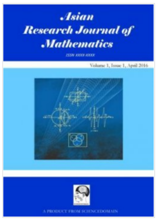

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D-optimal Designs for Multiple Poisson Regression Model with Random Coefficients

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Abstract

The majority of the Optimal design research has focused on linear models and binary data models. However, a couple of researches have recently called attention to Poisson regression models with random effects. In the present paper, we theoretically and numerically discuss the optimal designs for multiple Poisson regression model with random coefficients and two explanatory variables. Since there is no closed form for the information matrix, the quasi-information approach is applied in order to find the optimal designs in this study. Some special cases are illustrated and a new version of equivalence theorem is obtained.

Keywords: *Generalized linear mixed models; multiple poisson regression; optimal design; quasi-information; random effects.*

2010 Mathematics Subject Classification: 53C25, 83C05, 57N16.

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1 Introduction

The main goal of the optimal design is to obtain the best experimental setting x_i which maximizes the information matrix of parameters. Optimal experimental designs for generalized linear models have received increasing attention in recent years. The majority of investigations into optimal designs for generalized linear models (GLMs) have been dedicated to binary data models. Abdelbasit and Plackett [1], Minkin [2] and many others have studied the optimal designs for logistic models. Poisson regression model is an appropriate model to explain count data. Minkin [3] and Yanping et al. [4] have also conducted extensive research on the optimal designs for Poisson regression models.

In the above studies, they considered Poisson regression model for fixed effects, a fact may be in challange if we cannot suppose that the same effect for different individuals. In this study, we consider the multiple Poisson random coefficients regression model. This model is a special case of generalized linear mixed models (GLMMs)[5].

Information matrix plays a key role in optimal design theory. Apparently, this role originates from the asymptotic relation between information matrix and variance-covariance matrix of the maximum likelihood estimator of parameters. Due to the random effects of GLMMs, the likelihood function and consequently the information matrix cannot be obtained in an explicit form. We apply a quasi-likelihood approach which was extensively studied by McCulagh [6].

Niaparast [7] derived optimal designs for the quasi-likelihood estimation in a Poisson random intercept regression model. Furthermore, Niaparast and Schwabe [8] extended the results to general mixed effects Poisson regression.

The information matrix for GLMMs depends on the unknown parameters. Therefore, it poses a two-fold problem: first we must know the parameters to find the optimal designs, and second, we need to designs first in order to estimate the parameters. A simple approach to this problem is to look for locally optimal designs which are based on an initial guess of the parameters. Then, we can achieve the optimal designs which are optimal with respect to the initial guess.

The present paper is organized as follow. In section 2 we mention the results which have been obtained by Niaparast [7] and Niaparast and Schwabe [8]. The optimal designs for some special cases of general mixed effects Poisson are discussed in sections 3 and 4. Moreover, all proofs are presented in appendix following the discussion.

2 The Structure of Model and Design Specification

The results of this paper are in continuation of Niaparast [7] and Niaparast and Schwabe [8], who obtained some new results on D-optimal designs for Poisson regression models with random coefficients. Since we need their notation and results, we review them here.
Consider a Poisson regression model with random coefficients as following

$$Y_{ij}|\boldsymbol{b}_i \overset{ind}{\sim} Poisson(\lambda_{ij}) \quad ; \begin{cases} i = 1, \cdots, n \\ j = 1, \cdots, m_i \end{cases} \tag{2.1}$$

where Y_{ij} is the jth replication for the individual i at the experimental setting $\mathbf{x}_{ij}$ from the experimental region $\mathcal{X}$, and the mean of the response $\lambda_{ij} = \lambda(\mathbf{x}_{ij}, \boldsymbol{b}_i)$ is linked to the linear predictors by the following equation

$$\log(\lambda_{ij}) = \mathbf{f}^T(\mathbf{x}_{ij})\mathbf{b}_i$$

We also assume that $\mathbf{f} = (f_0, f_1, \cdots, f_{p-1})$ is the known regression function and $\mathbf{b}_i$ is a $p \times 1$ vector of random effects which is normally distributed with mean vector $\boldsymbol{\beta} = (\beta_0, \cdots, \beta_{p-1})$ and known

variance-covariance matrix $\mathbf{\Sigma}$. Moreover, we suppose $cov(b_i, b_j) = 0$ for $i \neq j$.
Let $\mathbf{Y}_i = (Y_{i1}, \cdots, Y_{im_i})$ be the vector of all m_i observations for individual i, regarding the definition of model (2.1), the global mean and the variance-covariance matrix of $\mathbf{Y}_i$ can be obtained as

$$E(\mathbf{Y}_i) = (\mu(\mathbf{x}_{ij}), \cdots, \mu(\mathbf{x}_{im_i})) \text{ with } \mu(\mathbf{x}_{ij}) = \exp(\mathbf{f}^T(\mathbf{x}_{ij})\boldsymbol{\beta} + \frac{1}{2}\sigma(\mathbf{x}_{ij}, \mathbf{x}_{ij}))$$

