Locally D-optimal Design for Sigmoid Model with Four Parameters

Tatik Widiharih*, Suparti and Moch. Abdul Mukid

Abstract— **Locally D-optimal design for a sigmoid model with four parameters is investigated. D-optimal criterion refers to the Generalized Equivalence Theorem of Kiefer Wolfowitz. Determining whether the design is minimally supported design based on the number of roots of the Tchebycheff system. This is done by checking the pattern of the standardized variance function curve whether the maximum value is equal to the number of parameters and occurring at the design points.Tchebycheff system and its properties are the main tools to create D-optimal design. The result in this paper for design region [a, b], the design is minimally supported and the design points are a , b, and two others are interior points of [a, b].**

Index Terms— **D-optimal design, equivalence theorem, minimally supported design, standardized variance function, Tcebychev system.**

I. Introduction

NONLINEAR models were originally used to determine the growth function. These models includ exponential, sigmoidal or S curve. The most frequently used for modelling are the sigmoidal model or S curve including Logistics, Gompertz, Richards, Brody, Weibull, and Morgan Mercer Flodin (MMF) models.

Originally the sigmoid models can be applied in many areas such as biology and animal husbandry sciencie, pharmacodynamics and pharmacokinetics, chemistry, agriculture and finance. Some researchers used this model in animal husbandry and agricultural science such as [1] used Logistic, Richards, Gompertz and Ontogenetic models for modeling the growth function of animals and plants. Fang et al [2] used Gompertz and Logistic models to study an empirical growth for predicting the growth of tomato in greenhouse. Ulkalska and Jastrzebowski [3] applied Richards, Logistic and Gompertz models to studi the dynamics of epicotyl emergence of pedunculate oak. Fernandes et al [4] utilized fruit height and diameter data over time through diphashic sigmoidal models including Brody, Gompertz and Logistic. Therefore [5] applied the Morgan Mercer Flodin model for two parameters specific model which is Michaelis Menten for modelling the effect of concentration of substrate on the velocity of reaction. Besides that [6] applied the Morgan Mercer Flodin model with three parameters which is EMAX for modelling the effect of this concentration on the drug. Furthermore, [7] investigated the Morgan Mercer Flodin model with three parameters. Al-Rahman et al [8] applied Brody, Logistic, Gompertz and Weibull models to describe the confirmed cases of COVID-19 in Egypt. Rochyani et al [9] utilized double sigmoidal model to investigate the growth of bacteria.

Optimal design is a design that contains design points and its proportions (replications) so that it meet the predetermined optimallity criteria. D-optimality criteria is the most important. The purpose of this criteria is minimizing the variance of the parameter estimates. Determining the D-optimal design by maximizing the generalized variance of the parameter estimates. This also means it can be done by minimizing the logarithm of the generalized variance of the parameter estimates ($-\log|M(\xi, \theta)|$). The main problem of this paper is determining the formula that used to create the D-optimal design criterion, including the number of design points and its proportions.

Minimizing $-\log|M(\xi, \theta)|$ is equivalent to maximizing $|M(\xi, \theta)|$. The main problem in determining the D-optimal design is to maximize the determinant of the information matrix. There are several methods for maximizing the function. The methods that are often used are the Newto method [10], Secant method [11], modified regularized newton raphson to overcome the singular hesian matrix [12]. Modified Newton could be used to find the maximum of $|M(\xi, \theta)|$ if impossible to maximize $|M(\xi, \theta)|$ analytically [13]. Maximizing $|M(\xi, \theta)|$ in this paper, we use modified Newton method because we impossible to maximize $|M(\xi, \theta)|$ analytically and this method is generally straightforward and strong [14]. The algotithm of modified Newton's method is presented in appendix 1.

Determination of D-optimal designs for the sigmoid model with four parameters is very difficult, because the Fisher information matrix $M(\xi, \theta)$ contains the unknown parameters. Methods that can be used to solve this problem by the local optimality approach. Evaluation of optimality criterion function by assuming the values of parameters. Chernoff [15] investigated the initial value $\theta = \theta_0$ as the unknown parameter vector than maximizing $|M(\xi, \theta)|$, evaluated it in initial value. The results obtained is locally optimal design.

Some researchers applied D-optimal designs for growth curve in different models such as [16] who used polynomials models, [17] also used sigmoidal growth models especially model Weibull and Richards. Li and Majummdar [18] constructed D-optimal design for Logistic models for three and four parameters, [19] investigated D-optimal design for Gompertz model, [20] applied regrowth model by double exponential and LINEX models. Hooghangifar et al [21] investigated D-optimal design for logistic model based on more precise approximation. Clarke and Haines [22] studied the optimal design for Richards model. Zhai et al [23] investigated the D-optimal design for two variables Logistic model. Widiharih et al [24] used generalized and weighted exponential models with two parameters. Furthermore [25]

Manuscript received August 7, 2024; revised March 28, 2025.

This work was supported in part by Faculty of Science and Mathematics, Diponegoro University, according to letter of dean no. 23.B/UN7.F8/PP/II/2023.

*T. Widiharih is a senior lecturer in Statistics Department at Faculty of Science and Mathematics, Diponegoro University Indonesia. (Corresponding author, e-mail: widiharih@live.undip.ac.id).

Suparti is a senior lecturer in Statistics Department at Faculty of Science and Mathematics, Diponegoro University Indonesia. (e-mail: suparti@live.undip.ac.id).

M. A. Mukid is a lecturer in Statistics Department at Faculty of Science and Mathematics, Diponegoro University Indonesia. (e-mail: mamukid@live.undip.ac.id).

used modified exponential model with three parameters. D-optimal designs for Morgan Mercer Flodin models without intercept have been done [26], and D-optimal designs for Morgan Mercer Flodin models with three parameters have been studied [27].

