Measurement error model with a general class of error distribution for the surrogate variable

Alexandre Galvão Patriota
joint work with Heleno Bolfarine

Department of Statistics
Institute of Mathematics and Statistics
University of São Paulo
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Motivating example
Sleep disordered breathing

One interest in epidemiological studies is to analyze the relation between:

**blood pressure** \((Y)\) and **sleep disordered breathing** \((x)\)

and other variable such as gender \((w_1)\), age \((w_2)\) and body mass index \((w_3)\).

**Problem:**

The sleep disordered breathing cannot be observed directly.
The surrogate variable

The **apnea-hypopnea index** \((X)\) is observed in the place of the sleep disordered breathing:

\[
\text{It is the number of occurrences of apnea and hypopnea per sleep hour.}
\]

- **Apnea** occurs when there is no breathing during 10 seconds;
- **Hypopnea** occurs when there is a breathing reduction detected by airway obstruction noises.

The AHI \((X)\) and SDB \((x)\) are assumed to be connected by (Li, Palta and Shao, 2004)

\[
X|x \sim \text{Poisson}(x).
\]
### Wisconsin sleep cohort study data

<table>
<thead>
<tr>
<th>Ind</th>
<th>SBP</th>
<th>AHI</th>
<th>AGE</th>
<th>BMI</th>
<th>Gender</th>
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</tbody>
</table>

**SBP**: systolic blood pressure  
**AHI**: apnea-hypopnea index  
**BMI**: body mass index  
**Sample size**: 130 males and 83 females
Wisconsin sleep cohort study data
On the simple measurement error model

Typically, the measurement error model is composed by two equations.

The regression equation:

\[ Y_i = \beta + \gamma x_i + e_i \]

The measurement equation:

\[ X_i = x_i + u_i \quad \text{or} \quad X_i = u_i x_i \]

where \( u_i, e_i, i = 1, \ldots, n \), are independent random variables (usually normally distributed).

**Structural model:** \( x_i, i = 1, \ldots, n \), are random variables.

**Functional model:** \( x_i, i = 1, \ldots, n \), are incidental parameters.
The measurement error equation

The measurement equations could simply be replaced by:

\[ X_i | x_i \overset{ind}{\sim} F_{X_i | x_i} \]

which contains all the probabilistic information of the measurement equation.

In this presentation, I consider the above expression in the place of the measurement error equation.
The proposed Model
The proposed model

Let \((Y_i, W_i^\top, X_i^\top)^\top, i \geq 1\), be vectors related by the following equations

\[
Y_i = \beta^\top W_i + \gamma^\top x_i + e_i, \\
X_i | x_i \sim \text{ind} F_{X_i | x_i} \in C(x_i, g_1, g_2),
\]

(1)

- \(Y_i\) is the dependent random variable,
- \(W_i \in \mathbb{R}^q\) is a vector of covariate measured without error,
- \(x_i \in \mathbb{R}^p\) is a vector of unobservable covariates
- \(X_i \in \mathbb{R}^p\) is the surrogate of \(x_i\),
- \(e_i \sim \text{iid} \mathcal{N}(0, \sigma^2)\) is the model error (it could be a skewed distribution).

Also, \(F_{X_i | x_i}\) is the unknown distribution of \(X_i\) given \(x_i\) which lies in the class of distributions \(C(x_i, g_1, g_2)\), where the functions \(g_1(.)\) and \(g_2(.)\) are known and must satisfy the following conditions

\[
E[g_1(X_i) | x_i] = x_i \quad \text{and} \quad E[g_2(X_i) | x_i] = x_i x_i^\top
\]

(2)
Remarks

- We use the corrected score method proposed by Nakamura (1990) to conduct inferences about the parameters $\beta$, $\gamma$ and $\sigma^2$.

- It is not necessary to know the shape of $F_{X_i|x_i}$.

- It is only required to know the shape of $g_1$ and $g_2$ to employ this methodology.

Next we present same examples of $g_1$ and $g_2$. 
Particular cases
Normal distribution and $p = 1$

Assume that $X_i|x_i \sim N(x_i, \phi)$, where $\phi > 0$ is known. Then,

- $E(X_i|x_i) = x_i$ and $E(X_i^2|x_i) = \phi + x_i^2$

- $g_1(X_i) = X_i$ and $g_2(X_i) = X_i^2 - \phi$.

It is the additive model: $X_i = x_i + u_i$, where $u_i \sim N(0, \phi)$.

