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A Class of Exponentiated Regression Model for Non Negative Censored Data with an Application to Antibody Response to Vaccine

Guillermo Martínez-Flórez [1,†], Sandra Vergara-Cardozo [2,†] and Roger Tovar-Falón [1,*,†]

1 Departamento de Matemáticas y Estadística, Facultad de Ciencias Básicas, Universidad de Córdoba, Montería 230027, Colombia; guillermomartinez@correo.unicordoba.edu.co
2 Departamento de Estadística, Facultad de Ciencias, Universidad Nacional de Colombia, Bogotá 111321, Colombia; svergarac@unal.edu.co
* Correspondence: rjtovar@correo.unicordoba.edu.co
† These authors contributed equally to this work.

Abstract: In this paper, an asymmetric regression model for censored non-negative data based on the centred exponentiated log-skew-normal and Bernoulli distributions mixture is introduced. To connect the discrete part with the continuous distribution, the logit link function is used. The parameters of the model are estimated by using the likelihood maximum method. The score function and the information matrix are shown in detail. Antibody data from a study of the measles vaccine are used to illustrate applicability of the proposed model, and it was found the best fit to the data with respect to an others models used in the literature.

Keywords: centred exponentiated log-skew-normal distribution; censored data; asymmetry two-part model

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1. Introduction

Statistical models for dealing with the issue of random variables with limited or censored responses have been approached by different authors, standing out among others, the censored normal (CN) model, widely known in the literature as the Tobit model, Tobin [1]. The CN or normal Tobit (NT) model is defined from the considering the random variable $y_i = \max\{y_i^*, 0\}$, with $y_i^* = \boldsymbol{x}_i^\top \boldsymbol{\beta} + \varepsilon_i$, for $i = 1, 2, \ldots, n$, where $\boldsymbol{\beta} = (\beta_1, \beta_2, \ldots, \beta_p)^\top$ is a $p \times 1$ unknown parameter vector, $\boldsymbol{x}_i = (x_{1i}, x_{2i}, \ldots, x_{pi})^\top$ is a $p \times 1$ vector of known independent variables, and the error term $\varepsilon_i \sim \mathrm{N}(0, \sigma^2)$, $i = 1, \ldots, n$. This can be written as:

$$y_i = \begin{cases} \boldsymbol{x}_i^\top \boldsymbol{\beta} + \varepsilon_i, & \text{if } \boldsymbol{x}_i^\top \boldsymbol{\beta} + \varepsilon_i > 0, \\ 0, & \text{otherwise} \end{cases} \tag{1}$$

The model (1) has been used in applications in various areas of knowledge, often in situations with excess of zeros in the censoring value; however, the probability of censoring is not well estimated by the Tobit model since the tails of the data distribution are heavier than the normal distribution and other assumptions of the error distribution are not satisfied. A similar situation is presented in the case of data with non-negative support, where usually log-normal Tobit model (LNT) is used.

In some situations, the degrees of asymmetry and kurtosis of the distribution of the errors in the model can not be captured by the normal or the log-normal models. In this case it is not advisable to fit the CN or censored log-normal (CLN) models. To consider more flexible models, such as the skew-normal (SN) model by Azzalini [2] or the power-normal (PN) model of Durrans [3] is another solution. In the case of non-negative data, it can be considered the log-skew-normal alpha-power model by Martínez-Flórez et al. [4] or the log-power-normal model of Martínez-Flórez et al. [5].

The Tobit model extension for censored data with high degree of kurtosis was proposed by Arellano-Valle et al. [6], while the case of censored data with high or low degree of asymmetry was studied by Martínez-Flórez et al. [7], the latter is known as the Tobit power-normal model (TPN). When the censored part does not fit well with the Tobit model, mixture of distributions can be used, in this situation as in the usual censored distribution, the mean and the variance of the response variable is associated with the linear predictor. In addition, the proportion of censored data can be explained by using the binomial model with the logit or probit link function. This type of model has been used in many areas of knowledge such as economics, biology, agriculture, medicine, among others. Cragg [8], Moulton and Halsey [9,10] and Chai and Bailey [11], for example, use a mixture of distribution (which is denoted by "/ ") between a Bernoulli distribution and other continuous distribution.

The probability density function (PDF) of the random variable Y_i proposed by Cragg [8], which is often called "two-part model", is given by

$$g(y_i) = p_i I_i + (1 - p_i) f(y_i)(1 - I_i), \tag{2}$$

where p_i is the probability that determines the relative contribution made by the point mass distribution to the overall mixture distribution, f is a density function with positive support and I_i is an indicator variable given by $I_i = 0$ if $y_i > T$ and $I_i = 1$ if $y_i \leq T$. The model (2) is more informative than the Tobit model because the two components are determined by different stochastic processes, see Chai and Bailey [11].

The two-part model of Cragg [8] was generalized by Moulton and Halsey [9], by introducing a new model in which the response limit can result from a censorship interval of the PDF f, that is, a zero point can result in mass or may be a value of f in the censorship interval $(0, T)$, where T is constant. Specifically, the model proposed by [9] is represented by the PDF given by

$$g_F(y_i) = \left[p_i + (1 - p_i)F(T)\right] I_i + (1 - p_i) f(y_i)(1 - I_i), \tag{3}$$

where $F(\cdot)$ is the cumulative distribution function (CDF) associated to the PDF $f(\cdot)$. In particular, a Bernoulli variable can be used with the logit or probit link functions, see Cragg [8]. Moulton and Halsey [9] consider asymmetric log-normal and log-gamma data, while the log-skew-normal model (LSN) and log-power-normal model (LPN) with limited response are studied by Chai and Bailey [11] and Martínez-Flórez et al. [5], respectively.

2. Models for Asymmetric Data

Important proposals to modelling data with high/low degree of asymmetry and/or kurtosis in relation to the normal model have arisen in recent decades. Two of these proposals widely discussed in the statistical literature are the SN model of Azzalini [2] and PN model by Durrans [3]. The SN model, with asymmetry parameter λ, which is denoted by $Z \sim \mathrm{SN}(\lambda)$ has PDF given by

$$\phi_{\mathrm{SN}}(z; \lambda) = 2\phi(z)\Phi(\lambda z), \quad z \in \mathbb{R}, \tag{4}$$

where $\lambda \in \mathbb{R}$ and, $\phi(\cdot)$ and $\Phi(\cdot)$ represent the PDF and CDF of the standard normal distribution, respectively. The λ parameter controls the asymmetry in the model. The associated CDF to the PDF in (4) is given by

$$\Phi_{\mathrm{SN}}(z; \lambda) = \int_{-\infty}^{z} \phi_{\mathrm{SN}}(t; \lambda)dt = \Phi(z) - 2T(z, \lambda), \quad z \in \mathbb{R}, \tag{5}$$

where $T(\cdot, \lambda)$ is the Owen's function, see [12]. The PN model is denoted by $Z \sim \mathrm{PN}(\alpha)$ and has the PDF given by

$$f_{\mathrm{PN}}(z; \alpha) = \alpha\phi(z)\{\Phi(z)\}^{\alpha - 1}, \quad z \in \mathbb{R}, \tag{6}$$

where $\alpha \in \mathbb{R}^+$ is a shape parameter. The model (6) was introduced by Durrans [3] and it has had multiple applications in the situations where the data distribution presents high or low asymmetry and/or kurtosis, which can not be fitted by the normal distribution.

The extension to the location and scale version of the SN model is obtained by applying the transformation $Y = \xi + \eta Z$, where $\xi \in \mathbb{R}$ is a location parameter, $\eta > 0$ is a scale parameter, and $Z \sim \mathrm{SN}(\lambda)$. This is denoted by $Y \sim \mathrm{SN}(\xi, \eta, \lambda)$. In a similar way, the extension of the location and scale version of the PN model is obtained, which is denoted by $Y \sim \mathrm{PN}(\xi, \eta, \alpha)$.

A special feature of the SN and PN models is that both containing the normal model as special case when $\lambda = 0$ and $\alpha = 1$, respectively, highlighting that the SN model has a range of asymmetry higher than the PN model, and at the same time, the PN model has a higher range of kurtosis than the SN model, see Pewsey et al. [13]. Therefore, it is natural to expect that respective extensions for positive data have similar characteristics. Martínez-Flórez et al. [5] studied the extension of the PN model to the case of positive data and they denoted it the log-power-normal (LPN) model, while the extension of the SN distribution for positive data was studied by Azzalini et al. [14], which is denominated the log-skew-normal (LSN) model.

The main difficult with the SN model, which does not present the PN model is that, for $\lambda = 0$ the Fisher information matrix for the parameters vector (ξ, η, λ) is singular, see Azzalini [2]. Hence, the regularity conditions are not satisfied in general and the usual $\sqrt{n}$-property for the maximum likelihood estimator is kept only for $\lambda \neq 0$. The information matrix problem for the case $\lambda = 0$ has been addressed by using the methodology proposed by Rotnitzky et al. [15], who devised an iterative algorithm that under certain conditions leads to a non-singular information matrix for $\lambda = 0$.

The singularity of the Fisher information matrix has been found in multiple extensions of SN model, such as the LSN model, the skew-exponential power distribution, DiCiccio and Monti [16] and the skew-flexible-normal model, Gómez et al. [17], to name some of these cases. The log-skew-normal alpha-power (LSNAP) distribution is an extension of LPN model, which is obtained by replacing in the LPN model, the PDF and the CDF of the normal distribution for the PDF and the CDF of the SN distribution. This proposal is based on the non-singularity property of the information matrix of the PN model, Pewsey et al. [13], and the flexibility in terms of asymmetry in the SN model, Azzalini [2]. So, it is natural that a new model based on these two distributions can fit the distributions with higher or lower asymmetry than the fitted by the LSN model and/or higher or lower kurtosis than the fitted by the LPN model.

