Numerical approach nonminimally supported design for two parameters generalized exponential model and its efficiency

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Abstract. Nonminimally supported designs is a design that the number of supported design is greater than the number of parameters of the model. We construct nonminimally supported design with the number of the supported designs is the number of parameters plus one and it has uniform weight. We use two methods to construct nonminimally supported design, first we create the formula of determinant information matrix then maximize it, second by adding one supported design from minimally supported design. The formula to determine the supported design is a complicated nonlinear function, so we use numerically approach. Furthermore we conclude the best of nonminimally supported design based on the highest value of determinant information matrix. Efficiency of nonminimally supported design to minimally supported design is ratio of determinant information matrix nonminimally supported design and determinant information matrix minimally supported design.

1. Introduction

The Exponential models can be used to describe a growth functions curve. Several types curves in the exponential model are always increasing, always decreasing, from the starting point up to the maximum point, then relatively constant and unimodal curve. Rusdiana et al [1] do research in pharmacokinetics, a scatterplot of this data can be approach by unimodal curve. Rao [2] does research in pharmacokinetics and the scatterplot at the data in the unimodal model. Hathout[3] describes the world population using exponential model. Archontoulis and Miguez[4] make a model in the agricultural area in exponential model always increasing and unimodal models.

D-optimal design is a design usually the number of supported as the same with the number of parameters model and have the same proportion[5,6]. The information matrix of nonlinear model is complicated because it contains the parameter that unknown value. The formula determinant of the information matrix becomes complicated. Supported designs can be obtained if we have the initial information about the value of parameters. Maximizing the determinant of the information matrix is done numerically. D-optimal design for the exponential model have been done, including [7,8,9].

In this paper, the two parameters generalized exponential model as follows:

\[ y = e^{-\theta_1 t} \left(1 - e^{-\theta_1 t}\right)^{\theta_2} + \varepsilon, \quad t \geq 0, \quad \theta_1, \theta_2 > 0 \]  \hspace{1cm} (1)
Nonminimally supported design will be built by adding one supported design from the minimally supported design, so we use three supported design with uniform proportion. We use two methods, first by deriving the formula of the determinant of the information matrix, then determining the points that maximize this determinant, second by adding one supported design to the D-optimal design which randomly selected from the design region. Based on the two methods, all of the alternatives of nonminimally supported design are calculated the information matrix and their determinant. Based on the value of the determinant, the best design is design that have the highest value of the determinant of the information matrix. The efficiency of nonminimally supported design to minimally supported design is the ratio of determinant information matrix nonminimally supported design and determinant information matrix minimally supported design.

2. Material and Methods
The nonlinear model is denoted by:

$$y = \eta(t, \theta) + \epsilon$$

(2)

with independent $\epsilon \sim N(0, \sigma^2)$

$$E(Y|t) = \eta(t, \theta)$$

(3)

Designs $\xi$ of 3 supported designs ($t_i, i = 1,2,3$) and their proportions ($w_i = \frac{1}{3}, i = 1,2,3$) is denoted by:

$$\xi = \begin{pmatrix} t_1 & t_2 & t_3 \\ \frac{1}{3} & \frac{1}{3} & \frac{1}{3} \end{pmatrix}$$

(4)

The information matrix of design $\xi$ for the model (4) is:

$$M(\xi, \theta) = \frac{1}{3} \sum_{i=1}^{3} h(t_i, \theta)h^T(t_i, \theta)$$

(5)

Where: $h(t, \theta) = \frac{\partial \eta(t, \theta)}{\partial \theta} = (h_1(t, \theta), h_2(t, \theta))^T$ is the vector of partial derivatives of equation (3) with respect to $\theta_1$ and $\theta_2$. $M(\xi, \theta)$ is $2 \times 2$ symmetrix matrix.

Nonminimally supported designs are built in two methods as follows:

A. Method I

Algorithm constructing the nonminimally supported designs as follows:

i. Determine $h(t, \theta) = \frac{\partial \eta(t, \theta)}{\partial \theta} = (h_1(t, \theta), h_2(t, \theta))^T$

ii. Determine formula of the element of information matrix based on equation (4) and (5).

iii. Construct the information matrix $M(\xi, \theta)$

iv. Determine the formula of determinant information matrix $M(\xi, \theta)$.

v. Enter the value of parameters based on prior information in (iv)

vi. Determine the supported designs by maximizing $|M(\xi, \theta)|$.