In this paper, we create a formula to construst locally D-optimal designs for sigmoid function with four parameters as follows:

$$y = \frac{\theta_1 + \theta_3 x^{\theta_4}}{\theta_2 + x^{\theta_4}} + \varepsilon, \theta_1, \theta_2, \theta_3, \theta_4 > 0, x \epsilon [a, b] \quad (1)$$

This model has an inflextion point at $x = \left(\frac{\theta_2(\theta_4 - 1)}{\theta_4 + 1}\right)^{1/\theta_4}$ and θ_3 is asymptotic or maximum response.

The curve of the model (1) for θ_1 = 3727.0890, θ_2 = 590.4906, θ_4 = 3.4571, θ_3 = 128 , 135 , 140 , 150 , 145 is presented in figure (1) and the curve of the model (1) for θ_1 = 3727.0890, θ_2 = 590.4906, θ_3 = 128.2863, θ_4 =2.50 , 2.75 , 3.30 , 3.25, 3.45 is presented in figure (2).

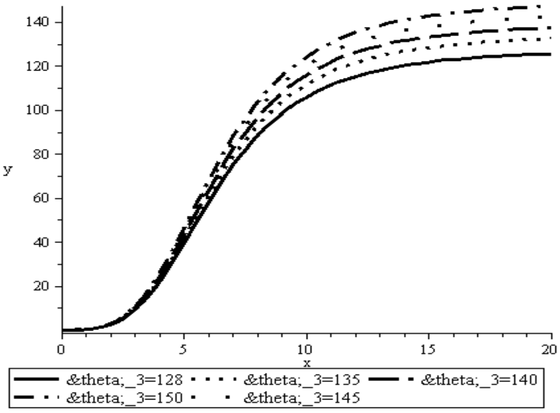

Fig. 1. Curve of Model (1) for θ_1 = 3727.0890, θ_2 = 590.4906, θ_4 = 3.4571, at Several Value of θ_3 = 128 , 135 , 140 , 150 , 145

Based on Figure (1) it can be see that for several curve the inflextion points at x= 5.3448 but asymptotic or maximum are different.

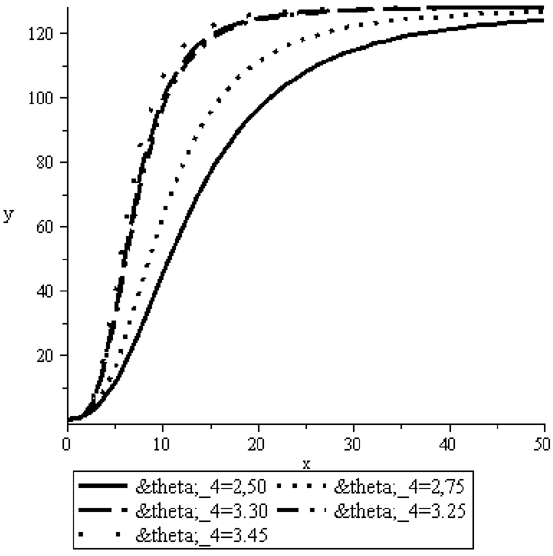

Fig. 2. Curve of Model (1) for θ_1 = 3727.0890, θ_2 = 590.4906, θ_4 = 128.2863, at Several Value of θ_4 =2.50 , 2.75 , 3.30 , 3.25, 3.45

Based on Figure (2) it can be seen that for several curves the inflextion points are different but the asymptotic or maximum at y=128.2863.

We organize the paper as follows. Section 2, contains the basic theory of D-optimal designs for nonlinear model, Generalized Equivalence Theorem, definition and properties of Tchebycheff System. Section 3, the mains result is the formula to construct D-optimal design of sigmoid model as in equation (1). The D-optimal design has four design points with the same proportion, the lower bound and the upper bound of the design region are design points and two others are interior points of the design region. Section 4, conclusion of research.

II. D-OPTIMAL DESIGN FOR NONLINEAR MODEL

In general, nonlinear models can be written as :

$$E(Y|x) = \eta(x, \theta) \quad (2)$$

Design of p points is denoted by:

$$\xi = \begin{pmatrix} x_1 & x_2 & \dots & x_p \\ w_1 & w_2 & \dots & w_p \end{pmatrix} \quad (3)$$

where: $w_i = \frac{rp_i}{N}$ as weight (proportion) of design point x_i, rp_i : number of replication or observation of the design point x_i, N : number of all observation, $N = \sum_{i=1}^{p} rp_i$ and total of weight is 1. The information matrix for design ξ in equation (3) is:

$$M(\xi, \theta) = \sum_{i=1}^{p} w_i h(x_i, \theta)\, h^T(x_i, \theta) \quad (4)$$

where : $h(x, \theta) = \frac{\partial \eta(x,\theta)}{\partial \theta} = \left(\frac{\partial \eta(x,\theta)}{\partial \theta_1}, \frac{\partial \eta(x,\theta)}{\partial \theta_2}, \dots, \frac{\partial \eta(x,\theta)}{\partial \theta_k}\right)^T$ is the vector that are partial derivatives of the model in equation (2) with respect to parameters $\theta = (\theta_1, \theta_2, \dots, \theta_k)$. A D-optimal design is obtained by maximizing: $|M(\xi, \theta)|$ that is the determinant of the information matrix. The function of standardized variance $d(\xi, x)$ is defined by :

$$d(\xi, x) = h^T(x, \theta) M^{-1}(\xi, \theta) h(x, \theta) \quad (5)$$

The Generalized Equivalence Theorem is the basic theory of optimum designs. At first this theory was used for linear models by [28] , after that [29] extended it for nonlinear. Principlely of the Generalized Equivalence Theorem, evaluates whether the value of $d(\xi, x)$ is less than or equal k.

