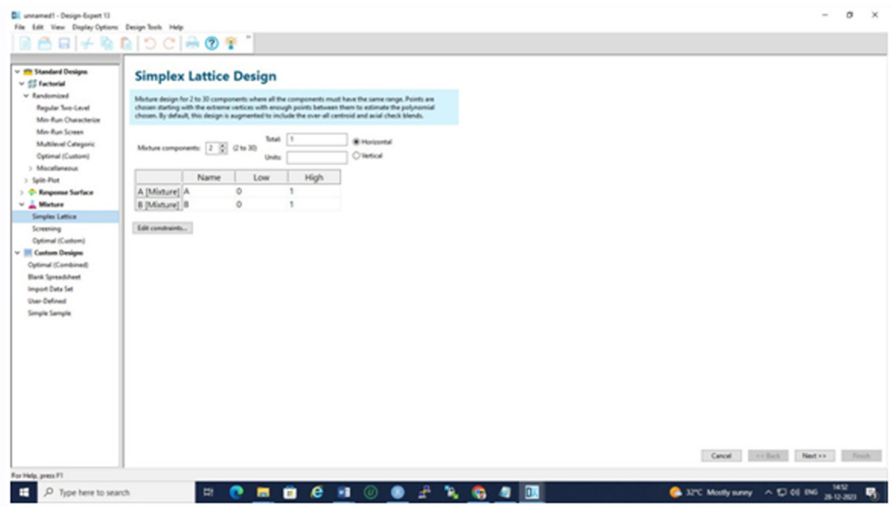
Layout of the design as follows:



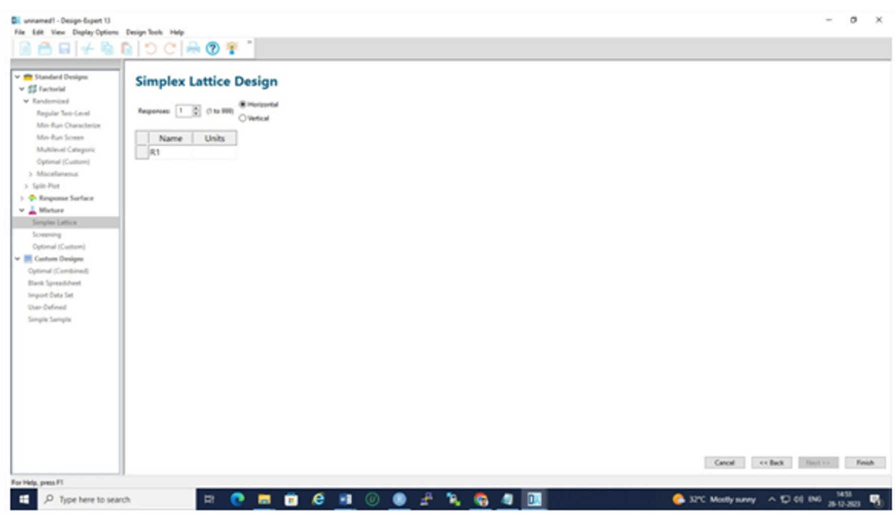
(iii) Construction of Simplex Lattice Designs for mixture experiments

Go to main menu and click Box-behnken under response surface tab Enter the number of factors and number of blocks and then continue

Select the number of response variables and continue



Layout of the design as follows:



SOME CASE STUDIES

Application of response surface design

An Experiment was conducted at Division of Food Science & Post Harvest Technology, ICAR-IARI, New Delhi (Anand et al., 2023) using a response surface design (central composite design) for optimizing the effects of 3 independent variables and their 5 levels; (A) MTS:WPC matrix ratio (0, 25, 50, 75, and 100 %), (B) homogenization pressure (10000 to 30,000 psi), (C) oil content (2to6%), where Chia seed oil (CSO) was encapsulated using whey protein concentrate (WPC) and modified tapioca starch (MTS) through freeze-drying. The responsevariables were encapsulation efficiency (EE) and α-linolenic acid (ALA). The experimental layout constituting five level-central composite designs was obtained from Design Expert software (ver. 13) (Licensed to ICAR-CMFRI, Kochi). Table 5.1.1 shows the layout of 28 experimental runs that include 2 replicates of factorial points, 1 axial, and 6 central points providing enough degrees of freedom for testing the lack of fit of the model.

Table 5.1.1 The experimental runs of emulsion and their observed responses.