$$cov(\mathbf{Y}_i) = \mathbf{A}_i + \mathbf{A}_i\mathbf{C}_i\mathbf{A}_i$$

where $\mathbf{A}_i = diag\{\mu(\mathbf{x}_{ij})\}_{j=1,\cdots,m_i}$ is a diagonal matrix with entries $\mu(\mathbf{x}_{ij})$ for $j = 1, \cdots, m_i$ and $\mathbf{C}_i = (c(\mathbf{x}_{ij}, \mathbf{x}_{ik}))_{j,k=1,\cdots,m_i}$. Here $c(\mathbf{x}_{ij}, \mathbf{x}_{ik}) = \exp(\sigma(\mathbf{x}_{ij}, \mathbf{x}_{ik}))-1$ and $\sigma(\mathbf{x}_{ij}, \mathbf{x}_{ik}) = \boldsymbol{f}^T(\mathbf{x}_{ij})\mathbf{\Sigma}\boldsymbol{f}(\mathbf{x}_{ik})$ are the variance correction and the dispersion function term, respectively.
Let $\xi = \left\{ \begin{array}{c} \mathbf{x_1}, \cdots, \mathbf{x_s} \\ p_1, \cdots, p_s \end{array} \right\}$ be the design through which we observe all individuals under that. In other words, we omitted index i of the individual designs, and hence, $m_i = m$ for $i = 1, \cdots, n$. Here $p_j = \frac{n_j}{m}$ $(j = 1, \cdots, s)$ stands for the proportion of observations taken at $\mathbf{x}_j$. Niaparast and Schwabe (2013) have obtained the quasi-information matrix for the vector of fixed effects parameters, $\boldsymbol{\beta}$ in Poisson regression model with random effects as follow,

$$\mathfrak{M}(\xi) = \mathbf{F}_\xi^T(\mathbf{A}_\xi^{-1} + \mathbf{C}_\xi)^{-1}\mathbf{F}_\xi \tag{2.2}$$

where $\mathbf{F}_\xi = (\mathbf{f}(\mathbf{x}_1), \cdots, \mathbf{f}(\mathbf{x}_s))^T$, $\mathbf{A}_\xi = diag(n_j\mu(\mathbf{x}_j))_{j=1,\cdots,s}$ and $\mathbf{C}_\xi = (c(\mathbf{x}_j, \mathbf{x}_k))_{j,k=1,\cdots,s}$.
Finally, the following theorem is essential to evaluate D-optimal designs for Poisson regression model with random coefficients.

Theorem 2.1. *An individual design ξ is locally D-optimal at $\boldsymbol{\beta}$ for the quasi-information in the mixed effects Poisson regression model, if and only if*

$$d(\mathbf{x}, \xi^*) \leq p - tr(\mathfrak{M}(\xi^*)^{-1}\mathbf{F}_{\xi^*}^T(\mathbf{A}_{\xi^*}^{-1} + \mathbf{C}_{\xi^*})^{-1}\mathbf{C}_{\xi^*}(\mathbf{A}_{\xi^*}^{-1} + \mathbf{C}_{\xi^*})^{-1}\mathbf{F}_{\xi^*})$$

for all $\mathbf{x} \in \mathcal{X}$. Moreover, equality holds for all support points of ξ^*.

Here $d(\mathbf{x}, \xi) = m\mu(\mathbf{x})(\mathbf{f}(\mathbf{x}) - \mathbf{F}_\xi^T(\mathbf{A}_\xi^{-1} + \mathbf{C}_\xi)^{-1}\mathbf{c}_{\xi,\mathbf{x}})^T\mathfrak{M}(\xi)^{-1}(\mathbf{f}(\mathbf{x}) - \mathbf{F}_\xi^T(\mathbf{A}_\xi^{-1} + \mathbf{C}_\xi)^{-1}\mathbf{c}_{\xi,\mathbf{x}})$ is the sensitivity function (in $\mathbf{x}$) of the design ξ and $\mathbf{c}_{\xi,\mathbf{x}} = (c(\mathbf{x}_j, \mathbf{x}))_{j=1,\dots,s}$ is a vector of joint correction terms for the settings $\mathbf{x}_1, \dots, \mathbf{x}_s$ of a design ξ for prediction of a further setting $\mathbf{x}$.
The proof can be found in Niaparast and Schwabe(2013).

3 D-optimal Designs for Multiple Poisson Regression Model with Random Intercept

We consider two cases of the multiple Poisson regression models with random intercept

$$i) Y_j|b_0 \overset{ind}{\sim} P(\lambda_j) \quad ;\lambda_j = \lambda(\mathbf{x}_j, b_0) = \exp(b_0 + \beta_1 x_{1j} + \beta_2 x_{2j}) \tag{3.1}$$

$$ii) Y_j|b_0 \overset{ind}{\sim} P(\lambda_j) \quad ;\lambda_j = \lambda(\mathbf{x}_j, b_0) = \exp(b_0 + \beta_1 x_{1j} + \beta_2 x_{2j} + \beta_3 x_{1j}x_{2j}) \tag{3.2}$$