The Generalized Equivalence Theorem used to prove that the design is D-optimal design. There are three condition. Any design ς^* meets one of the conditions then it meets all three conditions:

(1) ς^* maximizes $|M(\xi, \theta)|$
(2) ς^* minimizes $max_{x \in \chi} d(\xi, x)$
(3) $max_{x \in \chi} d(\xi, x) = k$, where k is number of parameters

The Generalized Equivalence Theorem can be simply written as:

$$\varsigma^* \text{ D-optimal design} \leftrightarrow d(\varsigma^*, x) \le k \quad (6)$$

The design is minimally supported if the number of parameters is same as the number of design points. This design points have the same weight, i.e. $w_i = \frac{1}{number\ of\ parameters}$. In these conditions, maximizing $|M(\xi, \theta)|$ more simply, this function have k variables which are the design points $x_1, x_2, \dots . x_k$. Theorem 1 part 3 of [18] investigated in a sufficient condition to ensure that the D-optimal design is minimally supported. Here, we will adopt this approach.

Theorem 2.1 (Li and Majumdar, [18]).
For $\chi = [a, b]$, if $\forall \xi \epsilon H, \exists \varepsilon > 0$ such that every function in $d(x, \xi) - k + c: 0 < c < \varepsilon$ has at most *2k-1* roots in χ, then there exist a unique D-optimal design that minimally supported and at least one of the lower bound or upper bound as a design point. If $d(x, \xi) - k + c: 0 < c < \varepsilon$ has at most *2k-2* roots in χ then both lower bound and upper bound are design points of the D-optimal design.

Tchebycheff system used to determine the number of roots d(x,ξ). Tchebycheff system was introduced by several authors including ([30], [31], [32]), they investigated the properties and definition of Tchebycheff system.

Definition 2.2. (Shadrin [31]).
A set of continuous independent functions $\Theta = v_0, \dots, v_n$ in K is a Tchebycheff system, if it fulfil the Haar condition: which any polynomial $f = a_0 v_0 + \dots + a_n v_n$ with $a_0, \dots, a_n$ not zero, and have at most *n* roots. Tchebycheff space is the (*n+1*) dimension that U_n spanned by such a Θ.

Lemma 2.3. (Shadrin [31])
The following three conditions are equivalent:

1. $(v_i)_0^n$ is a Tchebycheff system.
2. For every *n+1* different points $(x_i)_0^n \epsilon K$, the determinant which is appropriate the points exist that mean not zero

$$D(x_0, \dots, x_n) = \begin{vmatrix} v_0(x_0) & \dots & v_n(x_0) \\ \dots & \dots & \dots \\ v_0(x_n) & \dots & v_n(x_n) \end{vmatrix}$$

3. If $(x_i)_0^n$ are different points in K and $(y_i)_0^n$ are any numbers, then the interpolation problem: $a_0 v_0(x_i) + \dots + a_n v_n(x_i) = y_i$, $i = 1,2, \dots, n$ has a single solution for the unknown (a_j)

Lemma 2.4. (Shadrin [31])
Let $\{f_0, f_1, \dots, f_{n-1}, v_i\} (i = 1,2, \dots, k)$ be k sequences of Tchebycheff system, v_i are continous independen function, then $\{f_0, f_1, \dots, f_{n-1}, \sum_{i=1}^k v_i\}$ is also a Tchebycheff system.

III MAIN RESUTS

Consider sigmoid model with four parameters as in equation (1):

$$y = \frac{\theta_1 + \theta_3 x^{\theta_4}}{\theta_2 + x^{\theta_4}} + \varepsilon$$

with homoscedastic error. Here $\theta = (\theta_1, \theta_2, \theta_3, \theta_4)$ is the parameter of interest.

$$\eta(x, \theta) = \frac{\theta_1 + \theta_3 x^{\theta_4}}{\theta_2 + x^{\theta_4}}$$

Partial derivative of η(x,θ) with respect to their parameters is :

$$h(x) = \frac{\partial \eta(x, \theta)}{\partial \theta} = \begin{pmatrix} \dfrac{1}{(\theta_2 + x^{\theta_4})} \\ -\dfrac{\theta_1 + \theta_3 x^{\theta_4}}{(\theta_2 + x^{\theta_4})^2} \\ \dfrac{x^{\theta_4}}{\theta_2 + x^{\theta_4}} \\ \dfrac{x^{\theta_4} \ln(x) (\theta_2 \theta_3 - \theta_1)}{(\theta_2 + x^{\theta_4})^2} \end{pmatrix}$$

With our result we establish the basic properties of locally D-optimal design of model (1) in Theorem (3.1).

Theorem 3.1.
D-optimal design of model (1) with design region [a,b] have four design points denote by $x_1 = a, x_2, x_3$ and $x_4 = b$ with same weight for all design points i.e $\frac{1}{4}$. x_2, x_3 are points that maximize :

$$|M(\xi, \theta)| \propto \frac{A}{(\theta_2 + a^{\theta_4})^3 (\theta_2 + x_2^{\theta_4})^3 (\theta_2 + x_3^{\theta_4})^3 (\theta_2 + b^{\theta_4})^3} + B + C \quad (7)$$

where:

$$A = 2[A_1 . A_2 + A_3 . A_4 + A_5 . A_6]$$
$$A_I = 2x_3^{\theta_4} b^{\theta_4} + 2x_1^{\theta_4} - (x_3^{\theta_4} + b^{\theta_4})(x_1^{\theta_4} + x_2^{\theta_4})$$
$$A_2 = (\theta_1 + \theta_3 x_3^{\theta_4})(\theta_1 + \theta_3 b^{\theta_4}) x_1^{\theta_4} \ln(x_1) x_2^{\theta_4} ln(x_2) + (\theta_1 + \theta_3 x_1^{\theta_4})(\theta_1 + \theta_3 x_2{}^{\theta_4}) x_3^{\theta_4} \ln(x_3) b^{\theta_4} ln(b)$$
$$A_3 = 2x_1^{\theta_4} x_3^{\theta_4} + 2x_2^{\theta_4} x_4^{\theta_4} - (x_1^{\theta_4} + x_3^{\theta_4})(x_2^{\theta_4} + x_4^{\theta_4})$$
$$A_4 = (\theta_1 + \theta_3 x_1^{\theta_4})(\theta_1 + \theta_3 x_3^{\theta_4}) x_2^{\theta_4} ln(x_2) x_4^{\theta_4} ln(x_4) + (\theta_1 + \theta_3 x_2^{\theta_4})(\theta_1 + \theta_3 x_4^{\theta_4}) x_1^{\theta_4} ln(x_1) x_3^{\theta_4} ln(x_3)$$
$$A_5 = 2x_1^{\theta_4} x_4^{\theta_4} + 2x_2^{\theta_4} x_3^{\theta_4} - (x_1^{\theta_4} + x_4^{\theta_4})(x_2^{\theta_4} + x_3^{\theta_4})$$
$$A_6 = (\theta_1 + \theta_3 x_1^{\theta_4})(\theta_1 + \theta_3 x_4^{\theta_4}) x_2^{\theta_4} ln(x_2) x_3^{\theta_4} ln(x_3) + (\theta_1 + \theta_3 x_2^{\theta_4})(\theta_1 + \theta_3 x_3^{\theta_4}) x_1^{\theta_4} ln(x_1) x_4^{\theta_4} ln(x_4)$$

B is sum of 6 part with denominator has a form:

$$(\theta_2 + x_i^{\theta_4})^2 (\theta_2 + x_j^{\theta_4})^2 (\theta_2 + x_k^{\theta_4})^4 (\theta_2 + x_l^{\theta_4})^4, \quad i, j, k, l = 1,2,3,4$$

and numerator: $(x_i^{\theta_4} - x_j^{\theta_4})^2 . N$

$$N = \left[(\theta_1 + \theta_3 x_l^{\theta_4}) x_k^{\theta_4} ln(x_4) - (\theta_1 + \theta_3\, x_k^{\theta_4})\, x_l^{\theta_4} ln(x_l)\right]^2$$

C is sum of 12 part with denominator has a form:

$$(\theta_2 + x_i^{\theta_4})^2 (\theta_2 + x_j^{\theta_4})^4 (\theta_2 + x_k^{\theta_4})^3 (\theta_2 + x_l^{\theta_4})^3, \quad i, j, k, l = 1,2,3,4$$

and numerator:

$$2[x_i^{\theta_4} - x_k^{\theta_4}][x_l^{\theta_4} - x_i^{\theta_4}][D + E + F]$$

where:

$$D = x_j^{2\theta_4} ln^2(x_j)(\theta_1 + \theta_3 x_k^{\theta_4})(\theta_1 + \theta_3 x_l^{\theta_4})$$

$$E = (\theta_1 + \theta_3 x_j^{\theta_4})^2 x_k^{\theta_4} ln(x_k) x_l^{\theta_4} ln(x_l)$$

$$F = (\theta_1 + \theta_3 x_j^{\theta_4}) x_j^{\theta_4} ln(x_j)[(\theta_1 + \theta_3 x_k^{\theta_4}) x_l^{\theta_4} ln(x_l) + (\theta_1 + \theta_3 x_l^{\theta_4}) x_k^{\theta_4} ln(x_k)]$$

$x_1 = a, x_4 = b$

Proof.

Let m^{ij} denote $(i, j)^{th}$ elemen of $M^{-1}(\xi, \theta)$, then:

$$d(x, \xi) = h^T(x) M^{-1}(\xi, \theta) h(x) = \frac{1}{(\theta_2 + x^{\theta_4})^4} [G_1 + G_2 + G_3 + G_4 + G_5 + G_6 + G_7 + G_8 + G_9 + G_{10}]$$

where:

$$G_1 = m^{11}(\theta_2 + x^{\theta_4})^2$$
$$G_2 = m^{22}(\theta_1 + \theta_3 x^{\theta_4})^2$$
$$G_3 = m^{33} x^{2\theta_4}(\theta_2 + x^{\theta_4})^2$$
$$G_4 = m^{44} x^{2\theta_4} ln^2(x)(\theta_2 \theta_3 - \theta_1)^2$$
$$G_5 = 2m^{12}(\theta_2 + x^{\theta_4})(\theta_2 \theta_3 - \theta_1)$$
$$G_6 = 2m^{13} x^{\theta_4}(\theta_2 + x^{\theta_4})^2$$

$G_7 = 2m^{14}(\theta_2 + x^{\theta_4})x^{\theta_4}ln(x)(\theta_2\theta_3 - \theta_1)$
$G_8 = 2m^{23}x^{\theta_4}(\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4})$
$G_9 = 2m^{24}(\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4})x^{\theta_4}ln(x)(\theta_2\theta_3 - \theta_1)$
$G_{10} = 2m^{34}(\theta_2 + x^{\theta_4})x^{2\theta_4}ln(x)(\theta_2\theta_3 - \theta_1)$

We have some Tchebycheff systems:

1. $\left\{1, (\theta_2 + x^{\theta_4}), (\theta_1 + \theta_3 x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4}), x^{\theta_4}ln(x), (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4}), (\theta_2 + x^{\theta_4})^2\right\}$
2. $\left\{1, (\theta_2 + x^{\theta_4}), (\theta_1 + \theta_3 x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4}), x^{\theta_4}ln(x), (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4}), (\theta_1 + \theta_3 x^{\theta_4})^2\right\}$
3. $\left\{1, (\theta_2 + x^{\theta_4}), (\theta_1 + \theta_3 x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4}), x^{\theta_4}ln(x), (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4}), x^{2\theta_4}(\theta_2 + x^{\theta_4})^2\right\}$
4. $\{1, (\theta_2 + x^{\theta_4}), (\theta_1 + \theta_3 x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4}), x^{\theta_4}ln(x), (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4}), x^{2\theta_4}ln^2(x)\}$
5. $\left\{1, (\theta_2 + x^{\theta_4}), (\theta_1 + \theta_3 x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4}), x^{\theta_4}ln(x), (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4}), x^{2\theta_4}(\theta_2 + x^{\theta_4})^2\right\}$
6. $\left\{1, (\theta_2 + x^{\theta_4}), (\theta_1 + \theta_3 x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4}), x^{\theta_4}ln(x), (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4})^2 \ln(x)\right\}$
7. $\{1, (\theta_2 + x^{\theta_4}), (\theta_1 + \theta_3 x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4}), x^{\theta_4}ln(x), (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4}), (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4})x^{\theta_4}\ln(x)\}$

Let:

$$\begin{aligned} v(x) = {} & m^{11}(\theta_2 + x^{\theta_4})^2 + m^{22}(\theta_1 + \theta_3 x^{\theta_4})^2 \\ & + m^{33}x^{2\theta_4}(\theta_2 + x^{\theta_4})^2 + 2m^{13}x^{\theta_4}(\theta_2 + x^{\theta_4})^2 \\ & + m^{44}(\theta_2\theta_3 - \theta_1)^2 x^{2\theta_4} ln^2(x) \\ & + 2m^{14}(\theta_2\theta_3 - \theta_1)x^{2\theta_4}(\theta_2 + x^{\theta_4})\ln(x) \\ & + 2m^{24}(\theta_2\theta_3 - \theta_1)(\theta_2 + x^{\theta_4})x^{\theta_4}ln(x) \end{aligned}$$

$u_0 = 1, u_1 = (\theta_2 + x^{\theta_4}), u_2 = (\theta_1 + \theta_3 x^{\theta_4}),$
$u_3 = x^{\theta_4}(\theta_2 + x^{\theta_4}), \ u_4 = x^{\theta_4}ln(x),$
$u_5 = (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4}).$

Based on Lemma (2.4) then: $\{1, (\theta_2 + x^{\theta_4}), (\theta_1 + \theta_3 x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4}), x^{\theta_4}ln(x), (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4}), v(x)\}$ is an Tchebycheff system. So $\{d(x, \xi) - 4 + c\}$ is a linear combination of: $\{1, (\theta_2 + x^{\theta_4}), (\theta_1 + \theta_3 x^{\theta_4}), x^{\theta_4}(\theta_2 + x^{\theta_4}), x^{\theta_4}\ ln(x), (\theta_2 + x^{\theta_4})(\theta_1 + \theta_3 x^{\theta_4}), v(x)\}$. Based on Definition (2.2): $\{d(x, \xi) - 4 + c\}$ have $6 = 2k - 2$ roots, so we conclude by Theorem (2.1) that this design is D-optimal and minimally supported, $x_1 = a, x_4 = b$ are design points. We have

$$\xi = \begin{pmatrix} a & x_2 & x_3 & b \\ \frac{1}{4} & \frac{1}{4} & \frac{1}{4} & \frac{1}{4} \end{pmatrix} \tag{8}$$

Element of the information matrix are:

$$m_{11} = \sum_{i=1}^{4} \frac{1}{4} \frac{1}{\left(\theta_2 + x_i^{\theta_4}\right)^2}$$

$$m_{22} = \sum_{i=1}^{4} \frac{1}{4} \frac{\left(\theta_1 + \theta_3\, x_i^{\theta_4}\right)^2}{\left(\theta_2 + x_i^{\theta_4}\right)^4}$$

$$m_{33} = \sum_{i=1}^{4} \frac{1}{4} \frac{x_i^{2\theta_4}}{\left(\theta_2 + x_i^{\theta_4}\right)^2}$$

$$m_{44} = \sum_{i=1}^{4} \frac{1}{4} \frac{x_i^{2\theta_4} ln^2(x_i)(\theta_2\theta_3 - \theta_1)^2}{\left(\theta_2 + x_i^{\theta_4}\right)^4}$$

$$m_{12} = \sum_{i=1}^{4} \left[-\frac{1}{4} \frac{\theta_1 + \theta_3\, x_i^{\theta_4}}{\left(\theta_2 + x_i^{\theta_4}\right)^3}\right]$$

$$m_{13} = \sum_{i=1}^{4} \frac{1}{4} \frac{x_i^{\theta_4}}{\left(\theta_2 + x_i^{\theta_4}\right)^2}$$

$$m_{14} = \sum_{i=1}^{4} \frac{1}{4} \frac{x_i^{\theta_4} ln(x_i)(\theta_2\theta_3 - \theta_1)}{\left(\theta_2 + x_i^{\theta_4}\right)^3}$$

$$m_{23} = \sum_{i=1}^{4} \left[-\frac{1}{4} \frac{x_i^{\theta_4}\left(\theta_1 + \theta_3\, x_i^{\theta_4}\right)}{\left(\theta_2 + x_i^{\theta_4}\right)^3}\right]$$

$$m_{24} = \sum_{i=1}^{4} \left[-\frac{1}{4} \frac{(\theta_2\theta_3 - \theta_1)\left(\theta_1 + \theta_3\, x_i^{\theta_4}\right) x_i^{\theta_4} ln(x_i)}{\left(\theta_2 + x_i^{\theta_4}\right)^4}\right]$$

$$m_{34} = \sum_{i=1}^{4} \frac{1}{4} \frac{x_i^{2\theta_4} ln(x_i)(\theta_2\theta_3 - \theta_1)}{\left(\theta_2 + x_i^{\theta_4}\right)^3}$$