	Independent Variables			**Response Variables**	
Run	**MTS Levels (% w/w)**	**Pressure (psi)**	**Oil content (% w/v)**	**EE (%)**	**ALA (%)**
	A	B	C		
1	25	25000	5	93.68	56.17
2	50	20000	4	89.08	58
3	25	15000	5	95.84	57.94
4	25	25000	3	97.95	56.87
5	75	15000	5	43.12	60.33
6	50	10000	4	64.33	59.2
7	75	15000	3	59.97	61.01
8	50	20000	4	92.7	58.5
9	50	20000	4	88.01	58.14
10	100	20000	4	21.89	64.21
11	50	20000	4	97.83	58.6
12	75	25000	3	60.12	61.5

13	75	25000	5	43.32	60.1
14	50	20000	2	87.49	56.41
15	50	20000	4	76.27	59.34
16	75	25000	5	37.04	62.66
17	25	15000	5	94.36	57.46
18	75	25000	3	46.92	60.04
19	25	25000	3	95.52	55.08
20	50	20000	6	63.87	57.65
21	75	15000	5	41.28	61.8
22	50	30000	4	87.77	59.03
23	50	20000	4	77.86	59.44
24	25	25000	5	95.56	57.54
25	25	15000	3	97.23	55.4
26	0	20000	4	98.45	56.37
27	25	15000	3	87.18	55.36
28	75	15000	3	65.18	59.93

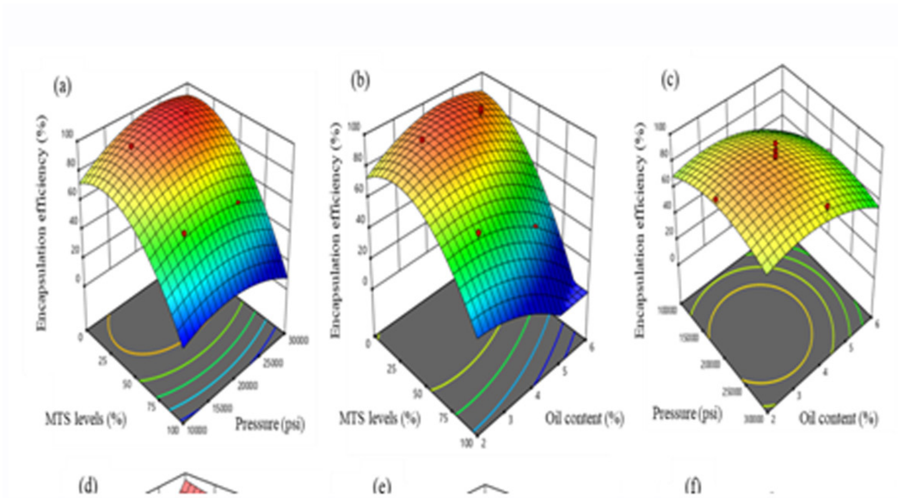
*MTS Levels is % of modified tapioca starch replacing whey protein concentrate from a total wall material of 25% (w/v) in the emulsion. EE is encapsulation efficiency. ALA is alpha-linolenic acid. A second order model was fitted to establish the functional relationship between input variablesand each response variables. The analysis of variance (ANOVA), R^2, adjusted R^2, predicted R^2 and lack of fit statistics were worked out and given in Table 5.1.2 to check the significance of the fitted model.

Table 5.1.2 Analysis of variance (ANOVA) results for response surface quadratic model forencapsulation efficiency (EE) and alpha-linolenic acid (ALA).

Source	df	SS	MS	F-Ratio	Prob > F
EE					
Model	9	13312.00	1479.11	28.68	<0.0001
Lack of fit	5	396.22	79.24	1.94	0.1564
Pure Error	13	532.21	40.94		
C. Total	27	14240.43			
				R^2	0.9348
				Adjusted R^2	0.9022
				Predicted R^2	0.8179
ALA					
Model	9	127.30	14.14	21.67	<0.0001
Lack of fit	5	1.28	0.2561	0.3181	0.8933
Pure Error	13	10.47	0.8052		
C. Total	27	139.05			
				R^2	0.9155
				Adjusted R^2	0.8733
				Predicted R^2	0.8006

*df = Degree of Freedom, SS = Sum of Square & MS = Mean Square

The values obtained through ANOVA resulted in R^2(0.9155), p (<0.0001), and a non-significant lack of fit (0.8933). The difference between adjusted R^2(0.87) and predicted R^2 (0.80) was <0.2. The statistical values suggest an excellent model-fit and good prediction of the influence ofvariables on ALA. Similar results can be seen for the response EE.