B. Method II

Algorithm constructing the nonminimally supported designs as follows:

a. Determine the minimally supported design ($t_1, t_2$) obtained from D-optimal design for model (1) by maximizing $|M(\xi, \theta)| \propto e^{-2\theta_1(t_1+t_2)}(1 - e^{-\theta_1 t_1})^{2\theta_2}(1 - e^{-\theta_1 t_2})^{2\theta_2}[A + B]^2$
where:

\[ A = t_1 \left( 1 - e^{-\theta_1 t_1} \right)^{-1} \left( (1 + \theta_2) e^{-\theta_1 t_1} - 1 \right) \ln(1 - e^{-\theta_1 t_1}) \]

\[ B = t_2 \left( 1 - e^{-\theta_1 t_2} \right)^{-1} \left( (1 + \theta_2) e^{-\theta_1 t_2} - 1 \right) \ln(1 - e^{-\theta_1 t_2}) \]

b. Adding one supported design \( (t_3) \) selected randomly in the design region.
c. Given uniform proportion to \( t_1, t_2, t_3 \)
d. Determine the determinant of the information matrix for all alternative nonminimally supported design.
e. Chose the design that has the highest value of the determinant of information matrix as the best of nonminimally supported design

3. Results and discussions

3.1. Nonminimally supported designs for two parameters generalized exponential model method I

Consider model (1):

\[ y = e^{-\theta_1 t_1} \left( 1 - e^{-\theta_2 t_1} \right)^{\theta_2} + \varepsilon, \quad t \geq 0, \theta_1, \theta_2 > 0. \]

The curve of model (1) for \( \theta_1 = 0.2 \) at several of \( \theta_2 \) and for \( \theta_2 = 0.4 \) at several of \( \theta_1 \) are presented in Figure 1 and Figure 2.

![Figure 1](https://via.placeholder.com/150)

**Figure 1.** The curve of model (1) for \( \theta_1 = 0.2 \) at several of \( \theta_2 \)

![Figure 2](https://via.placeholder.com/150)

**Figure 2.** The curve of model (1) for \( \theta_2 = 0.4 \) at several of \( \theta_1 \)

Based on Figure 1, if \( \theta_1 \) fixed with varying \( \theta_2 \) the smaller value of \( \theta_2 \) has a greater maximum, but the time \( t \) relatively the same. Based on Figure 2, if \( \theta_2 \) fixed and several of \( \theta_1 \) each curve has a maximum value that are relatively the same but the smaller of \( \theta_1 \) then the greater of \( t \) value.

Based on equation (1) and (2) so that:

\[ \eta(t, \theta) = e^{-\theta_1 t} \left( 1 - e^{-\theta_2 t} \right)^{\theta_2} \]

\[ \frac{\partial \eta(t, \theta)}{\partial \theta_1} = -t e^{-\theta_1 t} \left( 1 - e^{-\theta_1 t} \right)^{\theta_2 - 1} \left( (1 + \theta_2) e^{-\theta_1 t} - 1 \right) \]

\[ \frac{\partial \eta(t, \theta)}{\partial \theta_2} = e^{-\theta_1 t} \left( 1 - e^{-\theta_1 t} \right)^{\theta_2} \ln(1 - e^{-\theta_1 t}) \]
\[
\begin{align*}
\mathbf{h}(t, \theta) &= \begin{pmatrix}
-t e^{-\theta_1 t} \left(1 - e^{-\theta_1 t}\right)^{\theta_2 - 1} \left((1 + \theta_2) e^{-\theta_1 t} - 1\right) \\
-e^{-\theta_1 t} \left(1 - e^{-\theta_1 t}\right)^{\theta_2} \ln(1 - e^{-\theta_1 t})
\end{pmatrix}
\end{align*}
\] (6)

Designs \(\xi\) of three supported designs

\[
\xi = \begin{pmatrix}
t_1 \\
t_2 \\
t_3
\end{pmatrix}
\]

The information matrix based on equation (4) and (6) as follows:

\[
\mathbf{M}(\xi, \theta) = \begin{pmatrix}
m_{11} & m_{12} \\
m_{12} & m_{22}
\end{pmatrix}
\]