where b_0 is assumed to be normally distributed with the mean β_0 and known variance σ^2 . The first model is a special case of model (2.1) with $\boldsymbol{\beta} = (\beta_0, \beta_1, \beta_2)$, $\boldsymbol{f}^T(\mathbf{x}_j) = (1, x_{1j}, x_{2j})$ and $\mathbf{\Sigma} = diag(\sigma^2, 0, 0)$ and the mean function, dispersion function and correction term will be $\mu_j = \exp(\mathbf{f}^T(\mathbf{x}_j)\boldsymbol{\beta} + \frac{1}{2}\sigma^2)$, $(\sigma(\mathbf{x}_j, \mathbf{x}_k))_{j,k=1,2,3} = \sigma^2$ and $(c(\mathbf{x}_j, \mathbf{x}_k))_{j,k=1,2,3} = \exp(\sigma^2) - 1$ respectively.
The second model is also a special case of model (2.1) with $\boldsymbol{\beta} = (\beta_0, \beta_1, \beta_2, \beta_3)$, $\boldsymbol{f}^T(\mathbf{x}_j) = (1, x_{1j}, x_{2j}, x_{1j}x_{2j})$ and $\mathbf{\Sigma} = diag(\sigma^2, 0, 0, 0)$. The mean function, dispersion function and correction term will be $\mu_j = \exp(\mathbf{f}^T(\mathbf{x}_j)\boldsymbol{\beta} + \frac{1}{2}\sigma^2)$, $(\sigma(\mathbf{x}_j, \mathbf{x}_k))_{j,k=1,\dots,4} = \sigma^2$ and $(c(\mathbf{x}_j, \mathbf{x}_k))_{j,k=1,\dots,4} = \exp(\sigma^2) - 1$, respectively.

Suppose that $q_{1j} = \exp(\beta_1 x_{1j})$, $q_{2j} = \exp(\beta_2 x_{2j})$ and $\mu_0 = \exp(\beta_0 + \frac{1}{2}\sigma^2)$ the mean of Y_j will be as $\mu_j = q_{1j} q_{2j} \mu_0$. In practice, most applications of this model, like bioscience, pharmacokinetics etc., the design region is the non-negative real line or a subset of that. We also assume that the relation between response mean and regressor variables is negative, i.e. μ_j is a decreasing function of q_{1j} and q_{2j}. Therefore, canonical standardized mean $\tilde{\mu}_j = q_{1j} q_{2j}$ will be in (0,1]. So the design region can be limited to $0 \le q_{1j} \le 1$ and $0 \le q_{2j} \le 1$.

Theorem 3.1. *Consider the model* (3.1). *In terms of the canonical standardized mean, let* $\xi = \left\{ \begin{array}{ccc} (q_{11}, q_{21}) & (q_{12}, q_{22}) & (q_{13}, q_{23}) \\ p_1 & p_2 & p_3 \end{array} \right\}$ *be the design minimal supported points, the local D-optimal design to estimate* $\boldsymbol{\beta}$ *depends on the parameters only through* $\gamma(m, \beta_0, \sigma^2) = me^{\beta_0 + \frac{1}{2}\sigma^2}(e^{\sigma^2} - 1)$ *as follow*

$$\det(\mathfrak{M}(\xi)) \propto \frac{p_1 p_2 p_3 q_{11} q_{21} q_{12} q_{22} q_{13} q_{23} (det(\boldsymbol{F}^*))^2}{(1 + \gamma(m, \beta_0, \sigma^2)(p_1 q_{11} q_{21} + p_2 q_{12} q_{22} + p_3 q_{13} q_{23}))}$$

where $p_3 = (1 - p_1 - p_2)$,$\boldsymbol{F}^* = \begin{pmatrix} 1 & 1 & 1 \\ ln(q_{11}) & ln(q_{12}) & ln(q_{13}) \\ ln(q_{21}) & ln(q_{22}) & ln(q_{23}) \end{pmatrix}$ *and* $q_{1j} = \exp(\beta_1 x_{1j})$, $q_{2j} = \exp(\beta_2 x_{2j})$ *for* $(j = 1, 2, 3)$.

According to Theorem (3.1), numerical methods can be used to minimize $-log(det(\mathfrak{M}(\xi)))$ in order to find D-optimal designs. The D-optimal design for some representative values of $\gamma(m, \beta_0, \sigma^2)$ have been listed in Table 1.

Table 1. Locally D-optimal design for model (3.1)

$\gamma(m, \beta_0, \sigma^2)$	p_1	p_2	q_{11}	q_{21}	q_{12}	q_{22}	q_{13}	q_{23}
0	0.3333	0.3333	1	0.1353	1	1	0.1353	1
0.5	0.3400	0.3200	1	0.1303	1	1	0.1303	1
2	0.3500	0.3000	1	0.1222	1	1	0.1222	1
5	0.3799	0.2399	1	0.1133	1	1	0.1133	1
10	0.3954	0.2079	1	0.1061	1	1	0.1061	1
50	0.4131	0.1744	1	0.0961	1	1	0.0961	1
100	0.4150	0.1700	1	0.0947	1	1	0.0947	1
1000	0.4183	0.1633	1	0.0939	1	1	0.0939	1

Regarding Theorem (2.1) we have evaluated sensitivity function, over the experimental region for the Model (3.1), and the results in Table 1 have been confirmed. We have drawn sensitivity function with respect to q_{1j} and q_{2j}, for two special values of $\gamma(m, \beta_0, \sigma^2)$ in Fig. 1.