Notice that any distribution $F_{X_i|x_i}$ that yields the same $g_1$ and $g_2$ as above is such that $F_{X_i|x_i} \in C(x_i, g_1, g_2)$. 
Poisson distribution and $p = 1$

Assume that $X_i | x_i \sim \text{Poisson}(x_i)$. Then,

- $E(X_i | x_i) = x_i$ and $E(X_i^2 - X_i | x_i) = x_i^2$

- $g_1(X_i) = X_i$ and $g_2(X_i) = X_i^2 - X_i$.

Notice that any distribution $F_{X_i | x_i}$ such that

$$E(X_i | x_i) = \text{Var}(X_i | x_i) = x_i$$

produces the same $g_1$ and $g_2$ as above is such that $F_{X_i | x_i} \in C(x_i, g_1, g_2)$.
Multiplicative normal model or Gamma distribution and $p = 1$

Assume $X_i | x_i \sim N(x_i, x_i^2 \phi)$, with $\phi > 0$ known, then

- $E(X_i | x_i) = x_i$ and $E(X_i^2 | x_i) = (\phi + 1)x_i^2$
- $g_1(X_i) = X_i$ and $g_2(X_i) = X_i^2 / (\phi + 1)$.

It is the multiplicative model: $X_i = x_i u_i$, where $u_i \sim N(1, \phi)$.

Notice that, $X_i | x_i \sim \text{Gamma}(x_i, \phi)$, where $E(X_i | x_i) = x_i$ and $\text{Var}(X_i | x_i) = x_i^2 \phi$ also yields the same functions above. This gamma distribution is a reparameterization of the usual version.

That is, $N(x_i, x_i^2 \phi), \text{Gamma}(x_i, \phi) \in C(x_i, g_1, g_2)$
Examples of $g_1$ and $g_2$ for the multivariate normal distribution

Assume $X_i | x_i \sim N_p(x_i, \Sigma_i)$, where $\Sigma_i$ is known for each $i = 1, \ldots, n$. Then,

- $E(X_i | x_i) = x_i$ and $E(X_i X_i^\top | x_i) = \Sigma_i + x_i x_i^\top$

- $g_1(X_i) = X_i$ and $g_2(X_i) = X_i X_i^\top - \Sigma_i$. 
Examples of $g_1$ and $g_2$ for a ‘mixed’ multivariate distribution

Assume $X_i = (X_{1i}, X_{2i})^\top$ such that $X_{1i} \sim \mathcal{N}(x_{1i}, \phi_i)$, $X_{2i} \sim \text{Poisson}(x_{2i})$ and $\text{Cov}(X_{1i}, X_{2i}) = a_i$ known for each $i = 1, \ldots, n$. Then,

- $E(X_i | x_i) = x_i$ and $E(X_i X_i^\top | x_i) = \begin{bmatrix} x_{1i}^2 + \phi_i & x_{1i} x_{2i} + a_i \\ x_{1i} x_{2i} + a_i & x_{2i}^2 + x_{2i} \end{bmatrix}$

- $g_1(X_i) = X_i$, $g_2(X_i) = \begin{bmatrix} X_{1i}^2 - \phi_i & X_{1i} X_{2i} - a_i \\ X_{1i} X_{2i} - a_i & X_{2i}^2 - X_{2i} \end{bmatrix}$. 
Estimation procedure
Estimation procedure

We use the corrected score methodology proposed by Nakamura (1990).

We need to find a pseudo-log-likelihood function $\ell^+$ which depends only on the observed data $(Y, W, X)$ such that

$$E[\ell^+(\theta, Y, W, X)|Y, W, x] = \ell(\theta, Y, W, x)$$

where

$$\theta = (\beta^\top, \gamma^\top, \sigma^2)^\top$$

$\ell^+(\theta, Y, W, X)$ is the corrected log-likelihood function

$\ell(\theta, Y, W, x)$ is the “true” log-likelihood function as if $x$ were observed.
How to find $\ell^+$

In order to find $\ell^+$, we use the likelihood function attained by means of the model

$$Y_i = \beta^\top W_i + \gamma^\top x_i + e_i.$$  \hfill (3)

Let $\ell(\theta, Y, W, x)$ be the log-likelihood function related with (3), then

$$\ell(\theta, Y, W, x) = c - \frac{n}{2} \log \sigma^2 - \frac{1}{2\sigma^2} \sum_{i=1}^n \{ (Y_i - \beta^\top W_i)^2 +$$

$$- 2(Y_i - \beta^\top W_i) x_i^\top \gamma + \gamma^\top x_i x_i^\top \gamma \}$$
How to find $\ell^+$