The PDF of the location and scale version of a random variable with LSNAP distribution is given by

$$f_{\mathrm{LSNAP}}(y; \xi, \eta, \lambda, \alpha) = \frac{\alpha}{\eta y} \phi_{\mathrm{SN}}(z; \lambda) \left[\Phi_{\mathrm{SN}}(z; \lambda)\right]^{\alpha - 1}, \quad y \in \mathbb{R}^+, \tag{7}$$

where $z = (\log(y) - \xi)/\eta$, with $\xi \in \mathbb{R}$ being the location parameter and, $\eta > 0$ the scale parameter. The functions $\phi_{\mathrm{SN}}(\cdot)$ and $\Phi_{\mathrm{SN}}(\cdot)$ are the PDF and CDF of the SN distribution given in (4) and (5), respectively. The LSPN distribution is represented by the notation $Y \sim \mathrm{LSNAP}(\xi, \eta, \lambda, \alpha)$. One can see that, the model in (7) contains as special cases, the log-normal (LN) model when $\lambda = 0$ and $\alpha = 1$; the LSN model when $\alpha = 1$, and the LPN model when $\lambda = 0$. Thus, the LSPN model is more flexible in terms of asymmetry and kurtosis than the LN, LSN and LPN models.

The Centred Parametrization of the Skew-Normal Model

Facing the problem of the singularity of the information matrix of the SN model and the consequences in the estimation process of the parameters when $\lambda = 0$, Arellano-Valle and Azzalini [18] proposed an alternative parametrization to the SN model of Azzalini [2]. This new parametrization starts from the definition of the variable

$$Y = \mu + \sigma \frac{Z - \mathbb{E}(Z)}{\sqrt{\mathrm{Var}(Z)}},$$

where $\mu \in \mathbb{R}$ and $\sigma \in \mathbb{R}^+$ are parameters of the random variable Y, and $Z \sim \mathrm{SN}(\lambda)$. This representation is called centred parametrization, since $\mathbb{E}(Y) = \mu$ and $\mathrm{Var}(Y) = \sigma^2$. The centred parametrization of the SN model is denoted by $Y \sim \mathrm{SN}_c(\mu, \sigma, \gamma_1)$, where the parameters $\mu \in \mathbb{R}$, $\sigma \in \mathbb{R}^+$ and $\gamma_1 \in (-0.9953, 0.9953)$, represent the mean, standard deviation and coefficient of asymmetry of Y, respectively. One can see that, if $Z \sim \mathrm{SN}(\lambda)$, then $\mathbb{E}(Z) = b\delta$ and $\mathrm{Var}(Z) = 1 - (b\delta)^2$, where $b = \sqrt{2/\pi}$ and $\delta = \lambda/\sqrt{1+\lambda^2}$.

Thus, we have that the random variable Y is allowed to be written in the form $Y = \lambda_1 + \lambda_2 Z$, which follows a SN distribution of location and scale version denoted by $\mathrm{SN}(\lambda_1, \lambda_2, \lambda)$, where

$$\lambda_1 = \mu - c\sigma\gamma_1^{1/3}, \quad \lambda_2 = \sigma\sqrt{1 + c^2\gamma_1^{2/3}} \quad \text{and} \quad \lambda = \frac{c\gamma_1^{1/3}}{\sqrt{b^2 + c^2(b^2-1)\gamma_1^{2/3}}} \tag{8}$$

with $c = \{2/(4-\pi)\}^{1/3}$.

Under the centred parametrization of the SN model, the Fisher information matrix can be written as $\boldsymbol{I}_{\gamma_1} = \boldsymbol{D}\boldsymbol{I}_\lambda\boldsymbol{D}$, where $\boldsymbol{D}$ is a matrix representing the derivative of the parameters λ_1, λ_2 and λ of the standard representation, regarding to the new parameters μ, σ and γ_1. In addition, when $\lambda \to 0$, the information matrix converges to the diagonal matrix $\boldsymbol{\Sigma}_c = \mathrm{diag}(\sigma^2, \sigma^2/2, 6)$, which guarantees the existence and uniqueness of the maximum likelihood estimator (MLE) of the parameters λ_1 and λ_2, for each fixed value of λ.

Given the properties of the LSN and LPN models, the Bernoulli/log-skew-normal (BLSN) and the Bernoulli/log-power-normal (BLPN) mixture models are alternatives to the Bernoulli/log-normal (BLN) model for the case of positive data when the distribution of the continuous part presents greater or lower asymmetry and/or kurtosis than the LN model. Thus, the BLSN and BLPN mixture models are more flexible than the BLN mixture model. Details of the inferential properties of the MLE for the BSLN mixture model when $\lambda = 0$ are not presented by Chai and Bailey [11] , since it is expected that the same difficulties are arisen in relation to the continuous part that is fitted through the LSN model.

In this paper, we introduced a new model to fit asymmetric data, more flexible than LN, LSN and LPN models, and with non-singular Fisher information matrix. This model is obtained by replacing in the LPN model, the normal distribution by the $\mathrm{SN}_c(\mu, \sigma, \gamma_1)$ distribution. From the introduced model, a new regression model for censored data is proposed, which is a mixture of the proposed asymmetric model and a random variable with logit link function. The new model is more flexible in terms of asymmetry and kurtosis than the proposed by Moulton and Halsey [9], Chai and Bailey [11] and Martínez-Flórez et al. [5]. Data from a safety and immunogenicity study of measles vaccine conducted in Haiti during 1987–1990, see Job et al. [19] are used as an illustration. Here, the goal of the study was to demonstrate that the higher titer vaccines could effectively immunize infants as young as 12 months of age.

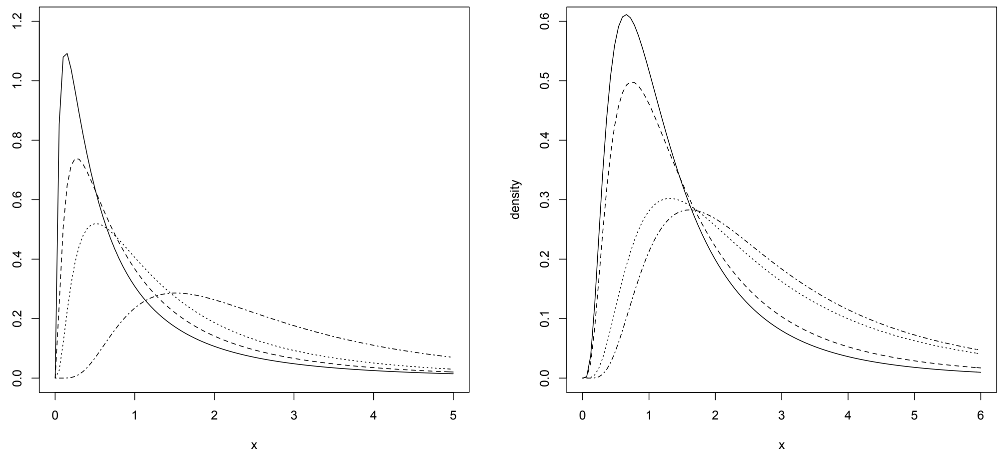
The rest of the paper is organized as follows. In Section 3, the centred exponentiated log-skew-normal distribution for censored data is presented. A small simulation study to evaluate the asymptotic properties of the parameter estimators is presented. In Section 4, the Bernoulli/centred log-skew-normal alpha-power mixture model is introduced. The inference process is carried out by using the maximum likelihood method. In Section 5, an application with measles vaccine data is presented to illustrate the proposed model.

3. The Centred Exponentiated Log-Skew-Normal Family of Distribution for Censored Data

Based on the flexibility and the non-singularity of the Fisher information matrix of the SN_c model, the LPN model is extended to the case of the SN_c model. This extension is denominated the centred exponentiated log-skew-normal (ELSN_c) distribution. The PDF of the ELSN_c distribution, with parameters μ, σ, γ_1 and α is given by

$$f_{\mathrm{ELSN}_c}(y;\mu,\sigma,\gamma_1,\alpha) = \frac{\alpha}{\lambda_2 y}\phi_{\mathrm{SN}}(z;\lambda)\{\Phi_{\mathrm{SN}}(z;\lambda)\}^{\alpha-1}, \quad \in \mathbb{R}^+ \tag{9}$$

where $z = \frac{\log(y)-\lambda_1}{\lambda_2}$ and λ_1, λ_2 and λ defined as in (8). This model is denoted by $\mathrm{ELSN}_c(\mu,\sigma,\gamma_1,\alpha)$. It is important to note that $\mathrm{ELSN}_c(\mu,\sigma,\gamma_1,\alpha) \equiv \mathrm{LSNAP}(\lambda_1,\lambda_2,\lambda,\alpha)$ with λ_1, λ_2 and λ defined in (8), that is, the ELSN_c model can be assumed as a reparametrization of LSNAP model, which corrects the problem of singularity in the Fisher information matrix. In addition, if $\gamma_1 = 0$, the $\mathrm{LPN}(\mu,\sigma,\alpha)$ model is obtained and, when $\alpha = 1$, the centred log-skew-normal model follows, which is denoted by $\mathrm{LSN}_c(\mu,\sigma,\gamma_1)$. Some forms of the PDF of the ELSN_c distribution are presented in the Figure 1. One can shown that, LSN_c model has non-singular information matrix. Finally, if $\gamma_1 = 0$ and $\alpha = 1$, the log-normal model is obtained, $\mathrm{LN}(\mu,\sigma^2)$. This shows that the ELSN_c model is more flexible in terms the asymmetry and kurtosis than LN, LSN and LPN models.



(**a**) (**b**)

Figure 1. (**a**) $\mathrm{ELSN}_c(0,1,0.75,\alpha)$ for $\alpha = 0.35$ (solid line), $\alpha = 0.5$ (dashed line), $\alpha = 0.75$ (dotted line), $\alpha = 2$ (dotted–dashed line), (**b**) $\mathrm{ELSN}_c(0,1,\gamma_1,2)$ with $\gamma_1 = -0.50$ (solid line), $\gamma_1 = -0.25$ (dashed line), $\gamma_1 = 0.50$ (dotted line), $\gamma_1 = 0.90$ (dotted–dashed line).