Where $x_1 = a$, $x_2 = b$

The determinant of information matrix is:

$$|M(\xi, \theta)| = \frac{1}{256} \frac{A}{(\theta_2 + a^{\theta_4})^3 \left(\theta_2 + x_2^{\theta_4}\right)^3 \left(\theta_2 + x_3^{\theta_4}\right)^3 (\theta_2 + b^{\theta_4})^3} + B + C$$

A, B, and C as in equation (7). Design points x_2 and x_3 are maximize of:

$$|M(\xi, \theta)| \propto \frac{A}{(\theta_2 + a^{\theta_4})^3 \left(\theta_2 + x_2^{\theta_4}\right)^3 \left(\theta_2 + x_3^{\theta_4}\right)^3 (\theta_2 + b^{\theta_4})^3} + B + C$$

■

Determination of D-optimal design needed the information value of the parameters model. Calculation of design points for some values of $a, \theta_1, \theta_2, \theta_3, \theta_4, b$, design region $[a, b]$, is presented in Table (1). The design points are $x_1 = a$, $x_4 = b$ and x_2, x_3 are determined by maximizing $|M(\xi, \theta)|$ in equation (7).

Each design points related to the values of $\theta_1, \theta_2, \theta_3, \theta_4$ and design region in Table (1) are satisfy the Equivalence Theorem i.e $d(\xi, x) \leq 4$. Example of the calculations by taking the case, $\theta_1 = 2.523684$, $\theta_2 = 12.371$, $\theta_3 = 6.318$, and $\theta_4 = 3.46$, the design region is $[1, 8]$. The curva of this model is presented in figure 3. The inflextion point in this curva at x=1.4345 and the asymptotic or maximum response is 6.318. The design points are $x_1 = 1$, $x_2 = 1.7138$, $x_3 = 2.9435$, $x_4 = 8$.

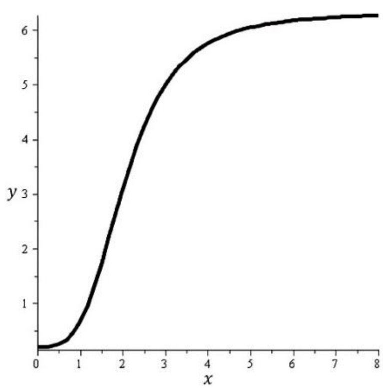

Fig.3. The Curva of Model (1) with Design Region [1, 8] and $\theta_1 = 2.523684$, $\theta_2 = 12.371$, $\theta_3 = 6.318$, $\theta_4 = 3.46$

TABLE I
DESIGN POINTS OF MODEL (1) FOR SOME VALUES OF $\theta_1, \theta_2, \theta_3, \theta_4, x \in [a, b]$

θ_1	θ_2	θ_3	θ_4	$[a, b]$	x_1	x_2	x_3	x_4
330.6616	9.441	50.093	1.717	[1, 20]	1.0	6.5645	2.4756	20.0
				[3, 25]	3.0	4.5605	9.7772	25.0
				[2, 30]	2.0	3.5548	8.6817	30.0
2.5237	12.371	6.318	3.460	[0.5, 10]	0.5	1.5494	2.7961	10.0
				[1, 8]	1.0	1.7136	2.9435	8.0
				[0.8, 9]	0.8	1.6299	2.8726	9.0
41.06462	0.912	429.618	3.952	[0.3, 8]	0.3	0.7667	1.2892	8.0
				[1.5, 7.5]	1.5	1.7168	2.4515	7.5
				[3, 6]	3.0	3.3205	4.2621	6.0
82.8856	1.558	293.486	3.060	[0.2, 8]	0.2	0.8299	1.6258	8.0
				[2.5, 7.5]	2.5	2.898970	4.2074	7.5
				[3, 9]	3.0	3.4650	5.0219	9.0
18383.5449	369.370	25486.460	1.830	[25, 300]	25.0	36.6816	79.8188	300.0
				[50, 250]	50.0	64.6909	116.8278	250.0
				[75, 200]	75.0	90.4125	135.4200	200.0
22736.6510	484.790	33980.680	1.740	[25, 300]	25.0	40.0799	91.9655	300.0
				[50, 250]	50.0	66.8915	123.4853	250.0
				[75, 200]	75.0	91.5791	138.2178	200.0

The information matrix is:

$$M(\xi, \theta) = \begin{pmatrix} 0.008757 & -0.11865 & 0.03876 & 0.06089 \\ -0.11865 & 0.02562 & -0.12021 & -0.19652 \\ 0.03876 & -0.12021 & 1.70075 & 1.26569 \\ 0.06089 & -0.19652 & 1.26569 & 1.91268 \end{pmatrix}$$

The inverse of information matrix is:

$$M^{-1}(\xi, \theta) = \begin{pmatrix} 1066.96938 & 1121.95444 & -10.88156 & 88.50372 \\ 1121.95444 & 1367.87310 & -13.58559 & 113.80924 \\ -10.88156 & -13.58559 & 1.29388 & -1.90559 \\ 88.50372 & 113.80924 & -1.90559 & 10.65920 \end{pmatrix}$$

The standardized variance at x_1, x_2, x_3, x_3 are 4.0000. The graph of the standardized variance function is presented in Figure (4).

