A Response Surface Approach to Factors Affecting Amplitude of Accommodation: A Case Study of Imo State University

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Abstract This study examines the effect age, quantity of caffeine intake and weight of an individual have on amplitude of accommodation. The purpose is to model the relationship age, quantity of caffeine intake and weight have on amplitude of accommodation among normal healthy adults in Imo State University, Owerri. A response surface methodology approach was employed using the Face centre cube central composite design and Analysis of Variance (ANOVA). The results show that the relationship is of quadratic model and it is significant (2.30 > 0.0347). From the model, the variables (Age, Amount of Caffeine intake) in the linear and squared terms of the model were significant while all the variables in interaction terms were not significant.

Keywords Amplitude of Accommodation, Response Surface Methodology, Central Composite Design

1. Introduction

The amplitude of accommodation (AA) is the maximum potential increase in optical power that an eye can achieve in adjusting its focus. According to [1], it refers to a certain range of object distances for which the retinal image is as sharply focused as possible. [2] identify AA as an important parameter in the diagnosis and treatment of accommodative anomalies, as well as the determination of reading addition of presbyopes. Accommodative abnormalities according [3] are the common visual disorders, which are associated at times with symptoms, such as headache, asthenopia, etc while reading. While [4] put the incidence of accommodative abnormalities of patients who come to optometry clinics at 20%, Amplitude of Accommodation is rarely integrated into routine clinical examinations by eye-care practitioners. This abnormality has in most cases result in inaccuracies in the assessment of accommodative function and prescription of reading addition. Amplitude of accommodation according to [5], reduces progressively from childhood to old age. Apart from age as having influence on AA, many researchers have also identified caffeine as having influence on Amplitude of Accommodation. [6], in their study suggested that Caffeine intake is associated with pupil dilation and enhanced accommodation. [7], though limited there study on healthy subjects of Benin metropolis of Nigeria, which revealed that the ingestion of caffeine has a significant positive effect on amplitude of accommodation. [8] studied the effects of caffeine on visual performance among youths. Their result showed Caffeine consumption has some effect on visual performance of the eye by increasing reading rate and tear film quality. [2], examined the amplitude of accommodation (AA) of healthy individuals' ages ranging from 5 and above 55 years in Owerri Municipal Council of Imo State using Donders' Push-up-to-blur (PUB) technique; and compared it with the average AA derived from Hofstetter's equation. Their results showed that age and AA were inversely but significantly correlated (p < 0.05), with the 5-14 and ≥ 55 years age categories having the highest (17.49D) and least (1.60D) AA values respectively.

Response Surface Methodology (RSM) is a rudimentary subject in statistical design of experiment which according to [9], is a collection statistical and mathematical methods that are useful for developing, improving and optimizing process. RSM experiments are designed to allow for the estimation of interaction and quadratic effects of a model. The true response function in most RSM problems are unknown. Therefore in order to develop a proper approximation for the function, it starts with a low order polynomial which is define by a linear function of an independent variable called a first order model. If there is a curvature in the response surface, then a higher degree polynomial is added to the first order model. In this, an approximating function with two or more variables is known as second order model given as follows.

$$y = \beta_0 + \sum_{i=1}^{k} \beta_i x_i + \sum_{i=1}^{k} \beta_{ii} x_{ii}^2 + \sum_{j=i+1}^{k}\sum_{i=1}^{k-1} \beta_{ij} x_i x_j + \varepsilon_{ij} \quad (1)$$

Where y is the measured response, β's are parameter coefficients; x_i's are the input variables and ε is an error term.

Most second order designs especially the Central composite design by [10] utilizes the above stated model. The central composite design (CCD) is made up of three parts namely; the factorial portion which consists of 2^k full or 2^{k-1} half replicate (*k* is the number of independent variables) coded as (± 1, ± 1, ..., ± 1), the axial or star points which consist of 2*k* coded in the form ($\pm\alpha$, 0,..., 0), (0, $\pm\alpha$,..., 0), and finally, a center point which is coded as (0, 0, ..., 0).