The importance of the proposed extension is that the information matrix of the model is non-singular, since for the parameter vector $\boldsymbol{\theta} = (\mu,\sigma,\gamma_1,\alpha)^\top$, the information matrix is given by $\boldsymbol{I_\theta} = \boldsymbol{D}\boldsymbol{I}_{\lambda,\alpha}\boldsymbol{D}$, where $\boldsymbol{I}_{\lambda,\alpha}$ is the information matrix of the model (7) given in Martínez-Flórez et al. [5] with $z = (\log(y) - \xi)/\eta$, and

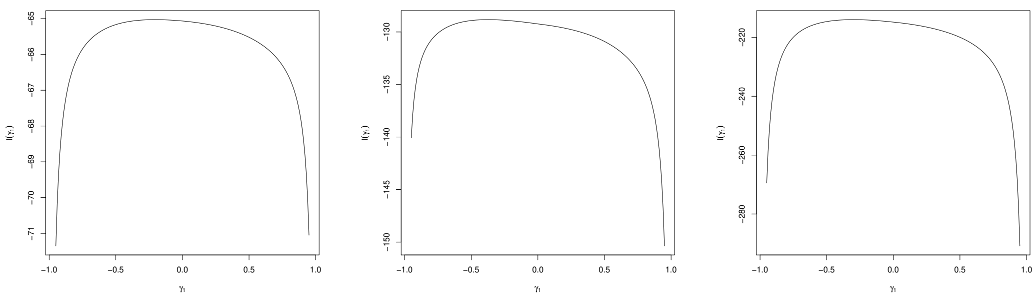
$$\boldsymbol{D} = \begin{pmatrix} 1 & -c\gamma_1^{1/3} & -\frac{1}{3}c\sigma\gamma_1^{-2/3} & 0 \\ 0 & \sqrt{1+c^2\gamma_1^{2/3}} & \frac{c^2\sigma\gamma_1^{-1/3}}{3\sqrt{1+c^2\gamma_1^{2/3}}} & 0 \\ 0 & 0 & \frac{cb^2\gamma_1^{-1/3}}{3(b^2+c^2(b^2-1)\gamma_1^{2/3})} & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}.$$

therefore, when $\lambda \to 0$ and $\alpha = 1$ it follows from Azzalini [2] and Pewsey et al. [13] that the information matrix of the ELSN$_c$ model converges to

$$\begin{pmatrix} \boldsymbol{\Sigma}_c & \boldsymbol{I}_{\boldsymbol{\theta}_1 \alpha} \\ \boldsymbol{I}_{\boldsymbol{\theta}_1 \alpha}^{\top} & 1 \end{pmatrix}$$

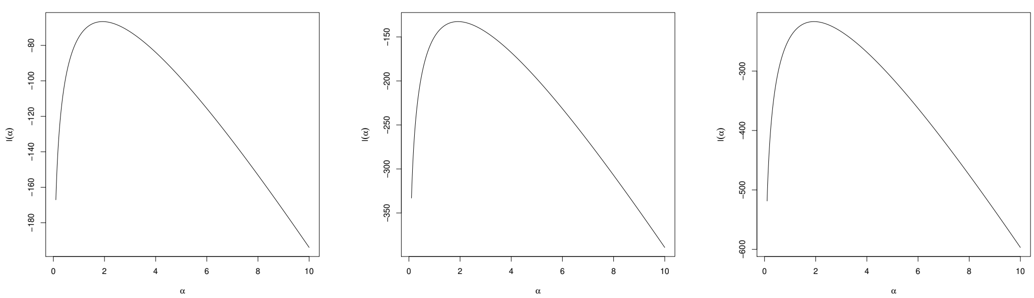
where $\boldsymbol{I}_{\boldsymbol{\theta}_1,\alpha}$ represents the vector of mixed second derivatives of α and the rests of the parameters $\boldsymbol{\theta}_1 = (\mu, \sigma, \gamma_1)^{\top}$. This turns out to be non-singular matrix, since its columns (or rows) are linearly independent. Hence, the regularity conditions are satisfied in general and the usual $\sqrt{n}$-property for the MLE $\hat{\boldsymbol{\theta}}$ of $\boldsymbol{\theta}$ is satisfied for all λ and α. This result guarantees the asymptotic distribution of the MLE for large samples, allowing to make inferences for the parameters of the ELSN$_c$ model, which is an advantage against to the LSN model whose information matrix is singular for $\lambda = 0$.

The Figures 2 and 3 represent of the log-likelihood profiled of the $\text{ELSN}_c(0,1,0,1) \equiv \text{LPN}(0,1,1) \equiv \text{LSN}_c(0,1,0) \equiv \text{LN}(0,1)$ distribution for samples sizes 50, 100 and 150. The graphics show a regularity in the behaviour of the log-likelihood function, which gives strong evidence for the existence and uniqueness of the MLE.



(**a**) (**b**) (**c**)

Figure 2. Log-likelihood profiled for γ_1 assuming ELSN$_c$ distribution with samples sizes (**a**) 50, (**b**) 100 and (**c**) 150 from a simulated $\text{LN}(0,1) \equiv \text{ELSN}_c(0,1)$ distribution.



(**a**) (**b**) (**c**)

Figure 3. Log-likelihood profiled for α assuming ELSN$_c$ distribution with samples sizes (**a**) 50, (**b**) 100 and (**c**) 150 from a simulated $\text{LN}(0,1) \equiv \text{ELSN}_c(0,1)$ distribution.

3.1. The ELSN$_c$ Regression Models

Azzalini [2] ensures that the properties of existence and uniqueness of the MLE model SN$_c$ can be extended to the more general models case such as $y_i = \boldsymbol{x}_i^{\top} \boldsymbol{\beta} + \sigma Z_i$, $i = 1, 2, \ldots, n$, where $\boldsymbol{x}_i$ is a $p \times 1$ vector of covariates, $\boldsymbol{\beta} = (\beta_0, \beta_1, \ldots, \beta_p)^{\top}$ is an unknown vector of regression coefficients and $z_1, \ldots, z_n$ are independent and identically distributed random variables $\text{SN}(\lambda)$.

In this section, the location and scale version of the $\text{ELSN}_c(\mu, \sigma, \gamma_1, \alpha)$ model, is extended to situations of the regression models, that is, we consider the regression model

$$\log(y_i) = \boldsymbol{x}_i^\top \boldsymbol{\beta} + \varepsilon_i, \quad i = 1, 2, \dots, n, \tag{10}$$

where $\varepsilon_i \sim \text{ELSN}_c(0, \sigma, \gamma_1, \alpha)$. The model (10) is denominated the centred exponentiated log-skew-normal regression (ELSNR_c) model and is denoted by $\text{ELSNR}_c(\boldsymbol{\beta}^\top, \sigma, \gamma_1, \alpha)$. Estimates for the components of the parameters vector $(\boldsymbol{\beta}^\top, \sigma, \gamma_1, \alpha)^\top$ of the ELSNR_c model can be obtained by using the maximum likelihood method.

To analyse the behaviour of the estimators of the parameters in the ELSNR_c model, we carried out a small Monte Carlo simulation study, so, we analysed the behaviour of the estimators in the model (10). Since the coefficients β_i, for $i = 0, 1, \dots, p$, have no restrictions on the values that can be assumed, without loss of generality we took $p = 1$ and the particular values $\beta_0 = 1.5$, $\beta_1 = 2.5$. Furthermore, without loss of generality, we took the value of the scale parameter equal to $\sigma = 1.0$; however, the following results can be obtained for any value of the scale parameter from the simple transformation $\varepsilon_i = \sigma\delta_i$ with $\delta_i \sim \text{ELSN}_c(0, 1, \gamma_1, \alpha)$. The values of shape parameter were taken as $\alpha = 0.75,\ 1.5$ to take into account different configurations in the form of the pdf of the random variable ε_i. Finally, we took values for the asymmetry parameter $\gamma_1 = 0.25, 0.50, 0.75$, to take into account different degrees of asymmetry in the distribution of the data.

To analyse some statistical measures of the MLE, we considered small, moderate and large sample sizes: $n = 60, 70, 80$ and 500, and 1000 iterations were performed for each sample size. The studied characteristics were the bias and the root of the mean square error (RMSE) of the MLEs of the parameters. All calculations and estimates were obtained by using `optim` function of R Development Core Team [20].

Table 1 presents the results of the simulation study, where it can be observed that the bias (in absolute value) and the RMSE of the MLEs tend to decrease when the sample size increases, which guarantees the asymptotic convergence of the MLEs. Another important fact, is the good estimation of the regression coefficients for all sample sizes considered, with a strong evidence that the model achieves to fit the high levels of skewness and kurtosis present in the response variable. On the other hand, the near zero values of the bias for the parameters γ_1 and α for large sample sizes ($n = 500$), the values indicate that average iterations fences were true parameter value and therefore, there are no problems of identifiability in the estimation process.

Table 1. Simulation study with 1000 iterations for $\alpha = 0.75, 1.5$, $\gamma = 0.25, 0.5, 0.75$, $\beta_0 = 1.5$, and $\beta_1 = 2.5$, with sample sizes of $n = 60, 70, 80$ and 500.