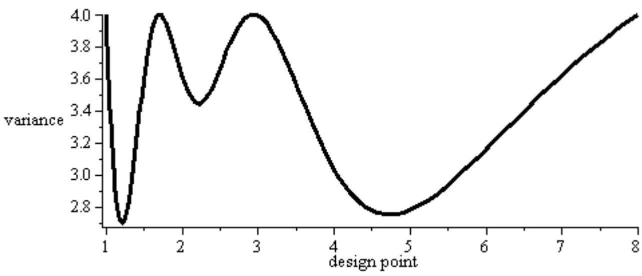

Fig.4. Standardized Variance Function Model (1) for Design Region [1, 8] and $\theta_1 = 2.523684$, $\theta_2 = 12.371$, $\theta_3 = 6.318$, $\theta_4 = 3.46$

Based on the Figure (4) we conclude that: $d(\xi, x) \leq 4$, maximum points at (1, 4.0000), (1.7138, 4.0000), $(2.9435, 4.0000)$ and $(8, 4.0000)$. It means that the maximum value occur on all of design points in this case: $x_1 = 1$, $x_2 = 1.7138$, $x_3 = 2.9435, x4 = 8$ are design points of D-optimal design of model (1) for $\theta_1 = 2.523684, \theta_2 = 12.371, \theta_3 = 6.318$, $\theta_4 = 3.46$, $x \in [1, 8]$.

IV. CONCLUSION

In this paper we have studied D-optimal design for sigmoid model with four parameters and homoscedastic error. Our tools to create D-optimal design is derived from the Generalized Equivalence Theorem of Kiefer-Wolowitz, we adopt Theorem 1 part 3 of [18], definition and properties of the Tchebycheff system in ([30], [31], [32]). The former, Theorem 3.1 is main result to create D-optimal design for sigmoid model with four parameters. The D-optimal design in this paper is a minimally supported design with the lower bound and upper bound of design region are design points and two others are interior points of the design region. Therefore, determination of design points by numerical approach , in this time we used Modified Newton Methods. Algorithm to determine the D-optimal designs for sigmoid model with four parameters is used Maple program in three steps, including a written formula of determinant of information matrix, the second maximize this formula to determine the supported design, information matrix and inverse of information matrix, the third construct the graph of $d(x, \xi)$ and to prove that the design ξ satisfy the Generalized Equivalence Theorem. The algorithm to determine D-optimal design is presented in the appendix 2.

APPENDIX

1. Algorithm of modified Newton's method.

Let $g(x)$ is a function being optimized, $\nabla g(x)$ is gradient vector of $g(x)$ and $Hg(x)$ is Hessian matrix of $g(x)$. Algorithm for modified Newton's Method as follows:

i. Select $x^{(0)}$ as the initial value and tolerance ε for the stoppping iteration and set k=0.
ii. Determine descent direction $d^{(k)} = -Hg(x^{(k)})^{-1} \nabla g(x^{(k)})$.
iii. Determine $\alpha_k = min_\alpha g\left(x^{(k)} + \alpha d^{(k)}\right)$.

iv. Calculate $s^{(k)} = \alpha^{(k)} d^{(k)}$
v. Calkulate $x^{(k+1)} = x^{(k)} + s^{(k)}$
vi. If $\left|\nabla g\left(x^{(k+1)}\right)\right| < \varepsilon$ then stop iteration, otherwise take $k = k + 1$ and go to step (ii).

2. Algorithm to create D-optimal designs for sigmoid model with four parameters.

   a. Define the formula of determinant of information matrix in equation (7).
   b. Initialize value of parameters $\theta_1, \theta_2, \theta_3$ and θ_4.
   c. Determine the design region $\xi = [a, b]$ wich appropriate with step (b)
   d. Maximizing the formula in step (a) to determine the design points x_1, x_2, x_3 , and x_4 by modified Newton's method.
   e. Determine the elements of information matrix and than the information matrix can be construct.
   f. Determine the inverse of information matrix.
   g. Create $d(\xi, x) = h^T(x, \theta) M^{-1}(\xi, \theta) h(x, \theta)$ and make this curva
   h. Evaluated the curva of standardize variance function, if $d(\xi, x) \leq 4$, $d(\xi, xi) = 4, i = 1, 2, 3, 4$ then x_1, x_2, x_3 , and x_4 in step (d) are supported design of D-optimal design. otherwise repeat to step (a).

REFERENCES

[1] L. Cao, P.J. Shi, L. Li and G. Chen, "A New Flexible Sigmoidal Growth Model," *Symmetry,* vol.11, no.204, p.1-16 , 2019.

[2] S.L. Fang. Y.H. Kuo, L. Kang, C.C. Chen, C.Y. Hsieh, M.H. Yao and B.J. Kuo, "Using Sigmoidal Growth Models To Simulated Greenhouse Tomato Growth And Development," Horticulturae, vol.8, no.1021, https://doi.org/10.3390/horticulturae8111021, 2022.

[3] J. Ukalska and S. Jastrzebowski, "Sigmoid Growth Curve, a New Approach to Study The Dynamics of The Epicotyl Emergence of Oak," *Folia Forestalia Polonica.*, vol.61, no.1, pp.30-41, 2019.

[4] J.G. Fernandes, E.M. da Silva, T.D. Ribeiro, E.M. Silva, T.J. Fernandes and J.A. Muniz, "Description of The Peach Fruit Growth Curve by Diphasic Sigmoidal Nonlinier Model," *Rev.Bras.Frutic:Jaboticabal,* vol.3 no. 9, pp. 1-10, 2022.

[5] Z. Jericevic, and Z. Kuster, "Nonlinear Optimization of Parameters in Michaelis Menten Kinetics," *Croatia Chemica Acta CCACCAA,* vo.78, no.4, pp.519-523, 2005.

[6] J. D. Knudsen, "*General Concepts of Pharmacodynamics*," Department of Clinical Microbiology, Rigshospitalet Copenhagen Denmark ,2001.