3D Response surface graph obtained for the varying levels of independent variables on response

Furthermore, the fitted model was optimized for the input variable and response by assigning goals. The optimum values for input variables to achieve these goals were done by multi-response optimization based on the desirability function (Derringerand Suich,1980). The optimized condition obtained to maximize the oil content and EE while setting ALA in the response range was; (MTS:WPC) ratio 25:75, 23,000 psi, and 5 % oil content for the desirability of 0.998. The optimized conditions resulted in high EE (97%), ALA content (59.54%), and a Ω-3:Ω-6 ratio (3.34). The validation of the predicted response was experimentally verified, and the values obtained were; 97.23% EE and 59.54% ALA showing a deviation of 1% and 4%, respectively.

APPLICATION OF MIXTURE DESIGN

An experiment was conducted at Central Plantation Crops Research Institute (ICAR-CPCRI), Kasaragod (Beegumet al., 2022) to find the optimum requirement of selected components suchas cocoa nibs (A), cocoa butter (B) and coconut sugar (C) to make dark chocolate based on the sensory perception. An Optimal mixture design was used for experimentation. Mixture design is a flexible design structure to accommodate models categorical factors, and irregular (constrained) regions. Optimal design begins with a pseudo-random set of model points (runs) that are capable of fitting the designed for model. The preliminary experiments on bean to barchocolate showed the acceptable minimal and maximal limit of cocoa nibs, cocoa butter andcoconut sugar as 35-50%, 15-30% and 20-35% respectively. Sensory attributes were selected asthe responses. Three components represent hundred weight-percent of the total formulation, thatis; cocoa nibs (A) + cocoa butter (B) +coconut sugar (C) = 100%. The constraint and component ranges were as follows.

Table 5.2.1 Limit and constraints in the selected variables and model

Low Limit		Constraint		High Limit
35.000	≤	A:C	≤	50.000
15.000	≤	B:CB	≤	30.000
20.000	≤	C:CS	≤	35.000
		A+B+C	=	100.000

Table 5.2.2 shows the experimental design in terms of actual components. An optimal mixture design with 14 runs (including two centre points) was generated for experimentation.

Table 5.2.2 Optimal Experimental design

A	B	C
42.5	30	27.5
47.5	20	32.5
47.5	27.5	25
40	27.5	32.5
42.5	22.5	35
45	25	30
50	22.5	27.5
50	15	35
50	30	20
35	30	35
50	30	20
50	15	35
42.5	30	27.5
35	30	35

The model used for establishing a relationship between the response and the input variable was in the form:

$$Y = \beta_1 A + \beta_2 B + \beta_3 C + \beta_{12} AB + \beta_{13} AC + \beta_{23} BC + e$$

where, Y represents sensory attributes (the response variable). A, B and C refers to the levels of independent factors being evaluated [viz., A=cocoa nibs (%), B=cocoa butter (%) and C= coconut sugar (%)]. β_i, β_{ii} and β_{ij} [$i<j=1$, 2 and 3].

The error term 'e' is assumed to follow normal distribution of independent and identical distribution characterized with zero mean andconstant variance. The suitability of the developed model was tested by calculating coefficient of determination (R^2), adjusted R^2 and predicted R^2. Statistical significance of the model was also assessed using ANOVA and the significance of the estimated regression equation was examined by t-test at $p<0.05$. Numerical optimization was used for the simultaneous optimization of multiple responses.

Table 5.2.3. ANOVA of the polynomial models for the response (Appearance)

ANOVA	Appearance
Model F value	14.21
Model p value	0.000835***
Linear Mixture (F value)	6.92**
AB (F value)	15.67**
AC(F value)	28.99**
BC (F value)	9.45**
R2	0.899
Adj-R2	0.835
Predicted R2	0.69
Adeq. precision	10.07
CV%	2.68
Mean	7.70
Standard deviation	0.21

(* P < 0.05, ** P < 0.01 and *** P < 0.001, ns– non-significant)