(7)

where the element of the information matrix as follows:

\[
m_{11} = \frac{1}{3} \sum_{i=1}^{3} t_i^2 e^{-2\theta_1 t_i} \left(1 - e^{-\theta_1 t_i}\right)^{2(\theta_2 - 1)} \left((1 + \theta_2) e^{-\theta_1 t_i} - 1\right)^2
\]

\[
m_{22} = \frac{1}{3} \sum_{i=1}^{3} e^{-2\theta_1 t_i} \left(1 - e^{-\theta_1 t_i}\right)^{2\theta_2} \ln^2(1 - e^{-\theta_1 t_i})
\]

\[
m_{12} = -\frac{1}{3} \sum_{i=1}^{3} t_i e^{-2\theta_1 t_i} \left(1 - e^{-\theta_1 t_i}\right)^{2\theta_2 - 1} \left((1 + \theta_2) e^{-\theta_1 t_i} - 1\right) \ln(1 - e^{-\theta_1 t_i})
\]

The formula of \(|\mathbf{M}(\xi, \theta)|\) is

\[
|\mathbf{M}(\xi, \theta)| \propto A + B + C
\]

(8)

where:

\[
A = e^{-2\theta_1 (t_1 + t_2)} \left(1 - e^{-\theta_1 t_1}\right)^{2(\theta_2 - 1)} \left(1 - e^{-\theta_1 t_2}\right)^{2(\theta_2 - 1)} A_1
\]

\[
A_1 = \left[t_1 \left(1 - e^{-\theta_1 t_1}\right) \ln(1 - e^{-\theta_1 t_1}) \left(1 - (1 + \theta_2) e^{-\theta_1 t_1}\right) - t_2 \left(1 - e^{-\theta_1 t_1}\right) \ln(1 - e^{-\theta_1 t_1}) \left(1 - (1 + \theta_2) e^{-\theta_1 t_1}\right)\right]^2
\]

\[
B = e^{-2\theta_1 (t_1 + t_2)} \left(1 - e^{-\theta_1 t_1}\right)^{2(\theta_2 - 1)} \left(1 - e^{-\theta_1 t_2}\right)^{2(\theta_2 - 1)} B_1
\]

\[
B_1 = \left[t_1 \left(1 - e^{-\theta_1 t_1}\right) \ln(1 - e^{-\theta_1 t_1}) \left(1 - (1 + \theta_2) e^{-\theta_1 t_1}\right) - t_3 \left(1 - e^{-\theta_1 t_1}\right) \ln(1 - e^{-\theta_1 t_1}) \left(1 - (1 + \theta_2) e^{-\theta_1 t_1}\right)\right]^2
\]

\[
C = e^{-2\theta_1 (t_2 + t_3)} \left(1 - e^{-\theta_1 t_2}\right)^{2(\theta_2 - 1)} \left(1 - e^{-\theta_1 t_3}\right)^{2(\theta_2 - 1)} C_1
\]

\[
C_1 = \left[t_2 \left(1 - e^{-\theta_1 t_2}\right) \ln(1 - e^{-\theta_1 t_2}) \left(1 - (1 + \theta_2) e^{-\theta_1 t_2}\right) - t_3 \left(1 - e^{-\theta_1 t_2}\right) \ln(1 - e^{-\theta_1 t_2}) \left(1 - (1 + \theta_2) e^{-\theta_1 t_2}\right)\right]^2
\]

Supported designs \(t_i, i = 1, 2, 3\) is obtained by maximizing \(|\mathbf{M}(\xi, \theta)|\), but in the \(|\mathbf{M}(\xi, \theta)|\) contains the unknown parameter \(\theta_i, i = 1, 2, 3\), so we need the initial information value of \(\theta_i, i = 1, 2, 3\). Numerical simulation nonminimally supported designs for model (1) by maximizing equation (8) for some value of \(\theta_i, i = 1, 2\) and design region (0 , 5) is presented in Table (1).
\[ \mathbf{M}(\xi, \theta) = e^{\theta_1 t_1 - \theta_2 t_2} \mathbf{A} + \mathbf{B} \]

where:

\[ A = t_1 (1 - e^{-\theta_1 t_1})^{-1} \left( (1 + \theta_2) e^{-\theta_2 t_2} - 1 \right) \ln(1 - e^{-\theta_2 t_2}) \]

\[ B = t_2 (1 - e^{-\theta_2 t_2})^{-1} \left( (1 + \theta_2) e^{-\theta_2 t_2} - 1 \right) \ln(1 - e^{-\theta_2 t_2}) \]