[7] C. Marianela, and M. Jose, "A New Approach to Modelling Sigmoidal Curve," *Technological Forecasting and Social Change,* vol. 69, pp.233-241, 2002.

[8] N.E.A. Al-Rahman, A.E.A. Hussien, E.G. Yehia and S.A. Mousa, "Modelling sigmoidal growt curves to study the confirmed cases of COVID-19 in Egypt," *An Academic Periodical Referred Journal,* vol.27, pp. 1-24, 2022.

[9] M.Y. Rochyani, D.G.R. Menufandu and R. Dapa, "Investigating the Growth of Bacteria Using Double Sigmoid Model with Reparameterization," *International Journal of Global Optimization and Its Application*, vol. 2, no. 4, pp. 200 - 208, 2023.

[10] A. Al-Shorman, M.A. Ajeel, K. and Al-Khaled, "Analyzing Newton's Method for Solving Algebraic Equations with Complex Variables: Theory and Computational Analysis," *IAENG International Journal of Applied Mathematics,* vol. 54, issue 6, pp. 1038-1047, 2014.

[11] S. Purwani, A.F. Ridwan, R.A. Hidayana and S. Sukono, "Secant Method with Aitken Extrapolation Outperform Newton-Raphson Method in Estimating Stock Implied Volatility," *IAENG International Journal of Computer Science*, vol.50, issue 2, pp.368-374, 2023.

[12] H. Wang and M. Qin, "A Modified Regularized Newton Method for Unconstrained Convex Optimization," *IAENG International Journal of Applied Mathematics,* vol.46, issue 2, pp. 130-134, 2016.

[13] A.C. Atkinson, A.N. Donev and R.D. Tobias, "Optimum experimental designs, with SAS," *OXFORD Universitu* Press Inc., New York, 2007, pp 129.

[14] A. Chauhan, "A study of Modified Newton-Raphson methods," *Journal of University of Shanghai for Science and Technology,* vol. 3, issue 8, pp. 129-134, 2021.

[15] H. Chernoff, "Locally Optimal Designs for Estimating Parameters," *The Annals of Statistics,* vol.24, pp. 586 - 602,1953.

[16] F. C. Chang, and C. F. Lay, "Optimal Designs for a Growth Curve Models," *Journal of Statistical Planning and Inference,* vol.104, pp. 427-438, 2002.

[17] H. Dette, and A. Pepelyshev, "Efficient Experimental Designs for Sigmoidal Growth Models," *Journal of Statistical Planning and Inference,* vol.138, pp. 2-17, 2008.

[18] G. Li, and D. Majumdar, "D-optimal Designs for Logistic Models with Three and Four Parameters," *Journal of Statistical Planning and Inference,* vol.138, pp.1950-1959, 2008.

[19] G. Li, "Optimal and Eficient Designs for Gompertz Regression Models," *Ann Inst Stat Math,* vol. 64, pp. 945-957, 2012.

[20] G. Li, and N. Balakrishnan, "Optimal Designs for Tumor Regrowth Models," *Journal of Statistical Planning and Inference,* vol.141, pp. 644 – 654, 2011.

[21] M. Hooshangifar, H. Talebi and D. Paursina, "D-optimal Design for Logistic Model Based on More Precise Approximation," *Communication in Statistics,* vol.5, no. 7, pp 1975-1992, 2022.

[22] G.P.Y. Clarke and L.M. Haines, "Optimal Design for Models Incorporating the Richards Function," in book *Statistical Modelling*, pp 61-66, doi:10.1007/978-1-4612-0789-48, 2011.

[23] Y. Zhai, C. Wang, H.Y. Lin and Z. Fang, "D-optimal Designs for Two-Variable Logistic Regression Model with Restricted Design Space," *Communication in Statistics-theory and Methods,* vol. 53, no.11, pp 3940-3957, 2024.

[24] T. Widiharih, S. Haryatmi, and Gunardi, "D-optimal Designs for Weighted Exponential and Generalized Exponential Models," *Applied Mathematical Sciences,* vol.7, no.22, pp. 1067-1079, 2013.

[25] T. Widiharih, S. Haryatmi, and Gunardi, "D-optmal designs for Modified Exponential Models with three parameters," *Journal Model Assisted Statistics and Application,* vol.11, pp. 153- 169, 2016.

[26] T. Widiharih, S. Haryatmi, and Gunardi, "D-optimal Designs for Morgan Mercer Flodin (MMF) Models Without Intercept," *International Journal of Applied Mathematics and Statistics,* vol. 53, no. 5, pp. 163-171, 2015.

[27] T. Widiharih, S. Haryatmi and Gunardi, "D-optimal Designs for Morgan Mercer Flodin (MMF) Models With Three Parameters," , In: *Proceeding AIP, 1707, 080015*, pp. 080015108001510, 2016.

[28] J. Kiefer, and J. Wolfowitz, "The equivalence of Two Extremum Problems," *Can. Jnl. Math,* vol.12, pp.363-366, 1960.

[29] L. White," An extension of the General Equivalence Theorem to Nonlinear Models," *Biometrika*, vol. 60, pp. 345-348, 1973.

[30] S. Karlin, and W. J. Studden, *Tchebyshev System: with application in analysis and statistics*, John Willey and Sons. Inc, 1966.

[31] A. Shadrin, Part III-Lent Term, "Approximation Theory-Lecture 6." A Short Course, Available: http://www.damtp.cam.uk/user/na/na.html , 2005 .

[32] V. K. Dzyadyk, and I. A. Shevchuk, "*Theory of Uniform Approximation of Functions by Polynomials*," Walter de Gruyter GmbH and CO. KG, 10785 Berlin, Germany, 2008. Ch.1