The center points provide information about the existence of curvature in the system. To provide flexibility and better estimate of the pure error and power for the test is determine by the number of center points. The scaled prediction variance of a design according to [11] is also affected by the choice of the number of center points. If the curvature is found in the system, then the addition of axial points allow for efficient estimation of the pure quadratic terms. The choice of axial distance α not only is based on the region of interest but choosing the appropriate values of α specifies the type of CCD for any study. The factorial portion of the design allows for the estimation of the first-order and interaction terms in the model. To make appropriate choice of central composite design, [12] in their study stipulated the criteria for selecting the right central composite design among the variations of CCD.

[13] Stressed on the biological applications rather than applications in the physical and engineering sciences of RSM. They applied the RSM in agriculture and biometric research in general. However, they emphasized the use of nonlinear models to describe the behavior of biological data.

[14] highlighted the practical applications of RSM in the chemical and processing fields and recently reviewed by [9]. In health science, [15] applied RSM in a study of the effect of demographic characteristics on HIV risk in South Africa. This study was a follow up on their previous work [16] where a two-level fractional factorial design was used to develop a ranked list of important and unimportant demographic characteristics affecting the HIV status of pregnant mothers in South Africa.

The main objective of this study is to develop an approach for better understanding of the relationship between variables for optimum amplitude of accommodation. This will be achieve by fitting an appropriate model for amplitude of accommodation and also determine the main and or interactive effects of a factorial combination age, quantity of caffeine intake and weight on amplitude of accommodation using the central composite design of a second order design.

2. Design of Experiments

The data for this study consist of randomly selected 50 healthy individuals from the optometry department of Imo State University of ages ranging from 18 to 35 years, who were administered 250, 200, 150 mg of caffeine drink and there amplitude of accommodation taken after 60 minutes.

In this study, CCD was used for experimental design model with 5-level- 3 factors experiment. A 5-level-3-factor of face centre cube central composite design was employed in the amplitude of accommodation optimization process requiring 50 experimental runs. Age (x_1), Caffeine quantity intake (x_2) and Weight of the individual (x_3) are the independent variables to optimize the response value of interest (Amplitude of Accommodation). In developing the regression model, the test factors were coded according to the formulae given as

$$x_i = X_0 \pm \alpha(X/2) \qquad (2)$$

Where x_i is a coded variable of the ith variable, X_0 is the average of the variable in high and low level, X is the range between the variable at high level and variable at low level and α is the axial parameter. Table 1 is the estimated values of the three factors at five levels.

Table 1. Three Factors at Five Levels Estimated Values

Factors	Symbol	-α (1) Lowest	-1 Low	0 Centre	1 High	α (1) Highest
Age	x_2	18	18	26.5	35	35
Caffeine Quantity	x_2	150	150	200	250	250
Body Weight	x_3	55	55	72.5	90	90

As earlier noted, the CCD consists of the following three parts: (i) A complete (or a fraction of) 2^k factorial design whose factors' levels are coded as -1, 1. This is called the factorial portion of the design. The factorial portion in this study was replicated three times and the number of factors *k* = 3 which are Age, Caffeine intake (mg) and weight (kg) of the individuals, (ii) An axial portion consisting of 2*k* points arranged so that two points are chosen on the axis of each control variable at a distance of α from the design center (chosen as the point at the origin of the coordinates system). We refer to α as the axial parameter. The axial portion of this study was also replicated three times and α = 1 which makes this design a Face-center cube central composite design. The choice of Face-center cube central composite design was as a result of other variations of CCD not being significant. (iii) A center point n_0. The center-point for this study is 8.

Therefore the total number of design points for a CCD is given as $N = 2^k + 2k + n_0$. But for this study $N = 3(2^k) + 3(2k) + 8n_0$ which makes the number of runs for study to be 50 runs that is $N = 3(2^3) + 3(2*3) + 8 = 50$.