Table 1. Nonminimally Supported Design Model (1) For Some Value Of \( \theta_i, i = 1,2 \) with Design Region \((0, 5)\)

| \( \theta_1 \) | \( \theta_2 \) | \( t_1 \) | \( t_2 \) | \( t_3 \) | \( \mathbf{M}(\xi, \theta) \) |
|---|---|---|---|---|---|
| 1 | 1 | 1.744779518 | 1.744779518 | 0.267734317 | 0.005969594 |
| 1 | 0.5 | 1.461052010 | 1.461052010 | 0.090526164 | 0.058767018 |
| 1 | 0.25 | 1.272272616 | 1.272272564 | 0.014952087 | 0.380044096 |
| 1 | 0.75 | 1.614736341 | 1.614736341 | 0.179810777 | 0.016302592 |
| 1 | 1.25 | 1.857656413 | 1.857656413 | 0.351186979 | 0.002594060 |
| 1 | 1.5 | 1.957472164 | 1.957472164 | 0.429380548 | 0.001268912 |
| 1 | 1.75 | 2.047001344 | 2.047001344 | 0.502678434 | 0.000677490 |
| 1 | 2 | 2.128210390 | 2.128210384 | 0.571390255 | 0.000387057 |
| 0.5 | 2 | 4.256420781 | 1.142780510 | 1.142780509 | 0.001548228 |
| 0.75 | 2 | 2.837613854 | 2.837613854 | 0.761853673 | 0.000688100 |
| 1.25 | 2 | 1.702568313 | 1.702568313 | 0.457122024 | 0.000247717 |
| 1.5 | 2 | 1.418806925 | 1.418806891 | 0.380926836 | 0.000172025 |
| 1.75 | 2 | 1.216120223 | 1.216120223 | 0.326508717 | 0.000126386 |
| 2 | 2 | 1.064105195 | 1.064105195 | 0.285709517 | 0.000897684 |
| 2.25 | 2 | 0.945871283 | 0.253951224 | 0.253951225 | 0.00076455 |

Based on Table (1) shows that from all of the cases value of \( \theta_i, i = 1,2 \) three supported designs two of them are equal. In order word nonminimally supported design have two supported design with the weight are 0.33333 and 0.66667 respectively.

3.2. Nonminimally supported designs for three parameters generalized exponential model method II

Supported design \((t_1, t_2)\) for D-optimal design model (1) obtained by maximized:

\[ \mathbf{M}(\xi, \theta) \propto e^{-2\theta_1 t_1 + t_2} (1 - e^{-\theta_1 t_1})^{2\theta_2} (1 - e^{-\theta_2 t_2})^{2\theta_2} [A + B]^2 \] (9)

The formula \( \mathbf{M}(\xi, \theta) \) in equation (9) contains the parameter \( \theta_i, i = 1,2 \), so we need the initial information value of \( \theta_i, i = 1,2 \). Besides that optimization, the formula in equation (9) is a nonlinear optimization, so we do it by numerical approach.

Numerical simulation D-optimal design model (1) by maximizing equation (9) for some value of \( \theta_i, i = 1,2 \) and design region \((0, 5)\) is presented in Table (2). 

Based on Table (2) shows that from all of the cases value of \( \theta_i, i = 1,2 \) two supported designs are equal to two supported design in table (1). Adding one supported design \((t_3)\) selected by trial and error in \((0, 5)\) is a very important to decided the best nonminimally supported design based on the value of determinant information matrix. In the cases \( t_2, t_3 \) have the same weight i.e 0.33333, so the information matrix as in equation (7). Based on the simulation, for all value of \( \theta_i, i = 1,2 \), the determinant of information matrix have the same pattern for all value of \( t_3 \). As an illustration, the scatterplot of the determinant of information matrix and \( t_3 \) for \( \theta_1 = 0.75, \theta_2 = 2.0 \) is presented in Figure 3.
Table 2. D-optimal Design Model (1) For Some Value Of $\theta_i, i = 1, 2$ with Design Region (0 , 5)