	$\beta_0 = 1.5$		$\beta_1 = 2.5$		$\alpha = 0.75$		$\gamma_1 = 0.25$	
n	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**
60	−0.0307	0.5331	0.0019	0.1405	−0.0168	0.3787	0.1614	0.5477
70	−0.0296	0.5073	0.0015	0.1305	−0.0130	0.3581	0.1410	0.5616
80	−0.0170	0.4640	−0.0012	0.1255	−0.0204	0.3342	0.1083	0.4157
500	0.0080	0.1700	0.0011	0.0462	−0.0046	0.1199	0.0068	0.1224
	$\beta_0 = 1.5$		$\beta_1 = 2.5$		$\alpha = 0.75$		$\gamma_1 = 0.50$	
n	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**
60	−0.0568	0.6625	0.0060	0.1384	−0.0048	0.3726	0.2956	1.0945
70	−0.0536	0.6290	−0.0015	0.1276	−0.0205	0.3309	0.2515	0.8024
80	−0.0301	0.6118	0.0031	0.1189	−0.0091	0.3135	0.2018	0.6585
500	0.0209	0.2970	−0.0006	0.0448	0.0023	0.1156	0.0197	0.2412
	$\beta_0 = 1.5$		$\beta_1 = 2.5$		$\alpha = 0.75$		$\gamma_1 = 0.75$	
n	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**
60	−0.0508	0.6767	0.0072	0.1211	0.1848	1.9833	0.3443	1.2177
70	−0.0481	0.67	0.0045	0.1174	0.184	2.0431	0.3243	1.1201
80	−0.0368	0.6483	0.003	0.1047	0.1284	1.0011	0.2918	1.0173
500	−0.0287	0.3889	−0.0015	0.0387	0.0201	0.1639	0.1173	0.4708

Table 1. *Cont.*

	$\beta_0 = 1.5$		$\beta_1 = 2.5$		$\alpha = 1.5$		$\gamma_1 = 0.25$	
n	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**
60	−0.0973	0.5842	0.0500	0.1251	0.0519	0.4253	0.8683	3.2124
70	−0.0815	0.5433	0.0102	0.1165	0.0360	0.4137	0.7459	3.0357
80	−0.0716	0.4592	−0.0068	0.1073	0.0081	0.3963	0.5457	2.2340
500	−0.0151	0.1480	0.0013	0.0408	0.0001	0.1253	0.0564	0.2874
	$\beta_0 = 1.5$		$\beta_1 = 2.5$		$\alpha = 1.5$		$\gamma_1 = 0.5$	
n	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**
60	−0.0179	0.6981	−0.0092	0.1203	0.0774	0.6987	1.0013	5.0588
70	0.0173	0.6716	0.0085	0.1153	0.0441	0.4326	0.6727	3.2734
80	0.0154	0.6311	0.0065	0.1057	0.0427	0.3569	0.6311	3.1535
500	−0.0404	0.2858	0.0005	0.0395	0.0190	0.1496	0.1793	0.6559
	$\beta_0 = 1.5$		$\beta_1 = 2.5$		$\alpha = 1.5$		$\gamma_1 = 0.75$	
n	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**	**Bias**	**RMSE**
60	0.0789	0.6885	0.0053	0.1218	0.1973	1.4280	0.4340	3.1930
70	0.0784	0.6413	0.0025	0.1134	0.1630	1.0152	0.4212	2.4414
80	0.0623	0.6046	0.0012	0.1059	0.1366	0.6108	0.3358	1.8002
500	0.0316	0.3572	−0.0005	0.0380	0.0723	0.3008	0.0890	0.6704

3.2. The Censored ELSN$_c$ Distribution

In this section, the centred ELSN$_c$ model for censored positive data is introduced. Suppose that random variable Y^* follows a ELSN$_c(\mu, \sigma, \lambda, \alpha)$ model, and let $Y_1^*, Y_2^*, \ldots, Y_n^*$ a random sample of size n, where only those values of Y^* greater than constant T are recorded; and for values $Y^* \leq T$ only the value T is recorded. The observed values, which we denote by Y_i can be written as

$$Y_i = \begin{cases} T, & \text{if } Y_i^* \leq T, \\ Y_i^*, & \text{if } Y_i^* > T. \end{cases}$$

The PDF of Y_i is

$$\begin{array}{ll} \Pr(Y_i = T) = \Pr(Y_i^* \leq T) = \{\Phi_{\text{SN}}(t_c; \lambda)\}^{\alpha}, & \text{if } Y_i = T, \\ Y_i \sim \text{ELSN}_c(\mu, \sigma, \lambda, \alpha), & \text{if } Y_i > T, \end{array} \tag{11}$$

where $t_c = \frac{\log(T) - \lambda_1}{\lambda_2}$, with λ, λ_1 y λ_2 defined in (8). This model is represented by the notation $Y_i \sim$ CELSN$_c(\mu, \sigma, \gamma_1, \alpha)$. One can see that, if $\gamma_1 = 0$ and $\alpha = 1$, the CELSN$_c$ distribution is identical to the log-normal Tobit model, see Moulton and Halsey [9]. This shows that the CELSN$_c$ model is much more flexible than the log-normal Tobit model. Furthermore, for $\alpha = 1$, the centred LSN model for censored data follows, while for $\gamma_1 = 0$ the censored LPN model of Martínez-Flórez et al. [5] is obtained.

Extensions of the CELSN$_c$ model to the case of regression models are defined in the same way, by assuming $\varepsilon_i \sim$ ELSN$_c(0, \sigma, \gamma_1, \alpha)$, and defining

$$t_{ci} = \frac{\log(T) - \boldsymbol{x}_i^\top \boldsymbol{\beta} + c\sigma\gamma_1^{1/3}}{\lambda_2} \quad \text{and} \quad t_i = \frac{\log(y_i) - \boldsymbol{x}_i^\top \boldsymbol{\beta} + c\sigma\gamma_1^{1/3}}{\lambda_2}, \tag{12}$$

with λ_2 defined as in (8).

4. The Bernoulli/ Centred Log-Skew-Normal Alpha-Power Mixture Model

This section aims to make an extension of the generalized two-part model presented by Moulton and Halsey [9], where the Logit/Log-normal model is proposed.

4.1. The Logit/Centred Log-Skew-Normal Alpha-Power Model

The extension of the Moulton and Halsey [9] model to the case of the ELSN_c distribution is obtained by following Martínez-Flórez et al. [5]. We assume the existence of two random variables which define two different stochastic processes, D with Bernoulli distribution and Y with ELSN_c distribution. According to the model (3), the PDF is given by

$$g_C(y_i) = \Big(p_{0i} + (1-p_{0i})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}\Big)^{I_i}\Big((1-p_{0i})\frac{\alpha}{\lambda_2 y_i}\phi_{\mathrm{SN}}(t_i;\lambda)\{\Phi_{\mathrm{SN}}(t_i;\lambda)\}^{\alpha-1}\Big)^{1-I_i}$$

where λ_2 and λ were defined in Equation (8).

One can get a more informative model if covariates are introduced to explain the response variable Y and covariates to explain the associated distribution to censored part, that is, the random variable D. Thus, we consider two sets of covariates,

- If $I_i = 0$, i.e., the non-censored part, the covariates vector will be denoted by $\boldsymbol{x}_{(2)i} = (1, X_{2i1}, X_{2i2}, \ldots, X_{2iq_0})^\top$ with the parameter vector given by $\boldsymbol{\beta}_{(2)} = (\beta_{20}, \beta_{21}, \ldots, \beta_{2q_0})^\top$.
- If $I_i = 1$ and $Y_i = T$, i.e., the censored part, the covariates vector will be denoted by $\boldsymbol{x}_{(1)i} = (1, X_{1i1}, X_{1i2}, \ldots, X_{1iq_1})^\top$ with the parameter vector given by $\boldsymbol{\beta}_{(1)} = (\beta_{10},\ \beta_{11}, \ldots,\ \beta_{1q_1})^\top$.

If $I_i = 1$ and $Y_i < T$, we will also have an associated distribution; however, in this case is assumed that there is no observations for $Y_i < T$ due the censorship. For the variable D, we consider the logit link function, so that

$$\mathrm{logit}\big(P[D = 1 \mid \boldsymbol{x}_{(1)}]\big) = \boldsymbol{x}_{(1)}^\top \boldsymbol{\beta}_{(1)},$$

then, we have

$$p_{0i} = \Big(1 + \exp\big(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}\big)\Big)^{-1},$$

For non-censored part is considered

$$Y_i \sim \mathrm{ELSN}_c(\boldsymbol{x}_{(2)i}^\top \boldsymbol{\beta}_{(2)}, \sigma_2, \gamma_1, \alpha), \quad Y_i > T. \tag{13}$$

The model (13) is a generalization of the models of Martínez-Flórez et al. [5], Moulton and Halsey [9] and Chai and Bailey [11]. It is denominated the Bernoulli/centred exponentiated log-skew-normal mixture model, and it will be represented by the notation $Y_i \sim \mathrm{BELSNM}_c(\boldsymbol{\beta}_{(1)}, \boldsymbol{\beta}_{(2)}, \sigma, \gamma_1, \alpha)$.

One can see that, when $\gamma_1 = 0$, the BELSNM_c model is identical to the Logit/log-power-normal (logit/LPN) mixture model, for $\alpha = 1$, the BELSNM_c model is identical to the Logit/centred log-skew-normal (Logit/LSN_c) mixture model, $\gamma_1 = 0$ and $\alpha = 1$, the BELSNM_c model is identical to the Logit/log-normal (Logit/LN) mixture model, see Martínez-Flórez et al. [5], Chai and Bailey [11] and Moulton and Halsey [9]. It can be concluded from the above results and the characteristics of the ELSN_c model to fit positive data with higher (or lower) degree of asymmetry and kurtosis than LPN and LSN models, that, the BELSNM_c model is a great extension of the logit/log-normal model. This new distribution turns out to be more flexible in terms of asymmetry and kurtosis than the models of Moulton and Halsey [9], Chai and Bailey [11] and Martínez-Flórez et al. [5], becoming a great alternative to censored asymmetric positive data or distributions with excess of zeros.