Theorem 3.2. *Consider the model* (3.2). *In terms of the canonical standardized mean, let* $\xi = \left\{ \begin{array}{cccc} (q_{11}, q_{21}) & (q_{12}, q_{22}) & (q_{13}, q_{23}) & (q_{14}, q_{24}) \\ p_1 & p_2 & p_3 & p_4 \end{array} \right\}$ *be the design with minimal support points, the local D-optimal design to estimate* $\boldsymbol{\beta}$ *depends on the parameters only through* $\gamma(m, \beta_0, \sigma^2) = me^{\beta_0 + \frac{1}{2}\sigma^2}(e^{\sigma^2} - 1)$ *and* $z = \frac{\beta_3}{\beta_1 \beta_2}$ *as follow*

$$\det(\mathfrak{M}(\xi)) \propto \frac{\prod_{j=1}^4 p_j \prod_{j=1}^4 q_{1j} q_{2j} \exp(z(\sum_{j=1}^4 ln(q_{1j}) ln(q_{2j})))(det(\boldsymbol{F}^*))^2}{(1 + \gamma(m, \beta_0, \sigma^2)(\sum_{j=1}^4 p_j q_{1j} q_{2j} \exp(z ln(q_{1j}) ln(q_{2j}))))} \tag{3.3}$$

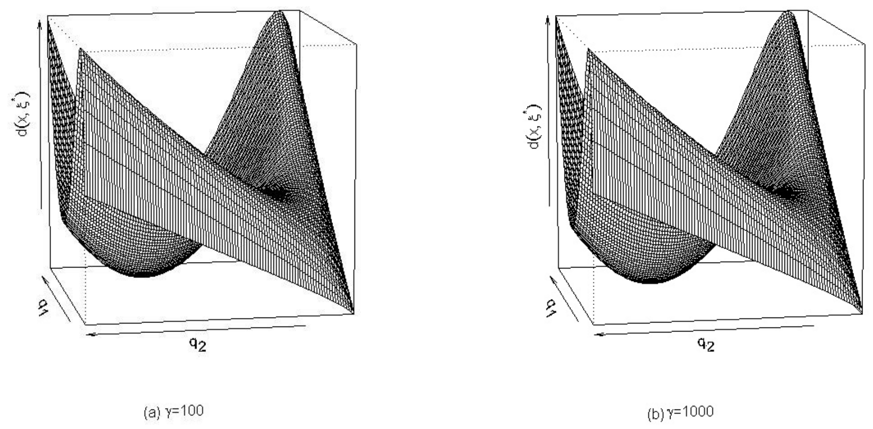

Fig. 1. Sensitivity function $d(\mathbf{x};\xi^*)$ over the unrestricted design region for model (3.1)

where $p_4 = (1 - p_1 - p_2 - p_3)$,

$$\boldsymbol{F}^* = \begin{pmatrix} 1 & 1 & 1 & 1 \\ ln(q_{11}) & ln(q_{12}) & ln(q_{13}) & ln(q_{14}) \\ ln(q_{21}) & ln(q_{22}) & ln(q_{23}) & ln(q_{24}) \\ ln(q_{11})ln(q_{21}) & ln(q_{12})ln(q_{22}) & ln(q_{13})ln(q_{23}) & ln(q_{14})ln(q_{24}) \end{pmatrix} \textit{ and } q_{1j} = \exp(\beta_1 x_{1j}), q_{2j} =$$

$\exp(\beta_2 x_{2j})$ *for* $(j = 1, 2, 3, 4)$.

Numerical methods lead us to obtain the locally D-optimal design for some representative values $\gamma(m, \beta_0, \sigma^2)$ and z which are listed in Table 2.

Table 2. D-optimal design for the model (3.2)

			$z=-\frac{1}{5}$								
$\gamma(m,\beta_0,\sigma^2)$	p_1	p_2	p_3	q_{11}	q_{21}	q_{12}	q_{22}	q_{13}	q_{23}	q_{14}	q_{24}
0	0.250	0.250	0.250	0.135	1	1	0.135	1	1	0.216	0.216
0.5	0.259	0.259	0.230	0.130	1	1	0.130	1	1	0.215	0.215
2	0.260	0.260	0.209	0.128	1	1	0.128	1	1	0.214	0.214
5	0.264	0.264	0.200	0.127	1	1	0.127	1	1	0.213	0.213
10	0.270	0.270	0.197	0.126	1	1	0.126	1	1	0.213	0.213
50	0.280	0.280	0.150	0.118	1	1	0.118	1	1	0.212	0.212
100	0.283	0.283	0.145	0.104	1	1	0.104	1	1	0.209	0.209
1000	0.290	0.290	0.137	0.100	1	1	0.100	1	1	0.206	0.206

Using Theorem (2.1), the results which have been obtained in Table 2, have been confirmed and shown in Fig. 2 for two different values of $\gamma(m, \beta_0, \sigma^2)$.

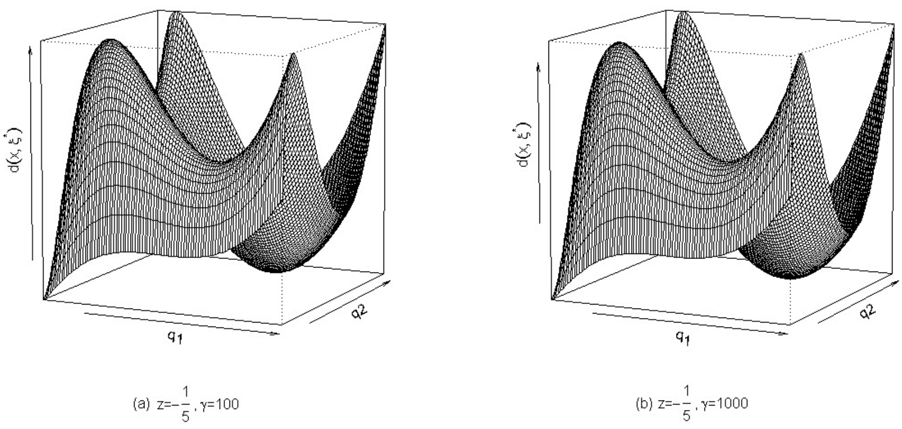

Fig. 2. Sensitivity function $d(\mathbf{x};\xi^*)$ over the design space for the Model (3.2)

