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# Insensitivity Region for Variance Components in General Linear Model

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## Abstract

In linear regression models the estimator of variance components needs a suitable choice of a starting point for an iterative procedure for a determination of the estimate. The aim of this paper is to find a criterion for a decision whether a linear regression model enables to determine the estimate reasonably and whether it is possible to do so when using the given data.

**Key words:** Linear regression model; variance components; insensitivity region.

**2000 Mathematics Subject Classification:** 62J05, 62F10

## 1 Notation

$\mathbf{Y} \sim N_n(\mathbf{X}\boldsymbol{\beta}, \boldsymbol{\Sigma}_\theta)$	the $n$ -dimensional random vector $\mathbf{Y}$ possesses the normal distribution with the mean value $\mathbf{X}\boldsymbol{\beta}$ and variance-covariance matrix $\boldsymbol{\Sigma}_\theta$
$\{\mathbf{A}\}_{i,j}$	the component of matrix $\mathbf{A}$ on its $(i,j)$ -th position
$r(\mathbf{A})$	the rank of the matrix $\mathbf{A}$
$\text{Tr}(\mathbf{A})$	the trace of the square matrix $\mathbf{A}$ , $\text{Tr}(\mathbf{A}) = \sum_i \{\mathbf{A}\}_{i,i}$
$\mathbf{A}^+$	the Moore–Penrose generalized matrix inverse (see [4] for more details)
$\mathbf{M}_\mathbf{A}$	the projection matrix on an orthogonal complement (in Euclidean sense) of the column space of the matrix $\mathbf{A}$
$\left. \frac{\partial \mathbf{A}}{\partial \mathbf{t}} \right _{\mathbf{t}=\mathbf{t}_0}$	the value of the partial derivative of the matrix $\mathbf{A}$ according to $\mathbf{t}$ for $\mathbf{t} = \mathbf{t}_0$

## 2 Introduction

The main aim of this paper is to describe how the variance components estimates in a linear regression model depend on small input prior variance components values changes. We need some input prior values of the variance components when computing their minimum norm quadratic unbiased estimators (MINQUE). The question is how to get these prior values and whether the choice is suitable. We can figure out the variances of the estimates based on the given prior values and then investigate how these variances change when using different prior values. Having the estimates variances not too high seems to be a comprehensible requirement. So the task now is to find a set of admissible changes of the input variance components values (for the given variance components prior values), it means a set of such changes of the input values which cause  $\varepsilon$ -multiple increase of the estimates variances at the most.

## 3 General linear regression model

Let's consider following regression model (according to [5], page 62):

$$\mathbf{Y} \sim N_n(\mathbf{X}\boldsymbol{\beta}, \boldsymbol{\Sigma}_\theta). \quad (1)$$

Suppose that  $n \times k$  matrix  $\mathbf{X}$  is known and of full column rank  $r(\mathbf{X}) = k$ ,  $\boldsymbol{\beta} = (\beta_1, \beta_2, \dots, \beta_k)'$  is a vector of unknown fixed effects parameters and the variance-covariance matrix  $\boldsymbol{\Sigma}_\theta$  satisfies

$$\boldsymbol{\Sigma}_\theta = \sum_{i=1}^r \theta_i \mathbf{V}_i. \quad (2)$$

$\theta_1, \theta_2, \dots, \theta_r$  in (2) are unknown variance components (the object of our interest) and  $\mathbf{V}_1, \mathbf{V}_2, \dots, \mathbf{V}_r$  are known symmetrical matrices. We suppose  $\boldsymbol{\Sigma}_\theta$  is positive definite. No restrictions such as  $\theta_i \geq 0$  or  $\mathbf{V}_i$  positive semidefinite need hold.

## 4 Variance components insensitivity region

### 4.1 Variance components estimator

According to [4], page 101 the  $\theta_0$ -MINQUE (it means the minimum norm quadratic unbiased estimator with prior variance components values  $\theta_0$ ) of variance components  $\boldsymbol{\theta} = (\theta_1, \dots, \theta_r)'$  in model (1) is

$$\widehat{\boldsymbol{\theta}}(\theta_0) = \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1} \begin{pmatrix} \mathbf{Y}'(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_1 (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{Y} \\ \vdots \\ \mathbf{Y}'(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_r (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{Y} \end{pmatrix} \quad (3)$$

and the variance-covariance matrix of the variance components estimates  $\widehat{\boldsymbol{\theta}}(\theta_0)$  is

$$\text{Var}_{\boldsymbol{\theta}_0} \left( \widehat{\boldsymbol{\theta}}(\theta_0) \right) = 2\mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1} \quad (4)$$

where (see [4], page 171)

$$(\mathbf{M}_{\mathbf{X}}\boldsymbol{\Sigma}_{\theta_0}\mathbf{M}_{\mathbf{X}})^+ = \boldsymbol{\Sigma}_{\theta_0}^{-1} - \boldsymbol{\Sigma}_{\theta_0}^{-1}\mathbf{X}(\mathbf{X}'\boldsymbol{\Sigma}_{\theta_0}^{-1}\mathbf{X})^{-1}\mathbf{X}'\boldsymbol{\Sigma}_{\theta_0}^{-1} \quad (5)$$

and  $\mathbf{S}_{(\mathbf{M}_{\mathbf{X}}\boldsymbol{\Sigma}_{\theta_0}\mathbf{M}_{\mathbf{X}})^+}$  is matrix with

$$\left\{ \mathbf{S}_{(\mathbf{M}_{\mathbf{X}}\boldsymbol{\Sigma}_{\theta_0}\mathbf{M}_{\mathbf{X}})^+} \right\}_{i,j} = \text{Tr} [\mathbf{V}_i(\mathbf{M}_{\mathbf{X}}\boldsymbol{\Sigma}_{\theta_0}\mathbf{M}_{\mathbf{X}})^+ \mathbf{V}_j(\mathbf{M}_{\mathbf{X}}\boldsymbol{\Sigma}_{\theta_0}\mathbf{M}_{\mathbf{X}})^+]$$

on its  $(i, j)$ -th position.

In practice in the first step the value  $\boldsymbol{\theta}_0$  in (3) can be chosen arbitrarily. In the second step the value of  $\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0)$  is chosen instead of  $\boldsymbol{\theta}_0$ . In this way we can proceed and stop the iterative procedure after a suitable number of the steps. The problem is to recognize whether the choice of the starting value  $\boldsymbol{\theta}_0$  is sufficient for deriving a reasonable estimate of  $\boldsymbol{\theta}$  and whether it is sufficient for stopping the iterative procedure already after the first step. This problem can be solved as follows.

It seems to be comprehensible to have the variances of the  $\theta_i$  estimators not too high. Let's use some given linear combination of the components of vector  $\boldsymbol{\theta}$ . Suppose that the coefficients of this linear combination are the components of vector  $\mathbf{g}$ . We will investigate the variance of the estimator of  $\mathbf{g}'\boldsymbol{\theta}$  instead of variances of all the variance components separately.