Table 2 is the full factorial central composite design matrix for the actual values of the data for the study with the coded values.

Table 2. Full Factorial Central Composite Design Matrix and Experimental Results

	Actual Values			Coded Values			
S/N	Age	Caffeine Intake	weight	x_2	x_2	x_3	AA after 60 mins
1	35	250	86	-1	-1	-1	6.0
2	24	200	71	-1	-1	-1	7.0
3	24	150	72	-1	-1	1	6.2
4	19	250	55	-1	-1	1	8.5
5	25	200	76	-1	1	-1	7.5
6	30	250	70	-1	1	-1	6.5
7	29	250	72	-1	1	1	7.8
8	20	200	55	-1	1	1	6.8
9	31	250	85	1	0	0	7.1
10	27	150	75	-1	0	0	8.1
11	23	200	70	0	1	0	6.2
12	18	150	57	0	-1	0	7.8
13	33	200	80	0	0	1	6.8
14	19	150	55	0	0	-1	6.2
15	18	200	55	0	0	0	7.2
16	35	150	82	0	0	0	7.5
17	21	150	60	0	0	0	6.1
18	22	150	60	-1	-1	-1	8.2
19	34	200	78	-1	-1	-1	7.8
20	25	150	71	-1	-1	1	7.5
21	35	200	90	-1	-1	1	8.1
22	24	150	74	-1	1	-1	6.8
23	26	150	75	-1	1	-1	6.8
24	18	250	60	-1	1	1	6.8
25	32	200	88	-1	1	1	8.0

Table 3. Full Factorial Central Composite Design Matrix and Experimental Results Cont'

	Actual Values			Coded Values			
S/N	Age	Caffeine Intake	weight	x_2	x_2	x_3	AA after 60 mins
26	24	150	60	1	0	0	6.5
27	20	250	65	-1	0	0	6.5
28	19	200	62	0	1	0	8.0
29	23	200	60	0	-1	0	5.8
30	22	250	68	0	0	1	6.5
31	27	150	80	0	0	-1	6.1
32	29	200	78	0	0	0	6.2
33	28	150	96	0	0	0	6.8
34	31	250	80	0	0	0	6.8
35	25	200	81	-1	-1	-1	7.0
36	30	200	80	-1	-1	-1	6.5
37	33	150	88	-1	-1	1	6.5
38	20	150	62	-1	-1	1	6.1
39	35	200	97	-1	1	-1	6.5
40	27	150	75	-1	1	-1	6.2
41	28	250	80	-1	1	1	5.8
42	34	250	90	-1	1	1	6.7
43	27	200	95	1	0	0	7.1

S/N	Actual Values			Coded Values			
	Age	Caffeine Intake	weight	x_2	x_2	x_3	AA after 60 mins
44	26	150	78	-1	0	0	6.8
45	22	150	66	0	1	0	6.3
46	22	200	62	0	-1	0	7.1
47	21	150	60	0	0	1	7.8
48	19	250	58	0	0	-1	6.0
49	27	200	74	0	0	0	6.5
50	28	150	76	0	0	0	6.8

Table 4. ANOVA Table for the Explanatory Variables

Source of Variation	Degree of Freedom	Sum of Squares	Mean Square	F
Model	P	$\sum(\hat{y}_i - \bar{y})^2$	$MSM = \dfrac{\sum(\hat{y}_i - \bar{y})^2}{p}$	$\dfrac{MSM}{MSE}$
Error	$N - p - 1$	$\sum(y_i - \hat{y}_i)^2$	$MSE = \dfrac{\sum(y_i - \hat{y}_i)^2}{N - p - 1}$	
Total	$N - 1$	$\sum(y_i - \bar{y})^2$		