4 D-optimal Designs for Multiple Poisson Regression Model with Random Slopes

We consider two cases of the multiple Poisson regression model with random slopes as following

$$iii) \qquad Y_j|b \overset{ind}{\sim} P(\lambda_j) \qquad ;\lambda_j = \lambda(\mathbf{x}_j, b) = \exp(\beta_0 + bx_{1j} + \beta_2 x_{2j}) \tag{4.1}$$

The above model is a special case of model (2.1) that b is assumed to be normally distributed with the mean β_1 and known variance σ^2 and vector of fixed effect parameters $\boldsymbol{\beta} = (\beta_0, \beta_1, \beta_2)$, variance-covariance matrix $\mathbf{\Sigma} = diag(0, \sigma^2, 0)$ and $\boldsymbol{f}^T(\mathbf{x}_j) = (1, x_{1j}, x_{2j})$.
The dispersion function, mean function and correction term could be indicated as $(\sigma(\mathbf{x}_j, \mathbf{x}_k))_{j,k=1,2,3} = \sigma^2 x_{1j}x_{1k}$, $\mu_j = \exp(\beta_0 + \beta_1 x_{1j} + \beta_2 x_{2j} + \frac{1}{2}\sigma^2 x_{1j}^2)$ and $(c(\mathbf{x}_j, \mathbf{x}_k))_{j,k=1,2,3} = \exp(\sigma^2 x_{1j}x_{1k}) - 1$, respectively.

$$iv) \qquad Y_j|b, b' \overset{ind}{\sim} P(\lambda_j) \qquad ;\lambda_j = \lambda(\mathbf{x}_j, b, b') = \exp(\beta_0 + bx_{1j} + b'x_{2j}) \tag{4.2}$$

This model is also a special case of general model (2.1) that b and b' are assumed to be normally distributed with the mean β_1 andβ_2 respectively. We also suppose that b and b' have the same known variance σ^2. Based on model (2.1), we have $\boldsymbol{\beta} = (\beta_0, \beta_1, \beta_2)$, $\mathbf{\Sigma} = diag(0, \sigma^2, \sigma^2)$ and $\boldsymbol{f}^T(\mathbf{x}_j) = (1, x_{1j}, x_{2j})$. Here $(\sigma(\mathbf{x}_j, \mathbf{x}_k))_{j,k=1,2,3} = \sigma^2(x_{1j}x_{1k} + x_{2j}x_{2k})$, $\mu_j = \exp(\beta_0 + \beta_1 x_{1j} + \beta_2 x_{2j} + \frac{1}{2}\sigma^2(x_{1j}^2 + x_{2j}^2)$ and $(c(\mathbf{x}_j, \mathbf{x}_k))_{j,k=1,2,3} = \exp(\sigma^2(x_{1j}x_{1k} + x_{2j}x_{2k})) - 1$ stand for dispersion function, mean function and correction term respectively.

We suppose that the design regions are also a non-negative subset of real numbers.

Considering $\mu_0 = \exp(\beta_0)$ using the same notation in the previous section, the mean functions, μ_j, can be represented as $\mu_j = q_{1j}q_{2j}\exp(\frac{1}{2}\sigma^2(\frac{ln(q_{1j})}{\beta_1})^2)\mu_0$ and $\mu_j = q_{1j}q_{2j}\exp(\frac{1}{2}\sigma^2((\frac{ln(q_{1j})}{\beta_1})^2 + (\frac{ln(q_{2j})}{\beta_2})^2)\mu_0$ for model (4.1) and model (4.2), respectively.

Theorem 4.1. *Consider model* (4.1) *and Model*(4.2). *Based on the canonical standardized mean, let* $\xi = \left\{ \begin{array}{ccc} (q_{11}, q_{21}) & (q_{12}, q_{22}) & (q_{13}, q_{23}) \\ p_1 & p_2 & p_3 \end{array} \right\}$ *be the design with minimal support points, and determinant* *of quasi-information matrix will be as follow*

$$\det(\mathfrak{M}(\xi)) \propto \frac{m^3 p_1 p_2 p_3 \mu_1 \mu_2 \mu_3 (det(\boldsymbol{F}^*))^2}{(1 + f(c_{ij}, p_j, m, \mu_j))}$$

where
$\boldsymbol{F}^* = \begin{pmatrix} 1 & 1 & 1 \\ ln(q_{11}) & ln(q_{12}) & ln(q_{13}) \\ ln(q_{21}) & ln(q_{22}) & ln(q_{23}) \end{pmatrix}$ *with* $q_{1j} = \exp(\beta_1 x_{1j})$ *and* $q_{2j} = \exp(\beta_2 x_{2j}) for (j = 1, 2, 3)$. *Also*