**Remark 4.1** We achieve the equality  $\mathbf{g}'\boldsymbol{\theta} = \theta_i$  when using the  $i$ -th unit vector for  $\mathbf{g}$ . It means we still have the possibility to take the variance of the estimator of each of the variance components under control and moreover we can monitor the variances of different linear combinations of the variance components.

As we know the  $\boldsymbol{\theta}$  estimator  $\widehat{\boldsymbol{\theta}}$  depends on the prior input value  $\boldsymbol{\theta}_0$ , it is  $\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0)$ . Next we find out the difference between the variance of  $\mathbf{g}'\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0)$  and the variance of  $\mathbf{g}'\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0 + \delta\boldsymbol{\theta})$ . A set  $\mathcal{N}_{\mathbf{g},\boldsymbol{\theta}_0}$  can be found such that  $\boldsymbol{\theta}_0 + \delta\boldsymbol{\theta} \in \mathcal{N}_{\mathbf{g},\boldsymbol{\theta}_0}$  leads to the inequality

$$\sqrt{\text{Var}_{\boldsymbol{\theta}_0} [\mathbf{g}'\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0 + \delta\boldsymbol{\theta})]} \leq (1 + \varepsilon) \sqrt{\text{Var}_{\boldsymbol{\theta}_0} [\mathbf{g}'\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0)]}, \quad (6)$$

where  $\varepsilon > 0$  is a sufficiently small real number.

We are looking after a set of  $\delta\boldsymbol{\theta}$ —small changes of input variance components values—holding (6) for a given  $r$ -dimensional vector  $\mathbf{g}$  and given  $\boldsymbol{\theta}_0$  in what follows.

In order to find such a set we need to express  $\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0 + \delta\boldsymbol{\theta})$ . We can approximate it like this

$$\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0 + \delta\boldsymbol{\theta}) \approx \widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0) + \sum_{i=1}^r \left. \frac{\partial \widehat{\boldsymbol{\theta}}(\boldsymbol{\theta})}{\partial \theta_i} \right|_{\boldsymbol{\theta}=\boldsymbol{\theta}_0} \cdot \delta\theta_i. \quad (7)$$

The appropriate linear combination  $\mathbf{g}'\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0 + \delta\boldsymbol{\theta})$  of variance components estimator fulfils

$$\mathbf{g}'\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0 + \delta\boldsymbol{\theta}) \approx \mathbf{g}'\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0) + \sum_{i=1}^r \left. \frac{\partial \mathbf{g}'\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta})}{\partial \theta_i} \right|_{\boldsymbol{\theta}=\boldsymbol{\theta}_0} \cdot \delta\theta_i. \quad (8)$$

Thus we need to know the partial derivative  $\frac{\partial \hat{\boldsymbol{\theta}}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}$ .

At first let us find the first derivative of  $\{\mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta} \mathbf{M}_X)^+}\}_{i,j}$  according to  $\theta_k$ :

$$\begin{aligned} \left. \left\{ \frac{\partial \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta} \mathbf{M}_X)^+}}{\partial \theta_k} \right\}_{i,j} \right|_{\boldsymbol{\theta}=\boldsymbol{\theta}_0} &= \frac{\partial}{\partial \theta_k} \text{Tr} \left[ \mathbf{V}_i (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta} \mathbf{M}_X)^+ \mathbf{V}_j (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta} \mathbf{M}_X)^+ \right] \Big|_{\boldsymbol{\theta}=\boldsymbol{\theta}_0} \\ &= \text{Tr} \left[ \mathbf{V}_i (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{M}_X \mathbf{V}_k \mathbf{M}_X (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_j (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \right. \\ &\quad \left. + \mathbf{V}_i (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_j (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{M}_X \mathbf{V}_k \mathbf{M}_X (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \right] \\ &= 2 \text{Tr} \left[ \mathbf{V}_i (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{M}_X \mathbf{V}_k \mathbf{M}_X (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_j (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \right]. \end{aligned}$$

If we denote matrix having

$$\text{Tr} (\mathbf{V}_i \mathbf{A} \mathbf{V}_j \mathbf{B}), \quad (9)$$

on its  $(i, j)$ -th position with  $\mathbf{C}_{\mathbf{A}, \mathbf{B}}$  (for arbitrary matrices  $\mathbf{A}, \mathbf{B}$  of  $n \times n$  dimension), we can continue as follows

$$\begin{aligned} \left. \frac{\partial \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta} \mathbf{M}_X)^+}}{\partial \theta_k} \right|_{\boldsymbol{\theta}=\boldsymbol{\theta}_0} &= 2 \mathbf{C}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{M}_X \mathbf{V}_k \mathbf{M}_X (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+, (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+} \\ &= 2 \mathbf{C}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+, (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}. \end{aligned}$$

Let's introduce following notation

$$\boldsymbol{\gamma} = \begin{pmatrix} \mathbf{Y}' (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_1 (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{Y} \\ \vdots \\ \mathbf{Y}' (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_r (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{Y} \end{pmatrix}.$$

Now we can write

$$\begin{aligned} \left. \frac{\partial \hat{\boldsymbol{\theta}}(\boldsymbol{\theta})}{\partial \theta_k} \right|_{\boldsymbol{\theta}=\boldsymbol{\theta}_0} &= -2 \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1} \\ &\quad \times \mathbf{C}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+, (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+} + \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1} \\ &\quad + \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1} \\ &\quad \times \begin{pmatrix} 2 \mathbf{Y}' (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_1 (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{Y} \\ \vdots \\ 2 \mathbf{Y}' (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_r (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{Y} \end{pmatrix}. \quad (10) \end{aligned}$$

According to (10) we have

$$\left. \frac{\partial \mathbf{g}' \hat{\boldsymbol{\theta}}(\boldsymbol{\theta})}{\partial \theta_k} \right|_{\boldsymbol{\theta}=\boldsymbol{\theta}_0} = -2 \mathbf{g}' \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1}$$

$$\begin{aligned}
 & \times \mathbf{C}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+, (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1} + \boldsymbol{\gamma}} \\
 & \quad + 2\mathbf{g}' \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1} \\
 & \times \begin{pmatrix} \mathbf{Y}' (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_1 (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{Y} \\ \vdots \\ \mathbf{Y}' (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_r (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{Y} \end{pmatrix}. \quad (11)
 \end{aligned}$$

If we denote

$$\begin{aligned}
 \mathbf{a}'_k &= \mathbf{g}' \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1} \\
 & \times \mathbf{C}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+, (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1}},
 \end{aligned}$$

$$\mathbf{b}'_g = \mathbf{g}' \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+}^{-1}$$

and

$$\boldsymbol{\zeta}_k = \begin{pmatrix} \mathbf{Y}' (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_1 (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{Y} \\ \vdots \\ \mathbf{Y}' (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{V}_r (\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{Y} \end{pmatrix},$$

we can write

$$\left. \frac{\partial \mathbf{g}' \widehat{\boldsymbol{\theta}}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}} \right|_{\boldsymbol{\theta}=\boldsymbol{\theta}_0} = -2 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \boldsymbol{\gamma} + 2 \begin{pmatrix} \mathbf{b}'_g \boldsymbol{\zeta}_1 \\ \vdots \\ \mathbf{b}'_g \boldsymbol{\zeta}_r \end{pmatrix}. \quad (12)$$