Is necessary to emphasize that $\hat{\beta}_{(2)0}$ is the biased estimation for the intercept in the regression model. In fact, since $\mathbb{E}(\boldsymbol{Y} \mid \boldsymbol{Y} > 0) \neq \boldsymbol{X}\boldsymbol{\beta}$, then, to correct the bias, it is necessary to calculate $\hat{\beta}^*_{(2)0} = \hat{\beta}_{(2)0} + \hat{\mathbb{E}}(\hat{e})$, where $\mathbb{E}(e) = \alpha\eta \int_0^1 \Phi_{\mathrm{ISN}}(y) y^{\alpha-1} dy$, where $\Phi_{\mathrm{ISN}}(\cdot)$ represents the inverse function of the SN_c distribution $\Phi_{\mathrm{SN}}(\cdot)$.

4.2. Fitting Model

The parameters vector $\boldsymbol{\theta} = (\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \sigma, \gamma_1, \alpha)^\top$ for the BELSNM$_c$ model can be estimated by using the maximum likelihood method. The log-likelihood function based on a random sample $Y_1, Y_2, \ldots, Y_n$, with $Y_i \sim \text{BELSNM}_c(\boldsymbol{\theta})$, given $\boldsymbol{X}_{(1)}$, $\boldsymbol{X}_{(2)}$ is given by

$$
\begin{aligned}
\ell(\boldsymbol{\theta}; \boldsymbol{X}_{(1)}, \boldsymbol{X}_{(2)}, \boldsymbol{Y}) = {} & \sum_i I_i \log\left[1 + \exp\left(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}\right) \{\Phi_{\text{SN}}(t_{ci}; \lambda)\}^\alpha\right] \\
& + \sum_i (1 - I_i) \left[\log(\alpha) - \log(\lambda_2 y_i) + \boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)} \right. \\
& \left. \qquad + \log\{\phi_{\text{SN}}(t_i; \lambda)\} + (\alpha - 1)\log\{\Phi_{\text{SN}}(t_i; \lambda)\}\right] \\
& - \sum_i \log\left\{1 + \exp\left(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}\right)\right\},
\end{aligned}
\tag{14}
$$

where t_{ci} and t_i are as defined in (12). The equations scores obtained by equating the score function to zero are given by (for $j = 1, 2, \ldots, q_1$ and $k = 1, 2, \ldots, q_0$).

$$
\begin{aligned}
& -\sum_i I_i \frac{x_{1ij} \exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})}{1 + \exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}) \{\Phi_{\text{SN}}(t_{ci}; \lambda)\}^\alpha} \frac{1 - \{\Phi_{\text{SN}}(t_{ci}; \lambda)\}^\alpha}{1 + \exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})} \\
& \qquad + \sum_i \frac{x_{1ij}}{1 + \exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})} = 0, \quad \text{for} \quad j = 1, 2, \ldots, q_1
\end{aligned}
$$

$$
\begin{aligned}
& -\sum_i I_i \frac{x_{2ik} \exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}) \phi_{\text{PSN}}(t_{ci}; \lambda, \alpha)}{1 + \exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}) \{\Phi_{\text{SN}}(t_{ci}; \lambda)\}^\alpha} \\
& \qquad - \frac{1}{\lambda_2} \sum_i (1 - I_i) x_{2ik} \{t_i + \lambda \omega(\lambda t_i) + (\alpha - 1)\omega_\lambda(t_i)\} = 0, \quad \text{for} \quad k = 1, 2, \ldots, q_0
\end{aligned}
$$

$$
\begin{aligned}
& -\sum_i I_i \frac{t_{ci} \exp(\mathbf{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}) \phi_{\text{PSN}}(t_{ci}; \lambda, \alpha)}{1 + \exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}) \{\Phi_{\text{SN}}(t_{ci}; \lambda)\}^\alpha} \\
& \qquad - \frac{1}{\lambda_2} \sum_i (1 - I_i) \times \left(1 - t_i^2 + \lambda t_i \omega(\lambda t_i) + \ (\alpha - 1) t_i \omega_\lambda(t_i)\right) = 0
\end{aligned}
$$

$$
\begin{aligned}
& -\sqrt{\frac{2}{\pi}} \frac{1}{1 + \lambda^2} \sum_i I_i \frac{\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}) \{\Phi_{\text{SN}}(t_{ci}; \lambda)\}^{\alpha - 1} \phi\left(\sqrt{1 + \lambda^2} t_{ci}\right)}{1 + \exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}) \{\Phi_{\text{SN}}(t_{ci}; \lambda)\}^\alpha} \\
& \qquad + \sum_i (1 - I_i) \left(t_i \omega(\lambda t_i) - \sqrt{\frac{2}{\pi}} \frac{\alpha - 1}{1 + \lambda^2} \nu_\lambda(t_i)\right) = 0
\end{aligned}
$$

$$
\begin{aligned}
& \sum_i I_i \frac{\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}) \{\Phi_{\text{SN}}(t_{ci}; \lambda)\}^\alpha \log\{\Phi_{\text{SN}}(t_{ci}; \lambda)\}}{1 + \exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)}) \{\Phi_{\text{SN}}(t_{ci}; \lambda)\}^\alpha} \\
& \qquad + \sum_i (1 - I_i) \left(\frac{1}{\alpha} + \log\{\Phi_{\text{SN}}(t_i; \lambda)\}\right) = 0
\end{aligned}
$$

where $\omega(t) = \phi(t)/\Phi(t)$, $\omega_\lambda(t) = \phi_{\text{SN}}(t; \lambda)/\Phi_{\text{SN}}(t; \lambda)$, $\nu_\lambda(t) = \phi(\sqrt{1 + \lambda^2} t)/\Phi_{\text{SN}}(t; \lambda)$ and $\phi_{\text{PSN}}(\cdot; \lambda, \alpha)$ is the PDF of the ELSN$_c$ model. The system of score equations has no closed form solution and have to be obtained numerically. The solutions of this system of equations provide the MLE of the parameters vector $(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \sigma, \gamma_1, \alpha)^\top$. The log-likelihood function can be maximized by implementing some statistical packages such as R Development Core Team [20], which has the x-Optim, optim, nlem, x-maxLIK or maxLIK commands to maximize non-linear functions.

The initial values for the parameters $\boldsymbol{\beta}_{(1)}$ and $\boldsymbol{\beta}_{(2)}$ can be obtained from the fit of a Tobit model, while, initial values for γ_1 and α can be obtained by fitting the ELSN$_c$ model for the response variable Y. The standard errors of the MLE can be obtained as the square root of the inverse of the observed information matrix $\boldsymbol{J}(\cdot)$, which converges asymptotically to the Fisher information matrix, this matrix is given by

$$\boldsymbol{J}(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \sigma, \gamma_1, \alpha) = \boldsymbol{B}^\top \boldsymbol{J}(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \eta, \lambda, \alpha)\boldsymbol{B}$$

where the elements of the $\boldsymbol{J}(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \eta, \lambda, \alpha)$ matrix are in the Appendix A, and

$$\boldsymbol{B} = \begin{pmatrix} \mathbf{I}_{q_1+1} & \mathbf{0}_{q_1+1} & \mathbf{0}_{(q_1+1)\times q_0} & \mathbf{0}_{q_1+1} & \mathbf{0}_{q_1+1} & \mathbf{0}_{q_1+1} \\ \mathbf{0}_{q_1+1}^\top & 1 & \mathbf{0}_{q_0}^\top & -c\gamma_1^{1/3} & -\frac{1}{3}c\sigma\gamma_1^{-2/3} & 0 \\ \mathbf{0}_{q_0\times(q_1+1)} & \mathbf{0}_{q_0} & \mathbf{I}_{q_0} & \mathbf{0}_{q_0} & \mathbf{0}_{q_0} & \mathbf{0}_{q_0} \\ \mathbf{0}_{q_1+1}^\top & 0 & \mathbf{0}_{q_0}^\top & \sqrt{1+c^2\gamma_1^{2/3}} & \frac{c^2\sigma\gamma_1^{-1/3}}{3\sqrt{1+c^2\gamma_1^{2/3}}} & 0 \\ \mathbf{0}_{q_1+1}^\top & 0 & \mathbf{0}_{q_0}^\top & 0 & \frac{cb^2\gamma_1^{-1/3}}{3(b^2+c^2(b^2-1)\gamma_1^{2/3})} & 0 \\ \mathbf{0}_{q_1+1}^\top & 0 & \mathbf{0}_{q_0}^\top & 0 & 0 & 1 \end{pmatrix}.$$

Then, the Fisher information matrix is given by

$$\boldsymbol{I}(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \sigma, \gamma_1, \alpha) = \mathbb{E}\Big(\boldsymbol{J}(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \sigma, \gamma_1, \alpha)\Big) = \boldsymbol{B}^\top \boldsymbol{I}(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \lambda_2, \lambda, \alpha)\boldsymbol{B},$$

where

$$\boldsymbol{I}\Big(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \lambda_2, \lambda, \alpha\Big) = \mathbb{E}\Big(\boldsymbol{J}(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \lambda_2, \lambda, \alpha)\Big). \tag{15}$$

From the information matrix in (15), it can be obtained the asymptotic distribution of the MLE for large samples with covariance matrix $\boldsymbol{\Sigma} = (\boldsymbol{I}(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \sigma, \gamma_1, \alpha))^{-1}$. Confidence intervals for the model parameters can be obtained from the MLE and the standard errors of the MLE.

5. An Application to Antibody Response to Vaccine

Data from a safety and immunogenicity study of measles vaccine conducted in Haiti during 1987–1990 are used as an illustration, see Job et al. [19]. In this case, the goal of the study was to demonstrate that the higher titer vaccines could effectively immunize infants as young as 12 months of age. The response variable was neutralization antibody and the covariates involved in the study were: *EZ* (vaccine type; 0 =: Schwarz, 1 =: Edmonston-Zagreb), *HI* (vaccine dose; 0 =: medium, 1 =: high) and *FEM* (gender; 0 =: male, 1 =: female). The sample size was 330 children, of which 86 were at or below the lower detection limit, (LDL). The number of expected zeros by considering the usual Tobit model was four. The response variable was the neutralization antibody, with LDL equal to 0.1 international units (UI), and the covariates involved in the study were encoded as $EZ = X_1$, $HI = X_2$ and $FEM = X_3$.