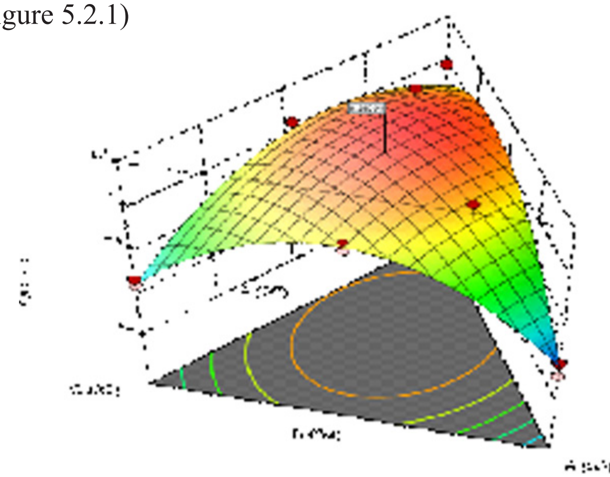
ANOVA reveal that the model was highly significant (Table 5.2.3). The linear effect of cocoanibs and cocoa butter as well as cocoa nibs and coconut sugar was highly significant ($p<0.01$). However, the interaction between cocoa butter and coconut sugar was found significant at 5% level. It was evident that the model comes out best with low standard deviation (0.21), high R-Squared (0.899) and low PRESS (1.04) values. Adequate precision ratio of 10.07 indicates an adequate signal. The data points were approximately linear suggesting no sign of any problem inthe data. It is evident from the 3D surface graph (Figure 5.2.1) that the effect of all three components was similar, showing an increasing trend followed by a peak and then a decline in the appearance. Main effect of all three independent variables was found to be negatively correlated with appearance. Nonetheless, the interaction effects were positively correlated. The linear and interaction equation in terms of real and actual components obtained for appearance is as follows,

Final equation in terms of real components:

$$\text{Appearance} = -29.20A - 45.10B - 45.09C + 142.70AB + 161.92AC + 110.83BC$$

Cocoa nibs and cocoa butter contribute much on the appearance including the shape and colour of the chocolate. The more the cocoa nibs, the darker the colour and vice versa. Similarly, pale yellowish colour of cocoa butter and coconut sugar provided lighter colour to chocolates.

The optimum combination of process variables for the best set of response properties were,44.7% cocoa nibs, 25.2% cocoa butter and 30.2% coconut sugar. The responses (sensory score) calculated at optimal extraction conditions consisted of hedonic score of 8.28 for appearance (Figure 5.2.1)



3D Response surface graph obtained for the varying levels of independent variables on response

SUGGESTED READINGS

Anand, V., Ksh, V., Kar, A., Varghese, E., Vasudev, S., &Kaur, C. (2023). Encapsulation efficiency and fatty acid analysis of chia seed oil microencapsulated by freeze -dryingusing combinations of wallmaterial, FoodChemistry.

Beegum P.P, S., Pandiselvam, R., S.V., R., P, S., Nooh, A., S, N., Gupta, A., Varghese,E., Balasubramanian, D., Apshara, E. S., Manikantan, M. R.,& Hebbar, K. B. (2022). Sensorial, textural, and nutritional attributes of coconut sugar and cocoa solids based"bean-to-bar" dark chocolate. Journal of Texture Studies,1–13.

Box, G. E. P. and Behnken, D. W. 1960. Some new three level designs for the study of quantitative variables. Technometrics, 2, 455–475.

Box, G. E. P. and Wilson, K. B. 1951. On the experimental attainment of optimumconditions. Journal of the Royal Statistical Society, SeriesB, 13, 1-45.

Box,G.E.P.,andN.R.Draper.2007.ResponseSurfaces,Mixtures,andRidgeAnalyses, 2nd ed. Hoboken, NJ: Wiley.

Hill, W. J. and Hunter, W. G. 1966. A review of response surface methodology, Aliterature survey. Technometrics, 84, 571- 590.

Hemavathi, M., Varghese, E., Shekhar, S., Jaggi, S., Bhowmik, A. and Sathianandan,T.V.,2022c.Run order consideration for sequential third order rotatable designs. Communications in Statistics-Simulation and Computation,1-14.

Khuri, A. I. (2006). Response surface methodology and related topics. Singapore: WorldScientific Publishing.

Khuri, A. I., & J. A. Cornell. (1996). Response surfaces, designs and analyses, 2nd ed. New York: Dekker.

Khuri, A.I.,& Mukhopadhyay, S. (2010). Response surface methodology. Wiley interdisciplinary reviews. Computational Statistics, 2(2), 128-149.

Mead, R. & Pike, D.J. (1975). Are view of response surface methodology from a biometrics viewpoint. Biometrics, 31, 803-851.

Myers, R. H. (1971). Response Surface Methodology. Allyn and Bacon, Boston.

Myers, R.H, Khuri A.I., & Carter W H. (1989). Response methodology, 1966-1988, Technometrics, 31, 137-157.

Myers R.H, Montgomery D.C, Vining GG, Borror C M and Kowalski S M. (2004). Response surface methodology a retrospective and literature survey. Journal of Quality Technology, 36(1), 53-77.

Myers, R. H., D. C. Montgomery, & C. M. Anderson-Cook. (2016). Response surface methodology: Process and product optimization using designed experiments, 4th ed. Hoboken, NJ: John and Wiley Sons.