Using (8) together with (12) we get

$$\mathbf{g}' \widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0 + \delta \boldsymbol{\theta}) \approx \mathbf{g}' \widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0) + (\delta \boldsymbol{\theta})' \left[ -2 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \boldsymbol{\gamma} + 2 \begin{pmatrix} \mathbf{b}'_g \boldsymbol{\zeta}_1 \\ \vdots \\ \mathbf{b}'_g \boldsymbol{\zeta}_r \end{pmatrix} \right]. \quad (13)$$

## 4.2 $\text{Var}_{\boldsymbol{\theta}_0} \left[ \mathbf{g}' \widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0 + \delta \boldsymbol{\theta}) \right]$ derivation

In order to find a set of  $\delta \boldsymbol{\theta}$  which is described in (6) we have to derive

$$\text{Var}_{\boldsymbol{\theta}_0} \left[ \mathbf{g}' \widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0 + \delta \boldsymbol{\theta}) \right].$$

According to (4)

$$\text{Var}_{\boldsymbol{\theta}_0} \left[ \mathbf{g}' \widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0) \right] = 2\mathbf{g}' \mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\theta_0} \mathbf{M}_X)^+ \mathbf{g}}^{-1}. \quad (14)$$

What we need to know further is  $\text{Var}_{\boldsymbol{\theta}_0} \frac{\partial \mathbf{g}'\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}$ .

$$\begin{aligned}
\text{Var}_{\boldsymbol{\theta}_0} \frac{\partial \mathbf{g}'\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}} &= \text{Var}_{\boldsymbol{\theta}_0} \left[ -2 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \gamma + 2 \begin{pmatrix} \mathbf{b}_g' \zeta_1 \\ \vdots \\ \mathbf{b}_g' \zeta_r \end{pmatrix} \right] \\
&= 4 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \text{Var}_{\boldsymbol{\theta}_0}(\gamma)(\mathbf{a}_1, \dots, \mathbf{a}_r) - 4 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \text{cov}_{\boldsymbol{\theta}_0} \left[ \gamma, \begin{pmatrix} \mathbf{b}_g' \zeta_1 \\ \vdots \\ \mathbf{b}_g' \zeta_r \end{pmatrix} \right] \\
&\quad - 4 \text{cov}_{\boldsymbol{\theta}_0} \left[ \begin{pmatrix} \mathbf{b}_g' \zeta_1 \\ \vdots \\ \mathbf{b}_g' \zeta_r \end{pmatrix}, \gamma \right] (\mathbf{a}_1, \dots, \mathbf{a}_r) + 4 \text{Var}_{\boldsymbol{\theta}_0} \begin{pmatrix} \mathbf{b}_g' \zeta_1 \\ \vdots \\ \mathbf{b}_g' \zeta_r \end{pmatrix}. \quad (15)
\end{aligned}$$

In view of (4) and of the definition of  $\gamma$

$$\text{Var}_{\boldsymbol{\theta}_0}(\gamma) = 2\mathbf{S}_{(\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+}. \quad (16)$$

Concerning  $\text{Var}_{\boldsymbol{\theta}_0} \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix}$ :

$$\begin{aligned}
\left\{ \text{Var}_{\boldsymbol{\theta}_0} \begin{pmatrix} \mathbf{b}_g' \zeta_1 \\ \vdots \\ \mathbf{b}_g' \zeta_r \end{pmatrix} \right\}_{k,l} &= \text{cov}_{\boldsymbol{\theta}_0}(\mathbf{b}_g' \zeta_k, \mathbf{b}_g' \zeta_l) = \mathbf{b}_g' \text{cov}_{\boldsymbol{\theta}_0}(\zeta_k, \zeta_l) \mathbf{b}_g \\
&= \mathbf{b}_g' \text{cov}_{\boldsymbol{\theta}_0} \left[ \begin{pmatrix} \mathbf{Y}'(\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_1 (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{Y} \\ \vdots \\ \mathbf{Y}'(\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_r (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{Y} \end{pmatrix}, \right. \\
&\quad \left. \begin{pmatrix} \mathbf{Y}'(\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_l (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_1 (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{Y} \\ \vdots \\ \mathbf{Y}'(\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_l (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_r (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{Y} \end{pmatrix} \right] \mathbf{b}_g \\
&= \mathbf{b}_g' \mathbf{D}_{\zeta_k, \zeta_l} \mathbf{b}_g, \quad (17)
\end{aligned}$$

where

$$\begin{aligned}
 \left\{ \mathbf{D}_{\zeta_k, \zeta_l} \right\}_{s,t} &= \text{cov}_{\boldsymbol{\theta}_0} \left[ \mathbf{Y}'(\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_s (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{Y}, \right. \\
 &\quad \left. \mathbf{Y}'(\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_l (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_t (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{Y} \right] \\
 &= 2 \text{Tr} \left[ (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_s (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \right. \\
 &\quad \left. \times (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_l (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_t (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \right] \\
 &= 2 \text{Tr} \left[ \mathbf{V}_s (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_l (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \right. \\
 &\quad \left. \times \mathbf{V}_t (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_k (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \right].
 \end{aligned}$$

Next

$$\begin{aligned}
 &\text{cov}_{\boldsymbol{\theta}_0} \left[ -2 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \gamma, 2 \begin{pmatrix} \mathbf{b}'_{g'} \zeta_1 \\ \vdots \\ \mathbf{b}'_{g'} \zeta_r \end{pmatrix} \right] = \\
 &= -4 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \text{cov}_{\boldsymbol{\theta}_0} \left[ \gamma, \begin{pmatrix} \mathbf{b}'_{g'} \zeta_1 \\ \vdots \\ \mathbf{b}'_{g'} \zeta_r \end{pmatrix} \right] = -4 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \mathbf{D}_{\gamma, \zeta}, \quad (18)
 \end{aligned}$$

where

$$\begin{aligned}
 &\left\{ \mathbf{D}_{\gamma, \zeta} \right\}_{i,j} = \text{cov}_{\boldsymbol{\theta}_0} (\gamma_i, \mathbf{b}'_{g'} \zeta_j) \\
 &= \text{cov}_{\boldsymbol{\theta}_0} \left[ \mathbf{Y}'(\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_i (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{Y}, \sum_{u=1}^r \mathbf{b}_{g_u} \mathbf{Y}'(\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_j \right. \\
 &\quad \left. \times (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_u (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{Y} \right] = \sum_{u=1}^r 2 \text{Tr} \left[ (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_i \right. \\
 &\quad \left. \times (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{b}_{g_u} (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_j (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \right. \\
 &\quad \left. \times \mathbf{V}_u (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \right] \\
 &= 2 \text{Tr} \left[ \mathbf{V}_i (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_j (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \sum_{u=1}^r \mathbf{b}_{g_u} \mathbf{V}_u (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \right] \\
 &= 2 \text{Tr} \left[ \mathbf{V}_i (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_j (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \mathbf{V}_g (\mathbf{M}_X \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_X)^+ \right].
 \end{aligned}$$

In the previous text following important fact was used (together with equality (5)).