The high asymmetry degree for values above 0.1 indicated by the sample asymmetry coefficient $\left(\sqrt{b_1}\right)$ reveals that it seems worthwhile trying to fit an asymmetric model for this data set, so we fit the Moulton and Halsey [9], Martínez-Flórez et al. [4] and the centred version of the Chai and Bailey [11] models, with $\boldsymbol{X}_{(1)} = \boldsymbol{X}_{(2)} = (X_1, X_2, X_3)^\top$, and the results are presented in Table 2. The parameter estimates of the fitted models were obtained by using the optim function of R Development Core Team [20]. The source codes of the fitted models can be obtained by requesting them by email to the authors.

Table 2. Estimated parameters (standard error) of the fitted model.

Density	AIC	β_{10}	β_{11}	β_{12}	γ_1/α	β_{20}	β_{23}
Logit/LN	986.19	0.652	0.808	0.422		−0.401	0.264
		(0.220)	(0.304)	(0.288)		(0.112)	(0.155)
Logit/LSN$_c$	944.15	0.503	0.648	0.974	0.899	−0.284	0.108
		(0.203)	(0.277)	(0.303)	(0.537)	(0.059)	(0.079)
Logit/LPN	976.11	0.640	0.765	0.357	9.660	−3.030	0.221
		(0.209)	(0.280)	(0.269)	(4.306)	(0.607)	(0.138)

We also fit the BELSNM$_c$ model, initially only with covariates in the continuous part and subsequently with covariates in the two components. The fitted models are shown in Table 3. To compare the fitted models, we computed the Akaike information criterion [21], namely $AIC = -2\ell(\cdot) + 2p$, where p is the number of parameters for the considered model. The best model is the one with the smallest AIC value.

Table 3. Parameter estimation (standard error) and model fitting.

AIC	β_{10}	β_{11}	β_{12}	β_{20}	β_{21}	β_{22}	β_{23}	γ_1	α
985.21	1.106	–	–	−1.786	−0.166	0.115	0.176	0.291	4.281
	(0.134)	–	–	(0.633)	(0.136)	(0.138)	(0.137)	(0.432)	(1.459)
938.32	0.349	0.975	0.689	0.045	–	–	0.156	0.923	0.613
	(0.199)	(0.274)	(0.295)	(0.101)	–	–	(0.084)	(0.407)	(0.090)

According to the AIC criterion, the best fit is presented by the BELSNM$_c$ model. To corroborate the good performance of the BELSNM$_c$ model, the proportion of the data set coming from units with low response was estimated. For the BELSNM$_c$ model without covariates the estimator of the Bernoulli intercept is 1.106, so that the estimator of the proportion of observations at or below the detection limit is $100 \times 1/[1 + \exp(1.106)] = 24.86\%$ which, compared to the observed 26.1%, indicates good agreement with the proposed model.

We also consider the problem of testing the null hypothesis of no difference between the BELSNM$_c$ model and the censored log-normal (CLN) model, i.e.,

$$H_0: \ (\gamma_1, \alpha) = (0, 1) \quad \text{versus} \quad H_1: \ (\gamma_1, \alpha) \neq (0, 1)$$

We use the likelihood ratio statistic

$$\Lambda = \frac{\mathcal{L}_{\mathrm{CLN}}(\hat{\boldsymbol{\theta}})}{\mathcal{L}_{\mathrm{BELSNM}_c}(\hat{\boldsymbol{\theta}})}.$$

where $\mathcal{L}_F(\cdot)$ is the likelihood function under model F. Numerical evaluations indicate that

$$-2\log(\Lambda) = -2(-511.18 + 461.36) = 99.63,$$

which is greater than the 5% chi-square critical value with two degree of freedom, $\chi^2_{2,5\%} = 5.991$. Hence, the null hypothesis is rejected and we conclude that the BELSNM$_c$ fits the data better than the logit/LN model.

Hypothesis testing for the Logit/LPN (CLPN) and Logit/LSN$_c$ (CLSN$_c$) models against the BELSNM$_c$ model are also conducted. Formally the hypotheses

$$H_{01}: \gamma_1 = 0 \quad \text{versus} \quad H_{11}: \gamma_1 \neq 0, \quad \text{and} \quad H_{02}: \alpha = 1 \quad \text{versus} \quad H_{12}: \alpha \neq 1$$

can be tested by using the statistics

$$\Lambda_1 = \frac{\mathcal{L}_{\mathrm{CLPN}}(\hat{\boldsymbol{\theta}})}{\mathcal{L}_{\mathrm{BELSNM}_c}(\hat{\boldsymbol{\theta}})} \quad \text{and} \quad \Lambda_2 = \frac{\mathcal{L}_{\mathrm{CLSN}_c}(\hat{\boldsymbol{\theta}})}{\mathcal{L}_{\mathrm{BELSNM}_c}(\hat{\boldsymbol{\theta}})}.$$

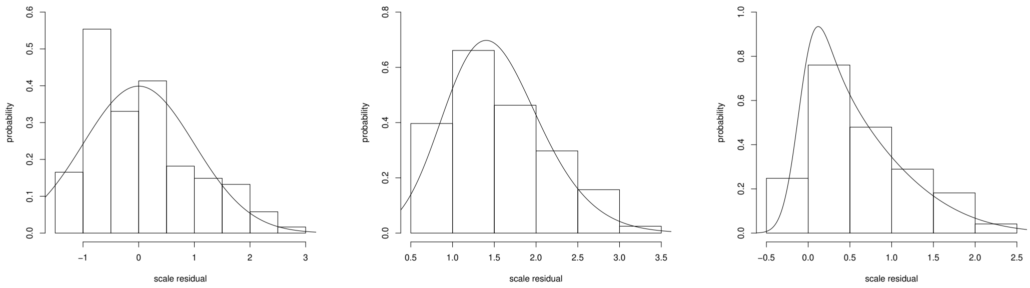
After numerical evaluations, we obtained

$$-2\log(\Lambda_1) = 39.39 \quad \text{and} \quad -2\log(\Lambda_2) = 11.66,$$

which are greater than the 5% chi-square critical value with one degree of freedom, $\chi^2_{1,5\%} = 3.8414$. The null hypothesis are rejected and we conclude that the BELSNM$_c$ model fits the data better than the Logit/LPN and Logit/LSN$_c$ models.

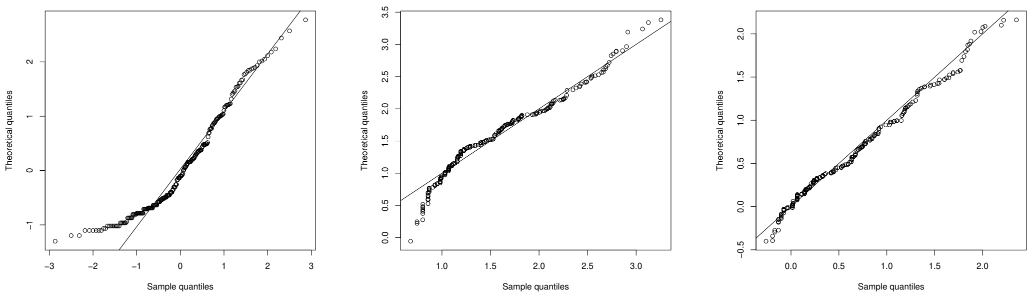
Using distributions LN, LPN and ELSN$_c$ for the continuous part, the scaled residuals $e_i = (\log(y_i) - \boldsymbol{x}_{(2)i}^\top \hat{\boldsymbol{\beta}}_{(2)})/\hat{\eta}$ are evaluated and presented in the Figures 4 and 5.

The figures reveal good performance of the BELSNM$_c$ distribution, further indicating that it is a viable alternative for asymmetric data with censored responses.



(**a**) (**b**) (**c**)

Figure 4. Histogram of the scaled residuals e_i for (**a**) LN model, (**b**) LPN model, (**c**) ELSN$_c$ model.



(**a**) (**b**) (**c**)

Figure 5. QQ-plots of the scaled residuals e_i for (**a**) LN model, (**b**) LPN model, (**c**) ELSN$_c$ model.

6. Final Discussion

In this paper, a more flexible model than the Logit/LN, Logit/LSN and Logit/LPN distributions is proposed. The new model is able to fit data with greater degree asymmetry and kurtosis than the Moulton and Halsey [9], Chai and Bailey [11] and Martínez-Flórez et al. [5] models. The score function and the maximum likelihood estimator (MLE) of the model parameters are presented. A small Monte Carlo simulation study carried out showed a good performance of the MLE. An illustration with safety and immunogenicity data was presented in which the BELSNM$_c$ model makes a better fit with respect to the Logit/LN, Logit/LSN and Logit/LPN models.

Among the main advantages that can be seen from the proposed models, there is greater flexibility with respect to the log-normal (log-Tobit), log-SN and log-PN models. On the other hand, the logit link function allows us to estimate the point mass probability with greater precision compared to the Tobit and log-Tobit models. As a disadvantage, the number of parameters in the model—although making it more flexible—also make it less parsimonious. However, even though the model is less parsimonious, it continues to be a good proposal, especially in cases where the asymmetry and kurtosis indices are high.