Table 5. Regression Coefficients Estimates

Factor	Coefficient Estimate	DF	Standard Error	95% CI low	95%CI High	VIF
Intercept	7.23	1	0.16	6.90	7.55	
x_1 -Age	0.043	1	0.12	-0.19	0.28	1.00
x_2 - Caffeine	0.057	1	0.12	-0.29	0.18	1.00
x_3 - Weight	-0.093	1	0.12	-0.33	0.14	1.00
$x_1 x_2$	-8.333E-003	1	0.13	-0.27	0.25	1.00
$x_1 x_3$	-0.14	1	0.13	-0.40	0.12	1.00
$x_2 x_3$	-0.17	1	0.13	-0.43	0.094	1.00
x_1^2	0.63	1	0.22	-1.08	-0.18	1.50
x_2^2	0.47	1	0.22	0.018	0.92	1.50
x_3^2	-0.41	1	0.22	-0.87	0.039	1.50

The analysis of variance (ANOVA) is used to examine the effect and role of each and every one of the linear, quadratic and cross models. The essence was to check and ascertain the model that is most statistically fit for the approximation of the response pattern. It also helped us to analyze the outstanding error that is responsible for Lack-of-Fit (LOF) and to check for the model that sufficiently represented the true response surface. The effect of each factor is inconsistent when compared to the level of statistical accuracy measure. It is also by the aid of analysis of variance that the experiment can be adequately predictable when varied factor is removed. The quotient of the Average (Mean) Sum of Squares of regression model (MSM) and Average (Mean) Sum of Squares of Error (MSE) give the value of F calculated.

The square of the sample correlation is equal to the ratio of the model sum of squares to the total sum of squares:

$$r^2 = \frac{SSM}{SST} \qquad (3)$$

This formalizes the interpretation of r^2 as explaining the fraction of variability in Model summary statistics focus on the model maximizing the Adjusted R-Squared and the Predicted R-Squared. R-Squared refer to a measure of proportion of the variation in the dependent variable that is explained by the independent variable for a regression model. Adjusted R-Squared it is used to adjust the statistic based on the number of independent variable in the model. It compares the explanatory power of regression model that contain different independent predictors. In this case, since the multiple regression models have more than one variable, Adjusted R-Squared is the most preferred.

3. Result and Analysis

3.1. Mathematical Model

The data obtained from the experiment were analyzed using the Design Expert software to develop the mathematical model. The multiple regressions was obtained by employing a least square technique to predict quadratic polynomial model for the amplitude of accommodation and results are presented in Table 5.

The following equation was generated for the model. The coded and actual equation of this study were relatively the same. It is a point of notice that both equations give true representation of the approximated quadratic model for the design of the experiment.

Coded Equation:

$$y = 7.23 + 0.043x_1 + 0.057x_2 - 0.093x_3 - 8.33E - 003x_1x_2$$
$$-0.14x_1x_3 - 0.17x_2x_3 - 0.63x_1^2 + 0.47x_2^2 - 0.41x_3^2$$

3.2. ANOVA for Response Surface Quadratic Model

Analysis of variance (ANOVA) was used to check the adequacy of the model for the response. The value of "Prob.> F" in Table 6 for the model is less than 0.05 which indicates that the model is significant and also adequate for the model. The Model F-value of 2.30 implies there is a 3.47% chance that a "Model F-Value" this large could occur due to noise. Age, Caffeine intake and weight were significant in the linear terms model while Age and Caffeine intake were significant in squared terms of the model.

Table 6. ANOVA for Response Surface Quadratic Model

SOV	SS	DF	MS	F	p-value
Model	8.27	9	0.92	2.30	0.0347
x_1 -Age	*0.056*	1	*0.056*	0.14	0.0594
x_2 - Caffeine	*0.096*	1	*0.096*	0.24	0.1263
x_3 - Weight	*0.26*	1	*0.26*	0.65	0.7237
x_1x_2	*1.667E-003*	1	*1.667E-003*	*4.167E-003*	*0.9489*
x_1x_3	*0.48*	1	*0.48*	1.20	0.2790
x_2x_3	*0.67*	1	*0.67*	1.67	0.2041
x_1^2	*3.18*	1	*3.18*	7.94	0.0075
x_2^2	*1.77*	1	*1.77*	*4.42*	*0.0419*
x_3^2	*1.37*	1	*1.37*	3.42	0.0719
Residual	16.00	40	0.40		
Lack of Fit	*0.74*	5	0.15	0.34	*0.8858*
Pure Error	*15.26*	35	0.44		
Cor Total	24.27	49			