**Lemma 4.1** (see [4], page 101) *Let  $n \times n$  matrices  $\mathbf{A}$ ,  $\mathbf{B}$  be symmetrical. Let  $\mathbf{Y} \sim N_n(\mathbf{X}\boldsymbol{\beta}, \boldsymbol{\Sigma}_{\boldsymbol{\theta}})$ , where  $\mathbf{A}\mathbf{X} = \mathbf{B}\mathbf{X} = \mathbf{0}$ . Then*

$$\text{cov}(\mathbf{Y}'\mathbf{A}\mathbf{Y}, \mathbf{Y}'\mathbf{B}\mathbf{Y}) = 2 \text{Tr}(\mathbf{A}\boldsymbol{\Sigma}_{\boldsymbol{\theta}}\mathbf{B}\boldsymbol{\Sigma}_{\boldsymbol{\theta}}).$$



Following notation was used as well:

$\gamma_i \dots i$ -th component of  $\boldsymbol{\gamma}$ ,  $\mathbf{b}_{\mathbf{g}_u} \dots u$ -th component of  $\mathbf{b}_{\mathbf{g}}$ ,  $\mathbf{V}_{\mathbf{g}} = \sum_{u=1}^r \mathbf{b}_{\mathbf{g}_u} \mathbf{V}_u$ .

According to (15), (16), (17) and (18) we have

$$\begin{aligned}
\mathbf{W}_{\mathbf{g}} &= \text{Var}_{\boldsymbol{\theta}_0} \frac{\partial \mathbf{g}' \widehat{\boldsymbol{\theta}}(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}} = 8 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \mathbf{S}_{(\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+} (\mathbf{a}_1, \dots, \mathbf{a}_r) \\
&+ 4 \mathbf{b}'_{\mathbf{g}} \begin{pmatrix} \mathbf{D}_{\zeta_1, \zeta_1} & \dots & \mathbf{D}_{\zeta_1, \zeta_r} \\ \vdots & & \vdots \\ \mathbf{D}_{\zeta_r, \zeta_1} & \dots & \mathbf{D}_{\zeta_r, \zeta_r} \end{pmatrix} \mathbf{b}_{\mathbf{g}} - 4 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \mathbf{D}_{\boldsymbol{\gamma}, \boldsymbol{\zeta}} - 4 \mathbf{D}'_{\boldsymbol{\gamma}, \boldsymbol{\zeta}} (\mathbf{a}_1, \dots, \mathbf{a}_r) \\
&= 8 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \mathbf{S}_{(\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+} (\mathbf{a}_1, \dots, \mathbf{a}_r) + 8 \mathbf{S}_{(\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+ + \mathbf{V}_{\mathbf{g}} (\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+} \\
&\quad - 8 \begin{pmatrix} \mathbf{a}'_1 \\ \vdots \\ \mathbf{a}'_r \end{pmatrix} \mathbf{C}_{(\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+, (\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+ + \mathbf{V}_{\mathbf{g}} (\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+} \\
&\quad - 8 \mathbf{C}'_{(\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+, (\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+ + \mathbf{V}_{\mathbf{g}} (\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+} (\mathbf{a}_1, \dots, \mathbf{a}_r). \quad (19)
\end{aligned}$$

Notation defined in (9) and denoting of matrix having on its  $(i, j)$ -th position  $\text{Tr}(\mathbf{A} \mathbf{V}_i \mathbf{A} \mathbf{V}_j)$  with  $S_{\mathbf{A}}$  was used.

#### 4.2.1 Insensitivity region formulation

If we determine the insensitivity region for the variance components as a set of all  $\boldsymbol{\theta}_0 + \delta \boldsymbol{\theta}$  with  $\delta \boldsymbol{\theta}$  satisfying (6), we get

$$\begin{aligned}
\mathcal{N}_{\mathbf{g}, \boldsymbol{\theta}_0} &= \left\{ \boldsymbol{\theta}_0 + \delta \boldsymbol{\theta} : \delta \boldsymbol{\theta}' \mathbf{W}_{\mathbf{g}} \delta \boldsymbol{\theta} \leq 2\varepsilon \text{Var}_{\boldsymbol{\theta}_0} (\mathbf{g}' \widehat{\boldsymbol{\theta}}) \right\} \\
&= \left\{ \boldsymbol{\theta}_0 + \delta \boldsymbol{\theta} : \delta \boldsymbol{\theta}' \mathbf{W}_{\mathbf{g}} \delta \boldsymbol{\theta} \leq 4\varepsilon \mathbf{g}' \mathbf{S}_{(\mathbf{M}_{\mathbf{X}} \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_{\mathbf{X}})^+}^{-1} \mathbf{g} \right\}. \quad (20)
\end{aligned}$$

**Remark 4.2** More precise form of  $\mathcal{N}_{\mathbf{g}, \boldsymbol{\theta}_0}$  is (see also [4] and [1])

$$\mathcal{N}_{\mathbf{g}, \boldsymbol{\theta}_0} = \left\{ \boldsymbol{\theta}_0 + \delta \boldsymbol{\theta} : \delta \boldsymbol{\theta}' \mathbf{W}_{\mathbf{g}} \delta \boldsymbol{\theta} \leq (2\varepsilon + \varepsilon^2) \text{Var} (\mathbf{g}' \widehat{\boldsymbol{\theta}}) \right\}.$$

Because  $\varepsilon$  is choiced to be a small positive number we usually can use  $2\varepsilon$  instead of  $(2\varepsilon + \varepsilon^2)$  as used in (20).

## 5 Numerical study

Let the Michaelis–Menten regression function

$$f(x) = \frac{\gamma_1 x}{\gamma_2 + x}$$

be considered. We can measure values of this function for  $x_1 = 0.5$ ;  $x_2 = 1.5$  with dispersion of  $\sigma_1^2 = 0.04$  and for  $x_3 = 7$ ;  $x_4 = 9$  with dispersion of  $\sigma_2^2 = 0.36$ . Let's suppose the true values of  $\gamma_1$  and  $\gamma_2$  are  $\gamma_1 = 10$  and  $\gamma_2 = 5$ . The values of  $\sigma_1^2$ ,  $\sigma_2^2$ ,  $\gamma_1$  and  $\gamma_2$  are apriori unknown for us. We have two measurements for each point  $x_1, x_2, x_3, x_4$ . Let's include the measured data into an observation vector

$$\mathbf{Y} = \begin{pmatrix} Y_1 \\ \vdots \\ Y_8 \end{pmatrix}.$$

The normal distribution of the random vector  $\mathbf{Y}$  is assumed. We need to describe such a nonlinear situation with a linear model. For  $f(x_i) = \frac{\gamma_1 x_i}{\gamma_2 + x_i}$ ,  $i = 1, 2, 3, 4$  we have

$$\frac{\partial f(x_i)}{\partial \gamma_1} = \frac{x_i}{\gamma_2 + x_i}, \quad \frac{\partial f(x_i)}{\partial \gamma_2} = -\frac{\gamma_1 x_i}{(\gamma_2 + x_i)^2}.$$