$$\begin{aligned} f(c_{ij}, p_i, m, \mu_j) &= mp_1c_{11}\mu_1 + mp_2c_{22}\mu_2 + mp_3c_{33}\mu_3 - m^2p_1p_2c_{12}^2\mu_1\mu_2 \\ &- m^2p_1p_3c_{13}^2\mu_1\mu_3 - m^2p_2p_3c_{23}^2\mu_2\mu_3 + m^2p_1p_2c_{11}c_{22}\mu_1\mu_2 + m^2p_1p_2c_{11}c_{33}\mu_1\mu_3 \\ &+ m^2p_2p_3c_{22}c_{33}\mu_2\mu_3 - m^3p_1p_2p_3c_{11}c_{23}^2\mu_1\mu_2\mu_3 - m^3p_1p_2p_3c_{13}^2c_{22}\mu_1\mu_2\mu_3 \\ &- m^3p_1p_2p_3c_{12}^2c_{33}\mu_1\mu_2\mu_3 + 2m^3p_1p_2p_3c_{12}c_{13}c_{23}\mu_1\mu_2\mu_3 \\ &+ 2m^3p_1p_2p_3c_{11}c_{22}c_{33}\mu_1\mu_2\mu_3 \end{aligned}$$

is a known function. Here c_{ij} *is the (i,j)th element matrix* $\boldsymbol{C}_\xi$ *which is defined as*
$\boldsymbol{C}_\xi = \begin{pmatrix} e^{\sigma^2 x_{11}^2} - 1 & e^{\sigma^2 x_{11}x_{21}} - 1 & e^{\sigma^2 x_{11}x_{31}} - 1 \\ e^{\sigma^2 x_{11}x_{21}} - 1 & e^{\sigma^2 x_{21}^2} - 1 & e^{\sigma^2 x_{21}x_{31}} - 1 \\ e^{\sigma^2 x_{31}x_{11}} - 1 & e^{\sigma^2 x_{31}x_{21}} - 1 & e^{\sigma^2 x_{31}^2} - 1 \end{pmatrix}$ *and*

$$\boldsymbol{C}_\xi = \begin{pmatrix} e^{\sigma^2(x_{11}^2+x_{21}^2)} - 1 & e^{\sigma^2(x_{11}x_{12}+x_{21}x_{22})} - 1 & e^{\sigma^2(x_{11}x_{13}+x_{21}x_{23})} - 1 \\ e^{\sigma^2(x_{11}x_{12}+x_{21}x_{22})} - 1 & e^{\sigma^2(x_{12}^2+x_{22}^2)} - 1 & e^{\sigma^2(x_{12}x_{13}+x_{22}x_{23})} - 1 \\ e^{\sigma^2(x_{13}x_{11}+x_{23}x_{13})} - 1 & e^{\sigma^2(x_{13}x_{23}+x_{23}x_{22})} - 1 & e^{\sigma^2(x_{13}^2+x_{23}^2)} - 1 \end{pmatrix}$$

for different models (4.1) *and* (4.2), *respectively* .

Using the above theorem, numerical methods can be used to minimize $-log(det(\mathfrak{M}(\xi)))$ in order to find D-optimal design for models (4.1) and (4.2), respectively. The locally D-optimal designs for some representative values of $\beta_0, \beta_1, \beta_2$ and m are listed in Tables 3 and 4 for models (4.1) and (4.2), respectively. The results have been evaluated by theorem (2.1).

Table 3. D-optimal design for model (4.1)

$m = 200$		$\beta_0 = -2$		$\beta_1 = -5$		$\beta_2 = -5$		
σ	p_1	p_2	q_{11}	q_{21}	q_{12}	q_{22}	q_{13}	q_{23}
0	0.3333	0.3333	0.1353	1	1	0.1353	1	1
0.5	0.3226	0.3385	0.1300	1	1	0.1353	1	1
1	0.2930	0.3532	0.1170	1	1	0.1353	1	1
1.5	0.2655	0.3767	0.1168	1	1	0.1353	1	1
2	0.2059	0.3967	0.1367	1	1	0.1353	1	1
2.5	0.1867	0.4066	0.1938	1	1	0.1353	1	1
3	0.1735	0.4151	0.2528	1	1	0.1353	1	1
4	0.1411	0.4295	0.3435	1	1	0.1353	1	1
5	0.1271	0.4541	0.4244	1	1	0.1353	1	1

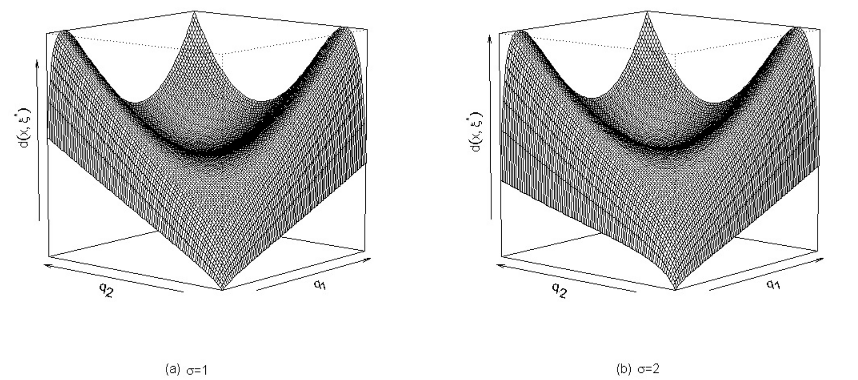

Fig. 3. Sensitivity function $d(\mathbf{x};\xi^*)$ over the design space for model (4.1)

Table 4. D-optimal design for model (4.2)