Table 7. Sequential Model Sum of Squares

SOV	SS	DF	MS	F	P-value
Mean vs Total	2369.47	1	2369.47		
Linear vs Mean	0.41	3	0.14	0.27	0.8495
2FI vs Linear	1.15	3	0.38	0.73	0.5420
Quadratic vs 2FI	6.70	3	2.23	5.59	0.0027
Cubic vs Quadratic	0.65	4	0.16	0.38	0.8195
Residual	15.35	36	0.43		
Total	2393.74	50	47.87		

Table 8. Model Summary Statistics

SOV	Std. Dev	R-Squared	Adjusted R-Squared	Predicted R-Squared	PRESS
Linear	0.72	0.0171	-0.0470	-0.1477	27.85
2FI	0.73	0.0644	-0.0661	-0.2535	30.42
Quadratic	0.63	0.3407	0.1924	-0.0157	24.65
Cubic	0.65	0.3676	0.1392	-0.1556	28.04

3.3. Model Fit Statistics

3.3.1. Sequential Model Sum of Squares

Sequential Model Sum of Squares focuses on the highest order polynomial where the additional terms are significant and the model is not aliased. This technique shows the effect of increasing terms to the complexity of the total model.

Table 7 shows that the quadratic model is more significant than the two-factor interaction model (5.59 > 0.0027) and also the two-factor interaction model is more significant than linear model (0.73 > 0.5420) that is (*F*-value > *P*-value).

3.3.2. Model Summary Statistics

Model Summary Statistics focus on the model maximizing the Adjusted R-Squared and the Predicted R-Squared. PRESS measures how well the model fits each point in the design. To calculate PRESS, the model is used to estimate each point using all of the design points except the one being estimated. PRESS is the sum of the squared differences between the estimated values and the actual values over all the points. A good model will have a low RMSE, a large predicted r^2, and a low PRESS. Table 8 shows that the quadratic model has the the least standard deviation with a negative Predicted R-Squared. This implies that the overall mean is a better predictor of the response than the current model.

Adeq Precision measures the signal to noise ratio. A ratio greater than 4 is desirable. Table 9 shows Adeq ratio of 5.386 which indicating an adequate signal. This model can be used to navigate the design space.

Table 9. Model Summary Statistics

Std. deviation	0.63	R-Square	0.3407
Mean	6.88	Adj R-Square	0.1924
C.V %	9.19	Pred R-Square	-0.0157
PRESS	24.65	Adeq R-Square	5.386

3.3.3. Lack of Fit

Non-significant lack of fit is good when one wants to fit a model. Table 10 shows that quadratic model lack of fit is not significant (Values of "Prob > F" less than 0.0500). F-value of 0.34 implies the Lack of Fit is not significant relative to the pure error. Also there is a 88.58% chance that a "Lack of Fit F-value" this large could occur due to noise.

Table 10. Lack of Fit Tests

SOV	SS	DF	MS	F-Value	P-Value
Linear	8.59	11	0.78	1.79	0.0936
2FI	7.44	8	0.93	2.13	0.0586
Quadratic	0.74	5	0.15	0.34	0.8858
Cubic	0.086	1	0.086	0.20	0.6589
Pure Error	15.26	35	0.44		

4. Conclusions and Recommendations

The RSM has shown to be useful for the design of experiments for investigating the effects of three evaluated factors: age, caffeine intake and body weight on the amplitude of accommodation. A quadratic model was found to best model for this study. This is because the model was significant and it had the least standard deviation with a negative Predicted R-Squared. The results also showed that, the variables (Age and Amount of Caffeine intake) were significant in the linear terms of the model but were not significant in interaction terms of the model. Also Age and Amount of Caffeine intake were significant in the squared terms of the model. In all, this proves that age and amount of caffeine intake have significant effect on the amplitude of accommodation. The response surface methodology added a new approach in studying the variables that affect amplitude of accommodation.