Replacing $x_i$ with $X_i$, we obtain the “naïve” log-likelihood function $\ell(\theta, Y, W, X)$:

$$\ell(\theta, Y, W, X) = c - \frac{n}{2} \log \sigma^2 - \frac{1}{2\sigma^2} \sum_{i=1}^{n} \{(Y_i - \beta^\top W_i)^2 +$$

$$- 2(Y_i - \beta^\top W_i)X_i^\top \gamma + \gamma^\top X_i X_i^\top \gamma\}$$

and from the naïve log-likelihood function we obtain the corrected log-likelihood function

$$\ell^+(\theta, Y, W, X) = c - \frac{n}{2} \log \sigma^2 - \frac{1}{2\sigma^2} \sum_{i=1}^{n} \{(Y_i - \beta^\top W_i)^2 +$$

$$- 2(Y_i - \beta^\top W_i)g_1(X_i)^\top \gamma + \gamma^\top g_2(X_i)\gamma\}$$

which satisfies

$$E\left[\ell^+(\theta, Y, W, X) | Y, W, x\right] = \ell(\theta, Y, W, x)$$
Maximizing $\ell^+$ with respect to the parameters, we obtain

$$\hat{\beta}_n = \left( \sum_{i=1}^{n} W_i W_i^\top \right)^{-1} \sum_{i=1}^{n} W_i \left[ Y_i - \gamma^\top g_1(X_i) \right],$$

$$\hat{\gamma}_n = H_n^{-1} \left[ \sum_{i=1}^{n} g_1(X_i) Y_i - \sum_{i=1}^{n} g_1(X_i) W_i^\top \left( \sum_{i=1}^{n} W_i W_i^\top \right)^{-1} \sum_{i=1}^{n} W_i Y_i \right]$$

and

$$\hat{\sigma}_n^2 = \frac{1}{n} \sum_{i=1}^{n} \left\{ (Y_i - \beta^\top W_i)^2 - 2(Y_i - \beta^\top W_i) g_1(X_i)^\top \gamma + \gamma^\top g_2(X_i) \gamma \right\},$$

where

$$H_n = \sum_i g_2(X_i)^\top - \sum_i g_1(X_i) W_i^\top \left( \sum_i W_i W_i^\top \right)^{-1} \sum_i W_i g_1(X_i)^\top.$$
Asymptotic distribution

Under certain regular conditions (Gimenez and Bolfarine, 1997), we have that

$$\sqrt{n}L_n^{1/2}(\hat{\theta}_n - \theta) \xrightarrow{D} \mathcal{N}_s(0, I)$$

where $s = p + q + 1$,

$$L_n^{1/2} = \bar{\Gamma}_n(\hat{\theta}_n)^{-1/2}\bar{\Lambda}_n(\hat{\theta}_n),$$

$$\bar{\Gamma}_n(\theta) = \frac{1}{n} \sum_{i=1}^{n} \frac{\partial \ell_i^+(\theta)}{\partial \theta} \frac{\partial \ell_i^+(\theta)}{\partial \theta^\top}, \quad \bar{\Lambda}_n(\theta) = \frac{1}{n} \sum_{i=1}^{n} \frac{\partial^2 \ell_i^+(\theta)}{\partial \theta \partial \theta^\top}$$

and

$$\ell^+(\theta) = \sum_{i=1}^{n} \ell_i^+(\theta)$$
Testing a general linear hypothesis

Wald statistics can be used to test the general null hypothesis $H_0 : C\theta = d$ against $H_1 : C\theta \neq d$, 

\[ \mathcal{W}_{H_0} = n(C\hat{\theta}_n - d)^\top [CL_n^{-1}C^\top]^{-1}(C\hat{\theta}_n - d) \xrightarrow{D} \chi^2_k \]

where $k = \text{rank}(C)$.

The asymptotic covariance matrix for $\hat{\theta}_n$ can be estimated by 

\[ \text{Cov}_a(\hat{\theta}_n) = \frac{1}{n}L_n^{-1} = \frac{1}{n}L_n^{-1/2}L_n^{-1/2\top} \]
Examples
Normal case

In the next slides, I consider the model: $Y_i = \beta + \gamma x_i + e_i$, where $e_i \sim \text{iid } N(0, \sigma^2)$.