Since

$$f(x_i, \gamma_1, \gamma_2) \approx f(x_i, \gamma_1^0, \gamma_2^0) + \frac{\partial f}{\partial \gamma_1}(\gamma_1 - \gamma_1^0) + \frac{\partial f}{\partial \gamma_2}(\gamma_2 - \gamma_2^0),$$

we can write:

$$\mathbf{Y} - \mathbf{f}_{\gamma_1^0, \gamma_2^0} \sim N_8 \left[ \mathbf{X} \begin{pmatrix} \delta \gamma_1 \\ \delta \gamma_2 \end{pmatrix}, \boldsymbol{\Sigma}_\theta \right]. \quad (21)$$

Here

$$\mathbf{f}_{\gamma_1^0, \gamma_2^0} = \begin{pmatrix} \frac{\gamma_1^0 x_1}{\gamma_2^0 + x_1} \\ \frac{\gamma_1^0 x_1}{\gamma_2^0 + x_1} \\ \frac{\gamma_1^0 x_2}{\gamma_2^0 + x_2} \\ \frac{\gamma_1^0 x_2}{\gamma_2^0 + x_2} \\ \frac{\gamma_1^0 x_3}{\gamma_2^0 + x_3} \\ \frac{\gamma_1^0 x_3}{\gamma_2^0 + x_3} \\ \frac{\gamma_1^0 x_4}{\gamma_2^0 + x_4} \\ \frac{\gamma_1^0 x_4}{\gamma_2^0 + x_4} \end{pmatrix}, \quad \mathbf{X} = \begin{pmatrix} \frac{x_1}{\gamma_2^0 + x_1} - \frac{\gamma_1^0 x_1}{(\gamma_2^0 + x_1)^2} \\ \frac{x_1}{\gamma_2^0 + x_1} - \frac{\gamma_1^0 x_1}{(\gamma_2^0 + x_1)^2} \\ \frac{x_2}{\gamma_2^0 + x_2} - \frac{\gamma_1^0 x_2}{(\gamma_2^0 + x_2)^2} \\ \frac{x_2}{\gamma_2^0 + x_2} - \frac{\gamma_1^0 x_2}{(\gamma_2^0 + x_2)^2} \\ \frac{x_3}{\gamma_2^0 + x_3} - \frac{\gamma_1^0 x_3}{(\gamma_2^0 + x_3)^2} \\ \frac{x_3}{\gamma_2^0 + x_3} - \frac{\gamma_1^0 x_3}{(\gamma_2^0 + x_3)^2} \\ \frac{x_4}{\gamma_2^0 + x_4} - \frac{\gamma_1^0 x_4}{(\gamma_2^0 + x_4)^2} \\ \frac{x_4}{\gamma_2^0 + x_4} - \frac{\gamma_1^0 x_4}{(\gamma_2^0 + x_4)^2} \end{pmatrix}, \quad \begin{pmatrix} \delta \gamma_1 \\ \delta \gamma_2 \end{pmatrix} = \begin{pmatrix} \gamma_1 - \gamma_1^0 \\ \gamma_2 - \gamma_2^0 \end{pmatrix}$$

and

$$\boldsymbol{\Sigma}_\theta = \theta_1 \mathbf{V}_1 + \theta_2 \mathbf{V}_2$$

with  $\theta_1 = \sigma_1^2$ ,  $\theta_2 = \sigma_2^2$ ,

$$\mathbf{V}_1 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \quad \mathbf{V}_2 = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

We consider a special case of a general linear regression model described in section 3—a mixed linear model, the variance components have to be non-negative and matrices  $\mathbf{V}_1, \mathbf{V}_2$  are evidently positive semidefinite. We have to take this fact into account when determining the insensitivity regions.

We will work with following measured data

$$\mathbf{Y} = \begin{pmatrix} 1.245 \\ 0.779 \\ 2.264 \\ 2.258 \\ 6.612 \\ 5.909 \\ 6.827 \\ 6.301 \end{pmatrix}$$

Components of this observation vector are the result of the data simulation from the normal distribution with mean equals to the real value of  $f$  for appropriate  $x_i$  and standard deviation  $\sigma_1 = 0.2$ ,  $\sigma_2 = 0.6$  respectively.

The next task is to decide whether we are able to get reasonable estimates of the variance components  $\theta_1$  and  $\theta_2$  when having this one observation vector only. We find some starting values  $\theta_1^0$  and  $\theta_2^0$  and establish the insensitivity region according to (20). Next we compute the variance components estimates based on these starting values and confidence region for the variance components. If the confidence region is inbedded into the insensitivity region, then the choice of starting  $\theta_1^0$  and  $\theta_2^0$  is good enough to determine the estimates based on them.

What we can do is to get a rough estimate  $\theta_{1,1}^0$  of  $\theta_1$  based on  $y_1$  and  $y_2$ —the first two components of observation vector:

$$\theta_{1,1}^0 = (y_1 - \bar{y}_{12})^2 + (y_2 - \bar{y}_{12})^2$$

and  $\theta_{1,2}^0$  based on  $y_3$  and  $y_4$

$$\theta_{1,2}^0 = (y_3 - \bar{y}_{34})^2 + (y_4 - \bar{y}_{34})^2,$$

where  $\bar{y}_{12}$  ( $\bar{y}_{34}$ ) denotes arithmetic average of  $y_1$  and  $y_2$  ( $y_3$  and  $y_4$  respectively). Since all the four values  $y_1, \dots, y_4$  were simulated with dispersion  $\theta_1$ , the starting

value  $\theta_1^0$  can be counted as an arithmetic average of  $\theta_{1,1}^0$  and  $\theta_{1,2}^0$ :

$$\theta_1^0 = \frac{\theta_{1,1}^0 + \theta_{1,2}^0}{2} = 0.0543.$$

Similarly

$$\theta_{2,1}^0 = (y_5 - \bar{y}_{56})^2 + (y_6 - \bar{y}_{56})^2, \quad \theta_{2,2}^0 = (y_7 - \bar{y}_{78})^2 + (y_8 - \bar{y}_{78})^2$$

and

$$\theta_2^0 = \frac{\theta_{2,1}^0 + \theta_{2,2}^0}{2} = 0.1927.$$

Next we need some starting values  $\gamma_1^0$  and  $\gamma_2^0$ . Lineweaver–Burke transformation (see [2] for more details) is frequently used to get the starting values of  $\gamma_1$  and  $\gamma_2$ . However following approach can be useful sometimes. Since

$$y = \frac{\gamma_1 x}{\gamma_2 + x},$$

$$\gamma_1 x - \gamma_2 y = xy. \quad (22)$$

According to this we can put together four systems of two linear equations:

$$\begin{aligned} \gamma_1 x_1 - \gamma_2 y_1 &= x_1 y_1 & \gamma_1 x_1 - \gamma_2 y_2 &= x_1 y_2 \\ \gamma_1 x_2 - \gamma_2 y_3 &= x_2 y_3 & \gamma_1 x_2 - \gamma_2 y_4 &= x_2 y_4 \\ \gamma_1 x_3 - \gamma_2 y_5 &= x_3 y_5 & \gamma_1 x_3 - \gamma_2 y_6 &= x_3 y_6 \\ \gamma_1 x_4 - \gamma_2 y_7 &= x_4 y_7 & \gamma_1 x_4 - \gamma_2 y_8 &= x_4 y_8 \end{aligned}$$