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Appendix A

Letting:
$\omega(t) = \phi(t)/\Phi(t),\ \omega_\lambda(t) = \phi_{\rm SN}(t;\lambda)/\Phi_{\rm SN}(t;\lambda),\ \nu_\lambda(t) = \phi(\sqrt{1+\lambda^2}t)/\Phi_{\rm SN}(t;\lambda)$, the elements of the observed information matrix $\boldsymbol{J}(\boldsymbol{\beta}_{(1)}^\top, \boldsymbol{\beta}_{(2)}^\top, \lambda_2, \lambda, \alpha)$, denoted $j_{\beta_{(1)j}\beta_{(1)j'}}$, $j_{\beta_{(2)k}\beta_{(1)j}}$, $\ldots, j_{\alpha\alpha}$, are given by

$$j_{\beta_{(1)j}\beta_{(1)j'}} = -\sum I_i \frac{x_{1ij}x_{1ij'}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\rm SN}(t_{ci};\lambda)\}^\alpha}{\left[1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\rm SN}(t_{ci};\lambda)\}^\alpha\right]^2} + \sum_i \frac{x_{1ij}x_{1ij'}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})}{\left\{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\right\}^2}$$

$$j_{\beta_{(1)j}\beta_{(2)k}} = \sum_i I_i \frac{x_{1ij}x_{2ik}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\rm PSN}(t_{ci};\lambda,\alpha)}{\left[1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\rm SN}(t_{ci};\lambda)\}^\alpha\right]^2}$$

$$j_{\eta\beta_{(1)j}} = \sum_i I_i \frac{x_{1ij}t_{ci}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\rm PSN}(t_{ci};\lambda,\alpha)}{\left[1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\rm SN}(t_{ci};\lambda)\}^\alpha\right]^2}$$

$$j_{\lambda\beta_{(1)j}} = \sqrt{\frac{2}{\pi}}\frac{\alpha}{1+\lambda^2}\sum_i I_i \frac{x_{1ij}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\rm SN}(t_{ci};\lambda)\}^{\alpha-1}\phi\left(\sqrt{1+\lambda^2}t_{ci}\right)}{\left[1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\rm SN}(t_{ci};\lambda)\}^\alpha\right]^2}$$

$$j_{\alpha\beta_{(1)j}} = -\sum_i I_i \frac{x_{1ij}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\rm SN}(t_{ci};\lambda)\}^\alpha\log\{\Phi_{\rm SN}(t_{ci};\lambda)\}}{\left[1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\rm SN}(t_{ci};\lambda)\}^\alpha\right]^2}$$

$$
\begin{aligned}
j_{\beta_{(2)k}\beta_{(2)k'}} = {} & \frac{1}{\lambda_2}\sum_i I_i \frac{x_{2ik}x_{2ik'}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha}\Big[t_{ci}-(\alpha-1)\omega_\lambda(t_i)\Big] \\
& - \sqrt{\frac{2}{\pi}}\frac{\alpha\lambda}{\lambda_2}\sum_i I_i \frac{x_{2ik}x_{2ik'}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)\phi\Big(\sqrt{1+\lambda^2}t_i\Big)\big(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\big)^{\alpha-1}}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha} \\
& + \sum_i I_i x_{2ik}x_{2ik'}\left[\frac{\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha}\right]^2 \\
& + \frac{1}{\lambda_2^2}\quad\sum_i(1-I_i)x_{2ik}x_{2ik'}\left[-1+\lambda^3 t_i\omega(\lambda t_i)+\lambda^2\big(\omega(\lambda t_i)\big)^2\right] \\
& + \frac{\alpha-1}{\lambda_2^2}\sum_i(1-I_i)x_{2ik}x_{2ik'}\left[t_i\omega_\lambda(t_i)+\big(\omega_\lambda(t_i)\big)^2-\sqrt{\frac{2}{\pi}}\lambda\nu_\lambda(t_i)\right]
\end{aligned}
$$

$$
\begin{aligned}
j_{\eta\beta_{(2)k}} = {} & \frac{1}{\eta}\sum_i I_i \frac{x_{2ik}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha}\Big(-1+t_{ci}^2-\alpha t_{ci}\omega_\lambda(t_{ci})\Big) \\
& - \sqrt{\frac{2}{\pi}}\frac{\alpha\lambda}{\eta^2}\sum_i I_i \frac{x_{2ik}t_{ci}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi\Big(\sqrt{1+\lambda^2}t_i\Big)\Big(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\Big)^{\alpha-1}}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha} \\
& + \sum_i I_i x_{2ik}t_{ci}\left(\frac{\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha}\right)^2 \\
& + \frac{1}{\eta^2}\sum_i(1-I_i)x_{2ik}\Big(2t_i+(\alpha-1)\big(-1+t_i^2+t_i\omega_\lambda(t_i)\big)\omega_\lambda(t_i)\Big) \\
& + \frac{\lambda(\alpha-1)}{\eta^2}\sum_i(1-I_i)x_{2ik}t_i\nu_\lambda(t_i) \\
& + \frac{\lambda}{\eta^2}\sum_i(1-I_i)x_{2ik}\omega(\lambda t_i)\Big(-1+\lambda^2t_i^2+t_i\omega(\lambda t_i)\Big)
\end{aligned}
$$

$$
\begin{aligned}
j_{\lambda\beta_{(2)k}} = {} & \sqrt{\frac{2}{\pi}}\sum_i I_i \frac{x_{2ik}t_{ci}\big[1+\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha\big]\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)\phi\Big(\sqrt{1+\lambda^2}t_{ci}\Big)}{\Big[1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha\Big]^2} \\
& - \sqrt{\frac{2}{\pi}}\frac{1}{1+\lambda^2}\sum_i I_i\Big(\big(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\big)^\alpha-(\alpha-1)\Big) \\
& \qquad\qquad \times \frac{x_{2ik}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)\phi\Big(\sqrt{1+\lambda^2}t_{ci}\Big)}{\Phi_{\mathrm{SN}}(t_i;\lambda)\Big(1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha\Big)^2} \\
& + \sqrt{\frac{2}{\pi}}\frac{\alpha-1}{\eta}\sum_i(1-I_i)x_{2ik}\Big((1-\lambda^2t_i^2)\omega(\lambda t_i)-t_i\{\omega(\lambda t_i)\}^2\Big) \\
& + \sqrt{\frac{2}{\pi}}\frac{\alpha-1}{\eta}\sum_i(1-I_i)x_{2ik}\nu_\lambda(t_i)\Big(t_i+\frac{1}{1+\lambda^2}\omega_\lambda(t_i)\Big)
\end{aligned}
$$

$$
\begin{aligned}
j_{\alpha\beta_{(2)k}} = {} & \sum_i I_i \frac{x_{2ik}\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{\left[1+\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha\right]^2} \\
& \qquad \times \left(\log\left(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\right) + \alpha^{-1}\left(1+\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha-1}\right)\right) \\
& + \frac{1}{\eta}\sum_i (1-I_i)x_{2ik}\omega_\lambda(t_i)
\end{aligned}
$$

$$
\begin{aligned}
j_{\lambda_2\beta_{(2)k}} = {} & \frac{1}{\lambda_2}\sum_i I_i \frac{x_{2ik}\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha}\left(-1+t_{ci}^2-\alpha t_{ci}\omega_\lambda(t_{ci})\right) \\
& - \sqrt{\frac{2}{\pi}}\frac{\alpha\lambda}{\lambda_2^2} \sum_i I_i \frac{x_{2ik}t_{ci}\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\phi\left(\sqrt{1+\lambda^2}t_i\right)\left(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\right)^{\alpha-1}}{1+\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha} \\
& + \sum_i I_i x_{2ik}t_{ci}\left(\frac{\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha}\right)^2 \\
& + \frac{1}{\lambda_2^2}\sum_i (1-I_i)x_{2ik}\left[2t_i+(\alpha-1)\left(-1+t_i^2+t_i\omega_\lambda(t_i)\right)\omega_\lambda(t_i)\right] \\
& - \sqrt{\frac{2}{\pi}}\frac{\lambda(\alpha-1)}{\lambda_2^2}\sum_i (1-I_i)x_{2ik}t_i\nu_\lambda(t_i) \\
& + \frac{\lambda}{\lambda_2^2}\sum_i (1-I_i)x_{2ik}\omega(\lambda t_i)\left(-1+\lambda^2 t_i^2+t_i\omega(\lambda t_i)\right)
\end{aligned}
$$

$$
\begin{aligned}
j_{\lambda\beta_{(2)k}} = {} & \sqrt{\frac{2}{\pi}}\sum_i I_i \frac{x_{2ik}t_{ci}\left(1+\left(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\right)^\alpha\right)\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)\phi\left(\sqrt{1+\lambda^2}t_{ci}\right)}{\left(1+\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha\right)^2} \\
& - \sqrt{\frac{2}{\pi}}\frac{1}{1+\lambda^2}\sum_i I_i\left(\left(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\right)^\alpha-(\alpha-1)\right) \\
& \qquad \times \frac{x_{2ik}\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)\phi\left(\sqrt{1+\lambda^2}t_{ci}\right)}{\Phi_{\mathrm{SN}}(t_i;\lambda)\left(1+\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha\right)^2} \\
& + \sqrt{\frac{2}{\pi}}\frac{\alpha-1}{\lambda_2}\sum_i (1-I_i)x_{2ik}\left((1-\lambda^2 t_i^2)\omega(\lambda t_i)-t_i\left(\omega(\lambda t_i)\right)^2\right) \\
& + \sqrt{\frac{2}{\pi}}\frac{\alpha-1}{\lambda_2}\sum_i (1-I_i)x_{2ik}\nu_\lambda(t_i)\left(t_i+\frac{1}{1+\lambda^2}\omega_\lambda(t_i)\right)
\end{aligned}
$$

$$
\begin{aligned}
j_{\alpha\beta_{(2)k}} = {} & \sum_i I_i \frac{x_{2ik}\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{\left(1+\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^\alpha\right)^2} \\
& \qquad \times \left(\log\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}+\alpha^{-1}\left(1+\exp(\boldsymbol{x}_{(1)i}^\top \boldsymbol{\beta}_{(1)})\left(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\right)^{\alpha-1}\right)\right) \\
& + \frac{1}{\lambda_2}\sum_i (1-I_i)x_{2ik}\omega_\lambda(t_i)
\end{aligned}
$$