1. Normal: $X_i | x_i \sim N(x_i, \phi_i^2)$ with $\phi_i$ known for each $i = 1, \ldots, n$.

\[
\hat{\beta}_n = \bar{Y} - \hat{\gamma}_n \bar{X}, \quad \hat{\gamma}_n = \frac{\sum_{i=1}^{n} Y_i X_i - n \bar{Y} \bar{X}}{\sum_{i=1}^{n} X_i^2 - n \bar{X}^2 - \sum_{i=1}^{n} \phi_i^2}
\]

and

\[
\hat{\sigma}_n^2 = \frac{1}{n} \sum_{i=1}^{n} \left\{ (Y_i - \hat{\beta}_n - \hat{\gamma}_n X_i)^2 - \phi_i^2 \hat{\gamma}_n^2 \right\}.
\]
2. Gamma: $X_i|x_i \sim \text{Gamma}(x_i, \phi)$ with $\phi$ known.

$$\hat{\beta}_n = \bar{Y} - \hat{\gamma}_n \bar{X}, \quad \hat{\gamma}_n = \frac{\sum_{i=1}^{n} Y_i X_i - n \bar{Y} \bar{X}}{(1 + \phi)^{-1} \sum_{i=1}^{n} X_i^2 - n \bar{X}^2}$$

and

$$\hat{\sigma}_n^2 = \frac{1}{n} \sum_{i=1}^{n} \left( Y_i - \hat{\beta}_n - \hat{\gamma}_n X_i \right)^2 - \frac{\phi}{1 + \phi} \hat{\gamma}_n^2 X_i^2.$$
Poisson distribution

Poisson: $X_i | x_i \sim \text{Poisson}(x_i)$.

$$
\hat{\beta}_n = \bar{Y} - \hat{\gamma}_n \bar{X}, \quad \hat{\gamma}_n = \frac{\sum_{i=1}^{n} Y_i X_i - n \bar{Y} \bar{X}}{\sum_{i=1}^{n} X_i^2 - n \bar{X} (1 + \bar{X})}
$$

and

$$
\hat{\sigma}_n^2 = \frac{1}{n} \sum_{i=1}^{n} \left\{ (Y_i - \hat{\beta}_n - \hat{\gamma}_n X_i)^2 - \hat{\gamma}_n^2 X_i \right\}.
$$

This case was studied by Li, Palta and Shao (2004).
Simulations
Consider the model \( Y_i = \beta_1 + \beta_2 T_i + \gamma x_i + e_i \), where \( T_i \) represents the treatment indicator. The parameter values are: \( \beta_1 = 1 \), \( \beta_2 = 2 \), \( \gamma = 1 \) and \( \text{Var}(e_i) = 5 \).

Consider also that \( x_i \sim \text{Uniform}\{1, \ldots, 10\} \), \( i = 1, \ldots, n \). We generate 25 000 Monte Carlo simulations under two scenarios:

i. \( X_i|x_i \sim \text{Gamma}(x_i, 0.01) \)

ii. \( X_i|x_i \sim \text{Poisson}(x_i) \),

The following sample sizes are considered \( n = 20 \), \( n = 50 \), \( n = 100 \) and \( n = 200 \).

The Bias and the Mean Square Error (MSE) are presented.
## Gamma distribution

<table>
<thead>
<tr>
<th>Sample size</th>
<th>Negative variance</th>
<th>( \beta_1 )</th>
<th>( \beta_2 )</th>
<th>( \gamma )</th>
<th>( \sigma^2 )</th>
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<tbody>
<tr>
<td>MSE n=50</td>
<td>0.58%</td>
<td>0.6749</td>
<td>0.3428</td>
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<td>1.6996</td>
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<td>Bias</td>
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<td>-0.2056</td>
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<td>MSE n=100</td>
<td>0%</td>
<td>0.2593</td>
<td>0.1470</td>
<td>0.0103</td>
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<td>Bias</td>
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<td>-0.1023</td>
<td>-0.0004</td>
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<td>-0.3618</td>
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<td>MSE n=200</td>
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<td>0.1576</td>
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### Poisson distribution

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<td>$\beta_1$</td>
<td>$\beta_2$</td>
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<tr>
<td>Bias</td>
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<td>-0.1877</td>
<td>0.0310</td>
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<tr>
<td>MSE n=100</td>
<td>0.32%</td>
<td>0.4037</td>
<td>0.1912</td>
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<tr>
<td>Bias</td>
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<td>0.0095</td>
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<tr>
<td>MSE n=200</td>
<td>0.01%</td>
<td>0.2221</td>
<td>0.0970</td>
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<tr>
<td>Bias</td>
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<td>-0.0075</td>
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Testing $H_0: \gamma = \gamma_0$: significance level 5%