When we denote the solutions of these systems with  $(\gamma_{1,1}^0, \gamma_{2,1}^0), \dots, (\gamma_{1,4}^0, \gamma_{2,4}^0)$ , we can get the starting values  $\gamma_1^0, \gamma_2^0$  as the arithmetic averages again:

$$\gamma_1^0 = \frac{\gamma_{1,1}^0 + \gamma_{1,2}^0 + \gamma_{1,3}^0 + \gamma_{1,4}^0}{4} \quad \text{and} \quad \gamma_2^0 = \frac{\gamma_{2,1}^0 + \gamma_{2,2}^0 + \gamma_{2,3}^0 + \gamma_{2,4}^0}{4}.$$

The results of this procedure are:

$$\gamma_1^0 = 16.068, \quad \gamma_2^0 = 8.250.$$

Now we are ready to determine the variance components insensitivity region for

$$\boldsymbol{\theta} = \boldsymbol{\theta}_0 = \begin{pmatrix} \theta_1^0 \\ \theta_2^0 \end{pmatrix}.$$

Let's consider  $\mathbf{g}_1 = (1, 0)'$  at first. In this case we have  $\mathbf{g}_1' \boldsymbol{\theta} = \theta_1$ .

Using (20),  $\varepsilon = 0.1$  and taking into account fact that the negative input variance components values does not make sense in our case we get:

$$\begin{aligned} \mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}_0} &= \left\{ \boldsymbol{\theta}_0 + \delta \boldsymbol{\theta} : \boldsymbol{\theta}_0 + \delta \boldsymbol{\theta} \geq 0 \right. \\ &\quad \left. \wedge \delta \boldsymbol{\theta}' \begin{pmatrix} 0.000806 & -0.000227 \\ -0.000227 & 0.000064 \end{pmatrix} \delta \boldsymbol{\theta} \leq 0.000393 \right\}. \end{aligned} \quad (23)$$

For  $\varepsilon = 0.1$  we get a set of all  $\boldsymbol{\theta}_0 + \delta\boldsymbol{\theta}$  which don't increase the standard deviation of  $\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta})$  more than by 10 %.

Now the same once more for  $\mathbf{g}_2 = (0, 1)'$  and  $\varepsilon = 0.1$

$$\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}_0} = \{ \boldsymbol{\theta}_0 + \delta\boldsymbol{\theta} : \boldsymbol{\theta}_0 + \delta\boldsymbol{\theta} \geq 0 \\ \delta\boldsymbol{\theta}' \begin{pmatrix} 0.0107 & -0.00300 \\ -0.00300 & 0.000846 \end{pmatrix} \delta\boldsymbol{\theta} \leq 0.00508 \}. \quad (24)$$

According to (3) we get (for  $\boldsymbol{\theta} = \boldsymbol{\theta}_0$ ) variance components estimate:

$$\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0) = \begin{pmatrix} 0.0474 \\ 0.165 \end{pmatrix}.$$

(Let's denote the real values of the variance components with  $\boldsymbol{\theta}^*$ , we have  $\boldsymbol{\theta}^* = \begin{pmatrix} 0.04 \\ 0.36 \end{pmatrix}$ . The difference  $(\boldsymbol{\theta}^* - \widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0))$  is compatible with the variance of the data.)

Let's determine another set—a rectangle with center  $\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0)$  which covers the real value of  $\boldsymbol{\theta}$  with probability of  $(1 - \alpha)$ — $\boldsymbol{\theta}$  confidence region. According to Chebyshev (see [6]) we have

$$P \left\{ |\widehat{\theta}_1(\boldsymbol{\theta}_0) - \theta_1| \leq k \sqrt{\text{Var}_{\boldsymbol{\theta}_0} [\widehat{\theta}_1(\boldsymbol{\theta}_0)]} \right\} \geq 1 - \frac{1}{k^2}$$

and

$$P \left\{ |\widehat{\theta}_2(\boldsymbol{\theta}_0) - \theta_2| \leq k \sqrt{\text{Var}_{\boldsymbol{\theta}_0} [\widehat{\theta}_2(\boldsymbol{\theta}_0)]} \right\} \geq 1 - \frac{1}{k^2}.$$

According to Bonferroni (see [3])

$$P \left\{ |\widehat{\theta}_1(\boldsymbol{\theta}_0) - \theta_1| \leq k \sqrt{\text{Var}_{\boldsymbol{\theta}_0} [\widehat{\theta}_1(\boldsymbol{\theta}_0)]} \wedge |\widehat{\theta}_2(\boldsymbol{\theta}_0) - \theta_2| \leq k \sqrt{\text{Var}_{\boldsymbol{\theta}_0} [\widehat{\theta}_2(\boldsymbol{\theta}_0)]} \right\} \\ \geq 1 - \frac{2}{k^2}. \quad (25)$$

In (25) we get a rectangle with center  $\widehat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0)$ . We determine this rectangle to include the variance components with probability of  $(1 - \alpha)$ . This means we need to have  $(1 - \frac{2}{k^2}) = (1 - \alpha)$ , so  $k = \sqrt{\frac{2}{\alpha}}$ . As mentioned above the variance components cannot be negative in this case as they are the variances in fact. We have to involve this into our consideration. The  $\boldsymbol{\theta}$  confidence region  $\mathcal{E}_{\boldsymbol{\theta}}$  is a set of non-negative  $\theta_1, \theta_2$  satisfying (25):

$$\mathcal{E}_{\boldsymbol{\theta}} = \left\{ \boldsymbol{\theta} = \begin{pmatrix} \theta_1 \\ \theta_2 \end{pmatrix} : |\widehat{\theta}_1(\boldsymbol{\theta}_0) - \theta_1| \leq \sqrt{\frac{2}{\alpha} \text{Var}_{\boldsymbol{\theta}_0} [\widehat{\theta}_1(\boldsymbol{\theta}_0)]} \right. \\ \left. \wedge |\widehat{\theta}_2(\boldsymbol{\theta}_0) - \theta_2| \leq \sqrt{\frac{2}{\alpha} \text{Var}_{\boldsymbol{\theta}_0} [\widehat{\theta}_2(\boldsymbol{\theta}_0)]} \wedge \theta_1 \geq 0 \wedge \theta_2 \geq 0 \right\}$$