$m = 200$		$\beta_0 = -2$		$\beta_1 = -5$		$\beta_2 = -5$		
σ	p_1	p_2	q_{11}	q_{21}	q_{12}	q_{22}	q_{13}	q_{23}
0	0.3333	0.3333	0.1353	1	1	0.1353	1	1
0.5	0.3277	0.3277	0.1299	1	1	0.1299	1	1
1	0.3104	0.3104	0.1170	1	1	0.1170	1	1
1.5	0.2655	0.2655	0.1168	1	1	0.1168	1	1
2	0.2462	0.2462	0.1474	1	1	0.1474	1	1
2.5	0.2219	0.2219	0.2024	1	1	0.2024	1	1
3	0.2056	0.2056	0.2528	1	1	0.2528	1	1
4	0.1872	0.1872	0.3668	1	1	0.3668	1	1
5	0.1765	0.1765	0.4501	1	1	0.4501	1	1

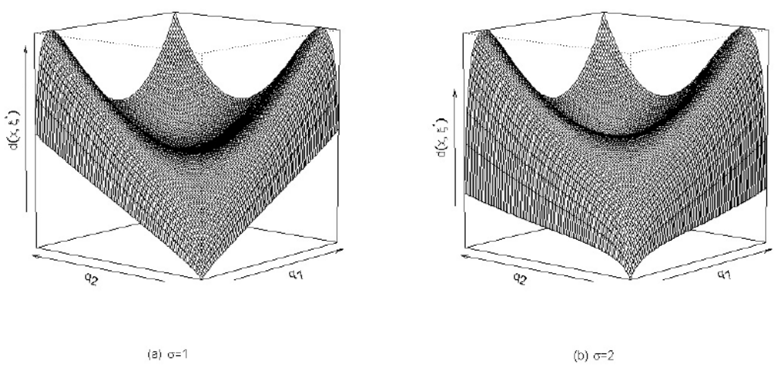

Fig. 4. Sensitivity function $d(\mathbf{x};\xi^*)$ over the design space for model (4.2)

Figs. 3 and 4 have been drawn for two cases in each model.

5 Conclusions

This paper aims at providing an extension and an application for the results in Niaparast and Schwabe (2013). We obtain some new theoretical results to find D-optimal designs for the quasi-likelihood estimators of parameters. The numerical results indicated the impact of the random coefficients on the D-optimal designs for some particular cases of multiple Poisson random coefficient regression model. Also the obtained results indicate that the D-optimal designs for different values of parameters are completely different from the standard experimental designs with the same proportion of design points.

For Poisson regression model, the explicit form for Information matrix cannot be obtained, hence, we applied a qusie-likelihood approach.

The point, which has not been considered here, is the efficiency of the D-optimal designs for quasi-likelihood estimation of the fixed effects parameters versus D-optimal designs for likelihood estimation of the same parameters.

A Bayesian approach could be applied as an alternative method for locally D-optimal designs.

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Competing Interests

Authors have declared that no competing interests exist.

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Appendix

Proof of Theorem (3.1)

Regarding the Equation (2.2), for the design $\xi = \left\{ \begin{array}{ccc} (q_{11}, q_{21}) & (q_{12}, q_{22}) & (q_{13}, q_{23}) \\ p_1 & p_2 & p_3 \end{array} \right\}$ the quasi-information matrix for $\boldsymbol{\beta}$ is given as follow

$$\mathfrak{M}(\xi) \quad = \quad \boldsymbol{F}_\xi^T(\boldsymbol{A}_\xi^{-1} + \boldsymbol{C}_\xi)^{-1}\boldsymbol{F}_\xi \tag{5.1}$$

where $\boldsymbol{F}_\xi^T = \begin{pmatrix} 1 & 1 & 1 \\ x_{11} & x_{12} & x_{13} \\ x_{21} & x_{22} & x_{23} \end{pmatrix}$, $\boldsymbol{A}_\xi = \begin{pmatrix} n_1\mu_1 & 0 & 0 \\ 0 & n_2\mu_2 & 0 \\ 0 & 0 & n_3\mu_3 \end{pmatrix}$ and $\boldsymbol{C}_\xi = (e^{\sigma^2} - 1)\begin{pmatrix} 1 & 1 & 1 \end{pmatrix}\begin{pmatrix} 1 \\ 1 \\ 1 \end{pmatrix}$.

For model (3.1) , we have:

$$\mu_0 = e^{\beta_0 + \frac{1}{2}\sigma^2} \qquad q_{1j} = e^{\beta_1 x_{1j}} \qquad q_{2j} = e^{\beta_2 x_{2j}}$$

then we can represent μ_j as follow

$$\mu_j = \exp(\beta_0 + \beta_1 x_{1j} + \beta_2 x_{2j} + \frac{1}{2}\sigma^2) = q_{1j}q_{2j}\mu_0$$

If we combine these expressions and replace in (5.1), after using some matrix algebra and a straightforward calculation the result follows.

Proof of Theorem (3.2)

We consider the four points design $\xi = \left\{ \begin{array}{cccc} (q_{11}, q_{21}) & (q_{12}, q_{22}) & (q_{13}, q_{23}) & (q_{14}, q_{24}) \\ p_1 & p_2 & p_3 & p_4 \end{array} \right\}$. For model (4.2), the design matrix, the diagonal matrix of the expectations and the matrix of the correction terms are:

$\boldsymbol{F}_\xi = \begin{pmatrix} 1 & 1 & 1 & 1 \\ x_{11} & x_{12} & x_{13} & x_{14} \\ x_{21} & x_{22} & x_{23} & x_{24} \\ x_{11}x_{21} & x_{12}x_{22} & x_{13}x_{23} & x_{14}x_{24} \end{pmatrix}$, $\boldsymbol{A}_\xi = \begin{pmatrix} n_1\mu_1 & 0 & 0 & 0 \\ 0 & n_2\mu_2 & 0 & 0 \\ 0 & 0 & n_3\mu_3 & 0 \\ 0 & 0 & 0 & n_4\mu_4 \end{pmatrix}$ and $\boldsymbol{C}_{\boldsymbol{\xi}} = (e^{\sigma^2} - 1)\begin{pmatrix} 1 & 1 & 1 & 1 \end{pmatrix}\begin{pmatrix} 1 \\ 1 \\ 1 \\ 1 \end{pmatrix}$ respectively. The mean function μ_j can be represented as

$$\mu_j = \exp(\beta_0 + \beta_1 x_{1j} + \beta_2 x_{2j} + \beta_3 x_{1j}x_{2j} + \frac{1}{2}\sigma^2) = q_{1j}.q_{2j}.\exp(z.ln(q_{1j}).ln(q_{2j})).\mu_0$$

where $\mu_0 = e^{\beta_0 + \frac{1}{2}\sigma^2}$, $q_{1j} = e^{\beta_1 x_{1j}}$, $q_{2j} = e^{\beta_2 x_{2j}}$ and $z = \frac{\beta_3}{\beta_1\beta_2}$. By replacing these expressions in the quasi-information matrix, relation (5.1), and after using some matrix algebra and a straightforward calculation the result follows.

Proof of Theorem (4.1)

Let $m_j = mp_j$. From Equation (2.2), for the design $\xi = \left\{ \begin{array}{ccc} (q_{11}, q_{21}) & (q_{12}, q_{22}) & (q_{13}, q_{23}) \\ p_1 & p_2 & p_3 \end{array} \right\}$, the quasi-information matrix is given as follow

$$\mathfrak{M}(\xi) \quad = \quad \boldsymbol{F}^T(\xi)(\boldsymbol{A}^{-1}(\xi) + \boldsymbol{C}_{\boldsymbol{\xi}})^{-1}\boldsymbol{F}(\xi) \tag{5.2}$$

with $\boldsymbol{F}^T(\xi) = \begin{pmatrix} 1 & 1 & 1 \\ x_{11} & x_{12} & x_{13} \\ x_{21} & x_{22} & x_{23} \end{pmatrix}$ and $\boldsymbol{A} = \begin{pmatrix} n_1\mu_1 & 0 & 0 \\ 0 & n_2\mu_2 & 0 \\ 0 & 0 & n_3\mu_3 \end{pmatrix}$. Here $\mu_j = \exp(\beta_0 + \beta_1 x_{1j} + \beta_2 x_{2j} + \frac{1}{2}\sigma^2 x_{1j}^2) = q_{1j}q_{2j}\exp(\frac{1}{2}\sigma^2(\frac{ln(q_{1j})}{\beta_1})^2)\mu_0$ for $(j = 1, 2, 3)$ and $\mu_j = \exp(\beta_0 + \beta_1 x_{1j} +$

$\beta_2 x_{2j} + \frac{1}{2}\sigma^2(x_{1j}^2 + x_{2j}^2) = q_{1j}q_{2j}\exp(\frac{1}{2}\sigma^2(\frac{ln(q_{1j})}{\beta_1})^2 + \frac{ln(q_{2j})}{\beta_2})^2)\mu_0$ for $(j = 1, 2, 3)$ stand for Model (4.1) and Model (4.2) respectively, where $\mu_0 = e^{\beta_0}$, $q_{1j} = e^{\beta_1 x_{1j}}$ and $q_{2j} = e^{\beta_2 x_{2j}}$ for $(j = 1, 2, 3)$. Also $\mathbf{C}_\xi$ can be represented as $\mathbf{C}_\xi = \begin{pmatrix} e^{\sigma^2 x_{11}^2} - 1 & e^{\sigma^2 x_{11}x_{12}} - 1 & e^{\sigma^2 x_{11}x_{13}} - 1 \\ e^{\sigma^2 x_{11}x_{12}} - 1 & e^{\sigma^2 x_{12}^2} - 1 & e^{\sigma^2 x_{12}x_{13}} - 1 \\ e^{\sigma^2 x_{13}x_{11}} - 1 & e^{\sigma^2 x_{13}x_{12}} - 1 & e^{\sigma^2 x_{13}^2} - 1 \end{pmatrix}$ and $\boldsymbol{C}_\xi = \begin{pmatrix} e^{\sigma^2 (x_{11}^2 + x_{21})^2} - 1 & e^{\sigma^2 (x_{11}x_{12} + x_{21}x_{22})} - 1 & e^{\sigma^2 (x_{11}x_{13} + x_{21}x_{23})} - 1 \\ e^{\sigma^2 (x_{11}x_{12} + x_{12}x_{22})} - 1 & e^{\sigma^2 (x_{12}^2 + x_{22}^2)} - 1 & e^{\sigma^2 (x_{12}x_{13} + x_{22}x_{23})} - 1 \\ e^{\sigma^2 (x_{13}x_{11} + x_{23}x_{13})} - 1 & e^{\sigma^2 (x_{13}x_{23} + x_{23}x_{22})} - 1 & e^{\sigma^2 (x_{13}^2 + x_{23}^2)} - 1 \end{pmatrix}$ for models (4.1) and (4.2), respectively. The result will be obtained after replacing the items in quasi-information (5.2) with the above corresponding expressions and a straightforward calculation.

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