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<td>3</td>
<td>5.31</td>
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Testing $H_0: \gamma = \gamma_0$: significance level 5%

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<th>$\gamma$</th>
<th>Gamma Proposed Model</th>
<th>Gamma Naïve Model</th>
<th>Poisson Proposed Model</th>
<th>Poisson Naïve Model</th>
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<tr>
<td>-3</td>
<td>5.44</td>
<td>$&lt;0.01$</td>
<td>5.83</td>
<td>1.32</td>
</tr>
<tr>
<td>-2</td>
<td>5.03</td>
<td>$&lt;0.01$</td>
<td>5.62</td>
<td>0.63</td>
</tr>
<tr>
<td>$\gamma_0$</td>
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<td>0.02</td>
<td>4.77</td>
<td>0.01</td>
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<tr>
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<td>4.86</td>
<td>0.02</td>
<td>4.80</td>
<td>0.03</td>
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<td>$&lt;0.01$</td>
<td>5.50</td>
<td>0.60</td>
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<tr>
<td>3</td>
<td>4.98</td>
<td>$&lt;0.01$</td>
<td>6.06</td>
<td>1.16</td>
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$n = 100$
Testing $H_0 : \gamma = \gamma_0$: significance level 5%

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<th>Gamma</th>
<th>Poisson</th>
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<td>Proposed Model</td>
<td>Naïve Model</td>
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<tr>
<td>$n = 200$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-3</td>
<td>5.16 &lt;0.01</td>
<td>5.88 0.51</td>
</tr>
<tr>
<td>-2</td>
<td>5.03 &lt;0.01</td>
<td>5.30 0.10</td>
</tr>
<tr>
<td>$\gamma_0$</td>
<td>4.71 0.01</td>
<td>4.73 &lt;0.01</td>
</tr>
<tr>
<td>1</td>
<td>4.91 &lt;0.01</td>
<td>4.74 &lt;0.01</td>
</tr>
<tr>
<td>2</td>
<td>4.75 &lt;0.01</td>
<td>5.22 0.14</td>
</tr>
<tr>
<td>3</td>
<td>5.44 &lt;0.01</td>
<td>5.95 0.48</td>
</tr>
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Application
Wisconsin sleep cohort study data

The model for the Wisconsin sleep cohort study data is

\[ Y_i = \beta_0 + \beta_1 W_{1i} + \beta_2 W_{2i} + \beta_3 W_{3i} + \gamma x_i + e_i, \]

where \( W_{1i} \): is the age; \( W_{2i} \): is the body mass index; \( W_{3i} \): is the gender (1=male; 0 = Female); \( x_i \): represents the sleep disordered breathing; and \( X_i \) is the observed apnea-hypopnea index (Poisson distribution).

<table>
<thead>
<tr>
<th></th>
<th>Naïve model</th>
<th>Proposed model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimative (SD)</td>
<td>Estimative (SD)</td>
</tr>
<tr>
<td>( \beta_0 )</td>
<td>78 (7.53)</td>
<td>78 (7.60)</td>
</tr>
<tr>
<td>( \beta_1 )</td>
<td>0.41 (0.11)</td>
<td>0.41 (0.11)</td>
</tr>
<tr>
<td>( \beta_2 )</td>
<td>0.80 (0.16)</td>
<td>0.79 (0.16)</td>
</tr>
<tr>
<td>( \beta_3 )</td>
<td>5.86 (1.82)</td>
<td>5.81 (1.84)</td>
</tr>
<tr>
<td>( \gamma )</td>
<td>0.59 (0.30)</td>
<td>0.62 (0.30)</td>
</tr>
<tr>
<td>( \sigma^2 )</td>
<td>150</td>
<td>145</td>
</tr>
</tbody>
</table>
Final remarks
Final remarks

- This work generalizes the results proposed in Li, Palta and Shao (2004). The authors considered only a Poisson distribution to the surrogate covariate.

- We are still working on a polynomial regression model:

\[
Y_i = \beta^\top W_i + \gamma_1 x_i + \gamma_2 x_i^2 + \ldots + \gamma_p x_i^p + e_i
\]

\[
X_i | x_i \sim \mathcal{G} \in \mathcal{C}(x_i, g_1, g_2, \ldots, g_{2p})
\]

- The distribution of the error \( e_i \) could be in the class of elliptical or skew distributions.
References
References


Thank you