According to (4) the variance-covariance matrix of variance components estimates  $\hat{\boldsymbol{\theta}}$  is

$$\text{Var}_{\boldsymbol{\theta}_0}(\hat{\boldsymbol{\theta}}) = 2\mathbf{S}_{(\mathbf{M}_x \boldsymbol{\Sigma}_{\boldsymbol{\theta}_0} \mathbf{M}_x)^+}^{-1} = \begin{pmatrix} 0.00197 & -0.0000894 \\ -0.0000894 & 0.0254 \end{pmatrix}.$$

For  $(1 - \alpha) = 0.95$  level of confidence we have

$$\mathcal{E}_{\boldsymbol{\theta}} = \langle 0; 0.328 \rangle \times \langle 0; 1.173 \rangle \quad (26)$$

This confidence region  $\mathcal{E}_{\boldsymbol{\theta}}$  is a subset of both  $\mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}_0}$  and  $\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}_0}$  as shown in figures 2 and 4 given bellow.

It means the starting values  $\theta_1^0, \theta_2^0$  are sufficient not only for deriving a reasonable estimate of  $\boldsymbol{\theta}$  based on them—it is enough to stop the iterative procedure after the first step already.

Since we know the real values of  $\theta_1, \theta_2$  we can repeat the same routine with these real values instead of the starting ones. Denote:

$$\boldsymbol{\theta}^* = \begin{pmatrix} \theta_1^* \\ \theta_2^* \end{pmatrix} = \begin{pmatrix} 0, 04 \\ 0, 36 \end{pmatrix}.$$

The insensitivity region for  $\mathbf{g}_1 = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$  and  $\varepsilon = 0.1$  is

$$\begin{aligned} \mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}^*} &= \{ \boldsymbol{\theta}^* + \delta \boldsymbol{\theta} : \boldsymbol{\theta}_0 + \delta \boldsymbol{\theta} \geq 0 \\ &\delta \boldsymbol{\theta}' \begin{pmatrix} 0.000143 & -0.0000159 \\ -0.0000159 & 0.00000177 \end{pmatrix} \delta \boldsymbol{\theta} \leq 0.000214 \}. \end{aligned} \quad (27)$$

For  $\mathbf{g}_2 = \begin{pmatrix} 0 \\ 1 \end{pmatrix}$  and  $\varepsilon = 0.1$

$$\begin{aligned} \mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}^*} &= \{ \boldsymbol{\theta}^* + \delta \boldsymbol{\theta} : \boldsymbol{\theta}_0 + \delta \boldsymbol{\theta} \geq 0 \\ &\delta \boldsymbol{\theta}' \begin{pmatrix} 0.0118 & -0.00131 \\ -0.00131 & 0.000145 \end{pmatrix} \delta \boldsymbol{\theta} \leq 0.0175 \}. \end{aligned} \quad (28)$$

$\hat{\boldsymbol{\theta}}(\boldsymbol{\theta}^*)$  is according to (3):

$$\hat{\boldsymbol{\theta}}(\boldsymbol{\theta}^*) = \begin{pmatrix} 0.0476 \\ 0.164 \end{pmatrix}.$$

The  $\boldsymbol{\theta}$  confidence region with center  $\boldsymbol{\theta}^*$  for  $(1 - \alpha) = 0.95$  level of confidence is

$$\mathcal{E}_{\boldsymbol{\theta}} = \langle 0; 0.254 \rangle \times \langle 0; 2.032 \rangle \quad (29)$$

In figures number 2 and 4 given bellow we can see the situation for  $\boldsymbol{\theta} = \boldsymbol{\theta}^*$  is quite similar to that for  $\boldsymbol{\theta} = \boldsymbol{\theta}_0$ . The confidence region is again a subset of both the insensitivity regions. This is exactly what we could expect and it shows that model (21) enables to determine reasonable variance components estimates.

The insensitivity regions (23) and (27) relating to  $\mathbf{g}_1 = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$  and confidence regions (26) and (29) are visible in Fig. 1.

The relative position of the insensitivity regions and confidence regions is not obvious in Fig. 1. Fig. 2 gives a more detailed view.

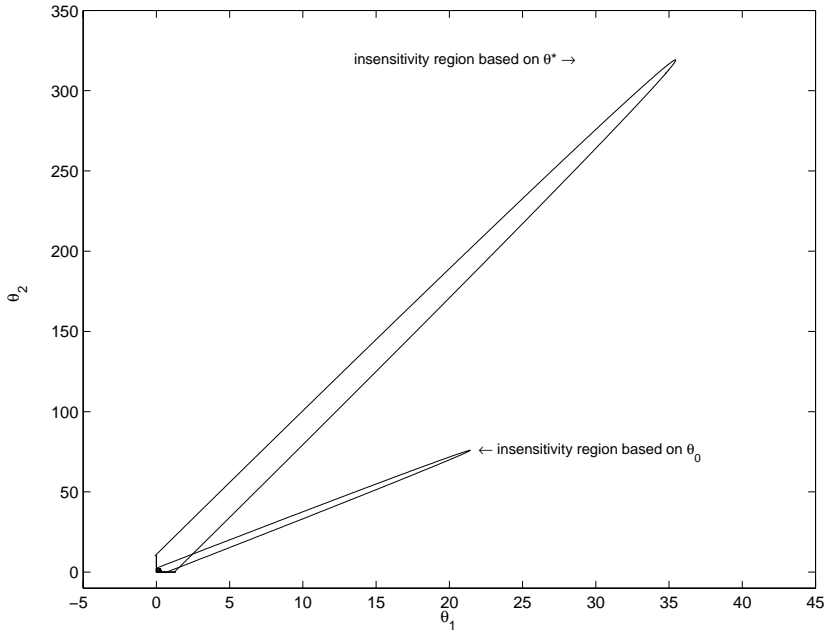


Figure 1: Insensitivity regions  $\mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}_0}$  and  $\mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}^*}$  for  $\varepsilon = 0.1$  and appropriate confidence regions for  $\alpha = 0.05$ .

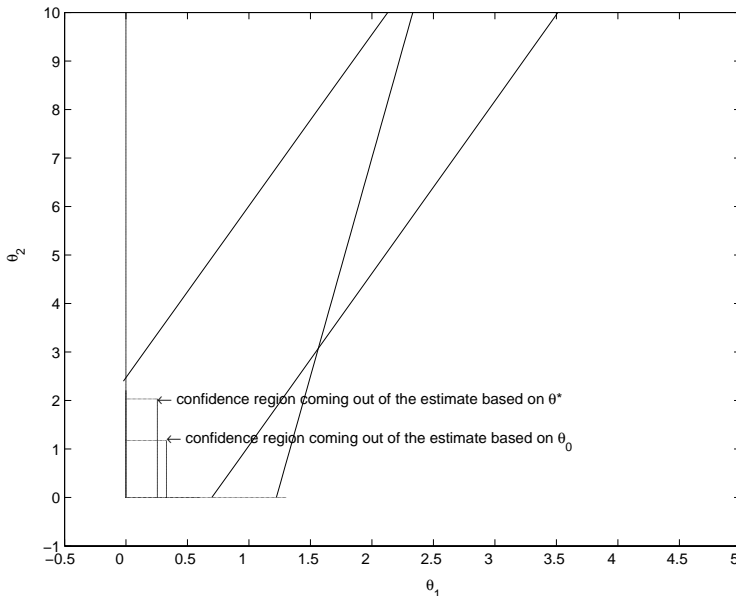


Figure 2. Relative position of insensitivity regions  $\mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}_0}$  and  $\mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}^*}$  and corresponding confidence regions—detail.