REFERENCES

[1] Atchinson D.A (1994), Clinical measurement of amplitude of accommodation. Australian Optometry Magazine 15.

[2] Akujobi A.U, Vincent C.L, Ekenze C.J, Obioma-Elemba J.E and Vincent C.C (2019), Assessment of Amplitude of Accommodation (AA) in Owerri Municipal Council, Southeast, Nigeria, *Journal of Ophthalmic Vis Res.* 14(3): 306–314. doi: 10.18502/jovr.v14i3.4787.

[3] Bailey R, (1998), Assessing the Predictive Ability of the Test-Positive Findings of an Elementary School Vision Screening. *Optometry Vision Science* 75(9): 682-691.

[4] Karania R and Evans BJ (2006) The Mallet Fixation Disparity Test: Influence Of Test Instructions And Relationship With Symptoms. *Ophthalmic Physiology Optomery* 26(5): 507-522.

[5] Majumder C & Ying LS (2015), Comparison of Amplitude of Accommodation in Different Vertical Viewing Angles. *Optometry and Visual Performance* 3(5): 276-280.

[6] S. Abokyi, J. Owusu-Mensah and K. A. Osei (2017), Caffeine intake is associated with pupil dilation and enhanced accommodation, *Eye (Lond)* 31(4): 615 -619.

[7] Stella E. Odjimogho and Efe S. Odjimogho (2011), Effects of caffeine on near vision of healthy subjects in Benin metropolis. Nigerian Society for Experimental Biology Journal, 11(3) 203-208.

[8] Murari, Swetha; Ho, Amiee; Hayes, John; and Cooper Scott, (2018) Effects of Caffeine intake on Visual Performance of the Eye Among Normal Healthy Adults. *College of Optometry*. 842. https://commons.pacificu.edu/opt/842.

[9] Myers R.H, Montgomery D.C, Vining G.G, (2004) Response Surface Methodology: A Retrospective and Literature Survey. *Journal of Quality Technology*. 36: 53–77.

[10] Box G.E.P & Wilson K.B. (1951), On the Experimental Attainment of Optimum Conditions. *Journal of the Royal Statistical Society* 13: 1– 45.

[11] Myers, R. H., Montgomery, D. C., and Vining, G. G. (2002), Generalized Linear Models with Applications in Engineering and the Sciences, John Wiley & Sons, NewYork.

[12] B.A. Oyejola and J.C. Nwanya (2015), Selecting the Right Central Composite Design, *International Journal of Statistics and Application*, 5(1), 21 - 30.

[13] Mead, R & Pike D.J (1975). A Review of Response Surface Methodology from a Biometric Viewpoint. *Biometrics*. 31: 803–851.

[14] Hill W.J & Hunter W.G. (1966), A Review of Response Surface Methodology: A Literature Survey. *Technometrics.* 8 (4): 571–590.

[15] Sibanda W & Pretorius P (2013), Comparative Study of the Application of Central Composite Face-Centre (CCF) and Box–Behnken Designs (BBD) To Study The Effect of Demographic Characteristics On HIV Risk In South Africa. *Network Model Anal Health Inform Bioinformatics* 2: 137–146.

[16] Sibanda W & Pretorius P (2011), Application of Two-Level Fractional Factorial Design to Determine and Optimize the Effect of Demographic Characteristics on HIV Prevalence Using the 2006 South African Annual Antenatal HIV and Syphilis zero prevalence Data. *International Journal of Computation Application* 35(12): 0975–8887.