| $\theta_1$ | $\theta_2$ | $t_1$   | $t_2$   | $|M(\xi, \theta)|$ |
|-----------|-----------|--------|--------|-----------------|
| 1         | 1         | 1.74477951 | 0.26773430 | 0.0007461993   |
| 1         | 0.5       | 1.46105201 | 0.09052616 | 0.0073458772   |
| 1         | 0.25      | 1.27227259 | 0.01495208 | 0.0475505120   |
| 1         | 0.75      | 1.61473633 | 0.17981075 | 0.0020378240   |
| 1         | 1.25      | 0.35111869 | 1.85765635 | 0.0003242575   |
| 1         | 1.5       | 1.95747207 | 0.42938054 | 0.0001586140   |
| 1         | 1.75      | 2.04700134 | 0.50267843 | 0.0000846863   |
| 0.5       | 2         | 2.12821038 | 0.57139025 | 0.0000483821   |
| 0.75      | 2         | 2.83761354 | 0.76185367 | 0.0000860127   |
| 1.25      | 2         | 1.70256831 | 0.45711220 | 0.0000309646   |
| 1.5       | 2         | 1.41880685 | 0.38092669 | 0.0000215032   |
| 1.75      | 2         | 1.21612022 | 0.32650871 | 0.0000157982   |
| 2         | 2         | 1.06410519 | 0.28569512 | 0.0000120955   |
| 2.25      | 2         | 0.94587128 | 0.25395121 | 0.0000095570   |

Figure 3. Scatterplot $|M(\xi, \theta)|$ vs $t_3$ for $\theta_1 = 0.75, \theta_2 = 2.0$

Based on the Figure (3) shows that the maximize value of the determinant of information matrix happens at twice of $t_3$, i.e $0.76185367$ and $2.83761354$ with the value of the determinant is $0.0000764557$. We can show that $t_3$ in this cases, is one of $t_1, t_2$ which is the same with nonminimally supported design method I. Efficiency of nonminimally supported design to minimally supported design is:

$$Eff = \frac{|M(\xi, \theta)|_{\text{of nonminimally supported design}}}{|M(\xi, \theta)|_{\text{of minimally supported design}}}.$$  

For all value of $\theta_1$ and $\theta_2$ the value of efficiency is 0.8889.
4. Conclusion
The results of this research indicate that the constructing nonminimally supported design with uniform proportion and based on the determinant of the value of information matrix can be carried out in two ways. First, by constructing the formula of the determinant of information matrix, than maximize it. Second, by adding one supported design to the D-optimal design, which maximize their determinant of the information matrix. The design I and Design II have the same result. The efficiency of nonminimally supported design to minimally supported design is 0.8889.

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References
[1] Rusdiono T, Sjuib F and Asyarie S 2009 Interaksi Farmakokinetik Kombinasi Obat Paracetamol dan Fenilpropanolamin Hidroklorida sebagai Komponen Obat Flu (pustaka.unpad.ac.id/wo-content/uploads/2009/interaksi farmakokinetik.pdf)
[2] Rao G S N K 2015 Pharmacokinetics One Compartment Oral Administration (RAGHU College of Pharmacy Visakhapatnam)
[3] Hathout D 2013 Appl. Math. 4 299
[4] Archontoulis S V and Miguez F E 2015 Agron. J. 107 2 786
[5] Li G and Majumdar D 2008 J. Stat. Plan. Inference 138 190
[6] Dette H and Pepelyshev A 2008 J. Stat. Plan. Inference 138 2
[7] Dette H, Melas V B and Wong W K 2006 Stat. Sin. 16 789
[8] Widiharih T, Haryatmi S and Gunardi 2016 Model Assist. Stat. Appl. 11 153
[9] Lall S, Jaggi S, Varghese E, Varghese C and Bhowmik A 2018 J. Indian Soc. Agric. Stat. 72 1 27
[10] Khinkis L A, Levasseur L, Faessel H and Greco W R 2003 Nonliniety Biol. Toxicol. Med. 1 363
[11] Su Y and Raghavaro D 2013 J. Biopharm. Stat. 23 2 281