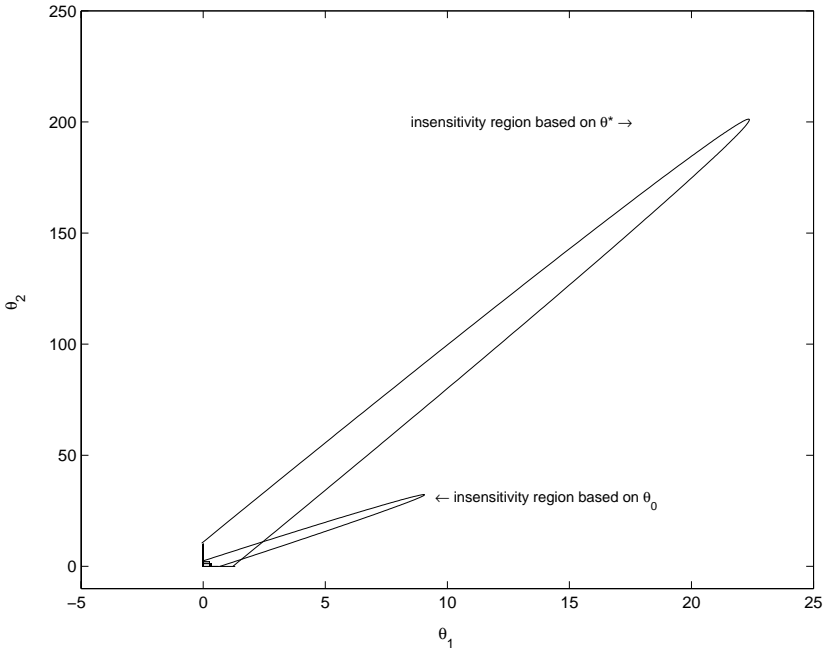


Figure 3. Insensitivity regions  $\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}_0}$  and  $\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}^*}$  for  $\varepsilon = 0.1$  and appropriate confidence regions for  $\alpha = 0.05$ .

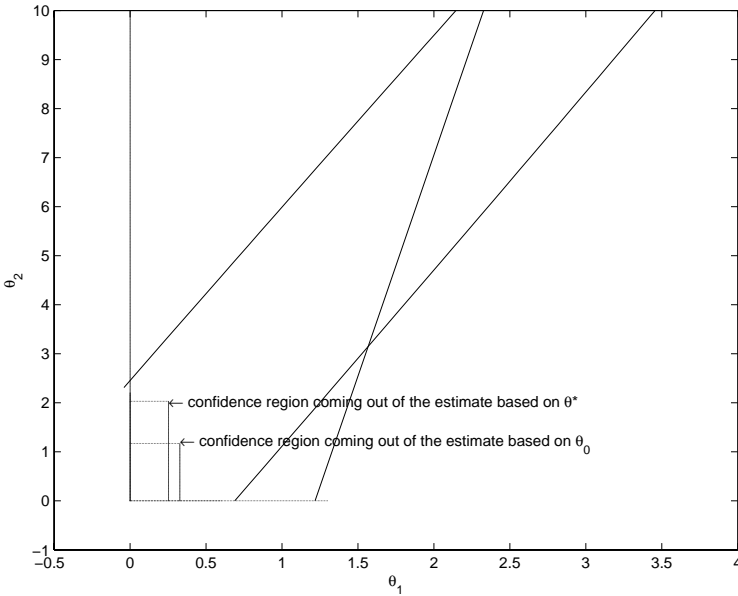


Figure 4. Relative position of insensitivity regions  $\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}_0}$  and  $\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}^*}$  and corresponding confidence regions—detail.



The insensitivity regions (24) and (28) relating to  $\mathbf{g}_2 = \begin{pmatrix} 0 \\ 1 \end{pmatrix}$  and confidence regions (26) and (29) are visible in Fig. 3.

The relative position of the insensitivity regions and confidence regions is again shown in Fig. 4 in detail.

The conclusion is that we can feel free to use the  $\hat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0)$  as a  $\boldsymbol{\theta}$  estimate without apprehension of the variance of the estimates being too large because both the insensitivity regions for  $\boldsymbol{\theta}_0$   $\mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}_0}$  and  $\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}_0}$  unambiguously cover the  $\boldsymbol{\theta}$  confidence region based on  $\hat{\boldsymbol{\theta}}(\boldsymbol{\theta}_0)$ .

The comparison of  $\mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}_0}$  and  $\mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}^*}$  is visible in Fig. 1. Fig. 3 contains similar comparison of  $\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}_0}$  and  $\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}^*}$ . When we compare the size of the insensitivity regions  $\mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}_0}$  and  $\mathcal{N}_{\mathbf{g}_1, \boldsymbol{\theta}^*}$  ( $\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}_0}$  and  $\mathcal{N}_{\mathbf{g}_2, \boldsymbol{\theta}^*}$  respectively) we can see the insensitivity regions based on the real values  $\boldsymbol{\theta}^*$  are much larger than those based on the prior values  $\boldsymbol{\theta}_0$ . This means the variance increase is slower when we base the estimates on the real values of the variance components compared to the estimates based on the prior values generated from the observation vector.

## References

- [1] Boháčová, H., Heckenbergerová, J.: *Insensitivity regions for fixed effects parameters in mixed linear model with type I constraints and calculation problems linked with them.* In: Forum Statisticum Slovacum 6/2007, ISSN 1336-7420, (in Czech).
- [2] Ebel, S., Alert, D., Schaefer, U.: *Calibration in TLC/HPTLC using the Michaelis-Menten function.* Chromatographia 1/1984.
- [3] Humak, K. M. S.: *Statistischen Methoden der Modellbildung Band I, Statistische Inferenz für lineare Parameter.* Akademie-Verlag, Berlin, 1977.
- [4] Kubáček, L., Kubáčková, L.: *Statistika a metrologie. Vyd. University Palackého, Olomouc,* 2000.
- [5] Rao, C. R., Kleffe, J.: *Estimation of Variance Components and Application.* North-Holland, Amsterdam-New York-Oxford-Tokyo, 1988.
- [6] Rényi, A.: *Probability theory.* Akadémiai Kiadó, Budapest, 1970.