$$
\begin{aligned}
j_{\lambda\lambda_2} = {} & \frac{\alpha}{\lambda_2}\sqrt{\frac{2}{\pi}}\sum_i I_i \frac{t_{ci}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi\Big(\sqrt{1+\lambda^2}t_{ci}\Big)\Big(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\Big)^{\alpha-1}}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}} \\
& \times\left(t_{ci}-\frac{\alpha-1}{1+\lambda^2}\omega_\lambda(t_{ci})+\frac{\lambda_2\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}}\right) \\
& +\frac{1}{\lambda_2}\sum_i(1-I_i)t_i\Big((1-\lambda^2t_i^2)\omega(\lambda t_i)-t_i\big(\omega(\lambda t_i)\big)^2\Big) \\
& +\sqrt{\frac{2}{\pi}}\frac{\alpha-1}{\lambda_2}\sum_i(1-I_i)t_i\nu_\lambda(t_i)\Big(t_i+\frac{1}{1+\lambda^2}\omega_\lambda(t_i)\Big)
\end{aligned}
$$

$$
\begin{aligned}
j_{\lambda\lambda} = {} & \sqrt{\frac{2}{\pi}}\sum_i I_i \frac{\alpha\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi\Big(\sqrt{1+\lambda^2}t_{ci}\Big)\Big(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\Big)^{\alpha-1}}{(1+\lambda^2)\Big(1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}\Big)} \\
& \times\left(\sqrt{\frac{2}{\pi}}\frac{1}{1+\lambda^2}\nu_\lambda(t_{ci})+\frac{2\delta}{\sqrt{1+\lambda^2}}+\lambda t_{ci}^2\right) \\
& -\frac{2}{\pi}\frac{\alpha}{(1+\lambda^2)^2}\sum_i I_i\left(\frac{\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi\Big(\sqrt{1+\lambda^2}t_{ci}\Big)\Big(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\Big)^{\alpha-1}}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}}\right)^2 \\
& +\frac{1}{\lambda_2}\sum_i(1-I_i)t_i^2\Big(\lambda t_i\omega(\lambda t_i)+\big(\omega(\lambda t_i)\big)^2\Big) \\
& -\sqrt{\frac{2}{\pi}}\frac{\alpha-1}{1+\lambda^2}\sum_i(1-I_i)\nu_\lambda(t_i)\left(-\left(\frac{2\delta}{\sqrt{1+\lambda^2}}+\lambda t_i^2\right)+\sqrt{\frac{2}{\pi}}\frac{1}{1+\lambda^2}\nu_\lambda(t_i)\right)
\end{aligned}
$$

$$
\begin{aligned}
j_{\alpha\lambda} = {} & \sqrt{\frac{2}{\pi}}\frac{1}{1+\lambda^2}\quad\sum_i I_i\Bigg(\Big(1+\alpha\log\big(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\big)\Big) \\
& -\frac{\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\big(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\big)^{\alpha-1}\phi\Big(\sqrt{1+\lambda^2}t_{ci}\Big)}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}} \\
& \times\frac{\alpha\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\big(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\big)^{\alpha}\log\big(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\big)}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}}\Bigg) \\
& +\sqrt{\frac{2}{\pi}}\frac{1}{1+\lambda^2}\sum_i(1-I_i)\nu_\lambda(t_i)
\end{aligned}
$$

$$
\begin{aligned}
j_{\lambda_2\lambda_2} = {} & \frac{1}{\lambda_2}\sum_i I_i\frac{t_{ci}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}}\Big(-2+t_{ci}\omega_\lambda(t_{ci})+t_{ci}^2\Big) \\
& +\alpha^{-1}\sum_i I_i+\frac{1}{\lambda_2^2}\sum_i(1-I_i)\Bigg[-1+3t_i^2 \\
& +\lambda t_i\left(\frac{t_{ci}\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^\top\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}}\right)^2(2+\lambda^2t_i^2)\omega(\lambda t_i)+\lambda^2t_i^2\big(\omega(\lambda t_i)\big)^2\Bigg] \\
& +\frac{\alpha-1}{\lambda_2^2}\sum_i(1-I_i)t_i\omega_\lambda(t_i)\Big(-2+t_i^2+t_i\omega_\lambda(t_i)\Big)
\end{aligned}
$$

$$j_{\alpha\lambda} = \sum_i I_i \frac{t_{ci} \log\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\} \exp(\boldsymbol{x}_{(1)i}^{\top}\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^{\top}\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}} \times \left(1 - \frac{\exp(\boldsymbol{x}_{(1)i}^{\top}\boldsymbol{\beta}_{(1)})\left(\Phi_{\mathrm{SN}}(t_{ci};\lambda)\right)^{\alpha}}{1+\exp(\boldsymbol{x}_{(1)i}^{\top}\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}}\right) + \alpha^{-1}\sum_i I_i \frac{t_{ci}\exp(\boldsymbol{x}_{(1)i}^{\top}\boldsymbol{\beta}_{(1)})\phi_{\mathrm{PSN}}(t_{ci};\lambda,\alpha)}{1+\exp(\boldsymbol{x}_{(1)i}^{\top}\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}} + \frac{1}{\lambda_2}\sum_i I_i t_i \omega_{\lambda}(t_i)$$

$$j_{\alpha\alpha} = -\sum_i I_i \frac{\exp(\boldsymbol{x}_{(1)i}^{\top}\boldsymbol{\beta}_{(1)})(\Phi_{\mathrm{SN}}(t_{ci};\lambda))^{\alpha}\log^2(\Phi_{\mathrm{SN}}(t_{ci};\lambda))}{\left(1+\exp(\boldsymbol{x}_{(1)i}^{\top}\boldsymbol{\beta}_{(1)})\{\Phi_{\mathrm{SN}}(t_{ci};\lambda)\}^{\alpha}\right)^2} + \sum_i (1-I_i)\frac{1}{\alpha^2}$$

References

1. Tobin, J. Estimation of relationships for limited dependent variables. *Econometrica* **1958**, *26*, 24–36. [CrossRef]
2. Azzalini, A. A class of distributions which includes the normal ones. *Scand. J. Stat.* **1985**, *12*, 171–178.
3. Durrans, S.R. Distributions of fractional order statistics in hydrology. *Water Resour. Res.* **1992**, *28*, 1649–1655. [CrossRef]
4. Martínez-Flórez, G.; Vergara-Cardozo, S.; González, L.M. The family of log-skew-normal alpha-power distributions using the precipitation data. *Rev. Colomb. EstadÍstica* **2013**, *36*, 351–361.
5. Martínez-Flórez, G.; Bolfarine, H.; Gómez, H.W. Asymmetric regression models with limited responses with an application to antibody response to vaccine. *Biom. J.* **2013**, *55*, 156–172. [CrossRef] [PubMed]
6. Arellano-Valle, R.B.; Castro, L.M.; González-Farias, G.; Muñóz-Gajardo K.A. Student-t censored regression model: Properties and inference. *Stat. Methods Appl.* **2012**, *21*, 453–473. [CrossRef]
7. Martínez-Flórez, G.; Bolfarine, H.; Gómez, H.W. The alpha-power tobit model. *Commun. Stat. Theory Methods* **2013**, *42*, 633–643. [CrossRef]
8. Cragg, J. Some statistical models for limited dependent variables with application to the demand for durable goods. *Econometrica* **1971**, *39*, 829–844. [CrossRef]
9. Moulton, L.; Halsey, N. A mixture model with detection limits for regression analyses of antibody response to vaccine. *Biometrics* **1995**, *51*, 1550–1578. [CrossRef]
10. Moulton, L.; Halsey, N. A mixed gamma model for regression analyses of quantitative assay data. *Vaccine* **1996**, *14*, 1154–1158. [CrossRef]
11. Chai, H.; Bailey, K. Use of log-normal distribution in analysis of continuous data with a discrete component at zero. *Stat. Med.* **2008**, *27*, 3643–3655. [CrossRef] [PubMed]
12. Owen, D.B. Tables for computing bi-variate normal probabilities. *Ann. Math. Stat.* **1956**, *27*,1075–1090. [CrossRef]
13. Pewsey, A.; Gómez, H.; Bolfarine, H. Likelihood-based inference for power distributions. *Test* **2012**, *21*, 775–789. [CrossRef]
14. Azzalini, A.; Cappello, D.; Kotz, S. Log-skew-normal and log-skew-t distributions as models for family income data. *J. Incone Distrib.* **2002**, *11*, 12–20.
15. Rotnitzky, A.; Cox, D.R.; Bottai, M.; Robins, J. Likelihood-based inference with singular information matrix. *Bernoulli* **2000**, *6*, 243–284. [CrossRef]
16. DiCiccio, T.J.; Monti, A.C. Inferential aspects of the skew exponential power distribution. *J. Am. Stat. Assoc.* **2004**, *99*, 439–450. [CrossRef]
17. Gómez, H.W.; Elal-Olivero, D.; Salinas, H.; Bolfarine, H. Bimodal extension based on the skew-normal distribution with application to pollen data. *Environmetrics* **2011**, *22*, 50–62. [CrossRef]
18. Arellano-Valle, R.B.; Azzalini, A. The centred parametrization for the multivariate skew-normal distribution. *J. Multivar. Anal.* **2008**, *99*, 1362–1382. [CrossRef]
19. Job, J.; Halsey, N.; Boulos, R.; Holt, E.; Farrel, D.; Albrecht, P.; Brutus, J.; Adrien, M.; Andre, J.; Chan, E.; et al. The cite soleil/JHU project team. Successful immunization of infants at 6 months of age with high dose Edmonston-Zagreb measles vaccine. *Pediatr. Infect. Dis. J.* **1991**, *30*, 303–311. [CrossRef] [PubMed]
20. R Development Core Team. *R: A Language and Environment for Statistical Computing*; R Foundation for Statistical Computing: Vienna, Austria, 2019. Available online: http://www.R-project.org (accessed on 22 February 2021).
21. Akaike, H. A new look at statistical model identification. *IEEE Trans. Autom. Control* **1974**, *AU–19*, 716–722. [CrossRef]