University of São Paulo
"Luiz de Queiroz" College of Agriculture

Nonlinear mixed models applied to broiler chickens performance data

Andréia Pereira Maria Hilário

Thesis presented to obtain the degree of Doctor in Science.
Area: Statistics and Agricultural Experimentation

Piracicaba
2020

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Degree in Mathematics

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versão revisada de acordo com a resolução CoPGr 6018 de 2011.

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Prof. Dr. **CÉSAR GONÇALVES DE LIMA**

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1. Frango de corte 2. Modelos mistos não lineares bivariados 3. Componentes de variância 4. Modelos de crescimento 5. Medidas repetidas. I. Título.

DEDICATION

I dedicate this work to my husband,
my children and my parents.

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First of all, to God, Our Lady and my Guardian Angel for health, peace, and strength in the most challenging times.

I would like to thank my family, for the immense love for me, for the patience and all affection, without you my life would not make sense.

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EPIGRAPH

"*If you are looking for the way by which you should go,*
take Christ, because he himself is the way."

St. Thomas Aquinas

CONTENTS

RESUMO

Modelos mistos não lineares aplicados a dados de desempenho de frangos de corte

Devido à grande demanda de mercado da carne de frango, existe grande interesse em pesquisas que visam melhorar ainda mais a eficiência na produção desse produto. Neste contexto, o estudo do desempenho de frangos de corte auxilia no processo de otimização da produção de carne e facilita a compreensão das necessidades de cada fase de crescimento até a idade de abate das aves. Embora seja comum a utilização de modelos não lineares para descrever o padrão de crescimento das aves, não é comum a inclusão de efeitos aleatórios nesses modelos e muito menos a modelagem conjunta das variáveis observadas no experimento. Neste trabalho forma ajustados os modelos de crescimento Gompertz, logístico de quatro parâmetros, von Bertalanffy e Richards com efeitos fixos e aleatórios em seus parâmetros para descrever a curva de crescimento de 1080 frangos da linhagem Ross. Além disso, foi realizada a modelagem conjunta das variáveis peso corporal e consumo de ração utilizando modelos mistos. Adicionalmente, comparou-se os modelos ajustados utilizando os critérios de informação AICc e BIC. Os resultados indicaram o modelo misto logístico de quatro parâmetros como o mais adequado aos dados de desempenho de frangos de corte, tanto para o modelo univariado como para o modelo bivariado.

Palavras-chave: Frango de corte; Modelos mistos não lineares bivariados; Componentes de variância; Modelos de crescimento; Medidas repetidas

ABSTRACT

Nonlinear mixed models applied to broiler chickens performance data

Due to the large market demand for chicken meat, there is great interest in research aimed at further improving the production efficiency of this product. In this context, the study of broiler performance assists in the process of optimizing meat production and facilitates the understanding of the needs of each growth phase until the poultry slaughtering age. Although it is common to use nonlinear models to describe the growth pattern of birds, it is not common to include random effects in these models, much less the combined modeling of the variables observed in the experiment. In this work, we adjusted the Gompertz, four-parameter logistic, von Bertalanffy, and Richards growth models with fixed and random effects in their parameters to describe the growth curve of 1080 Ross broilers. Additionally, we performed the joint modeling of body weight and feed consumption variables using mixed models. Additionally, we compared the adjusted models using the AICc and BIC information criteria. The results indicated that the four-parameter mixed logistic model was the most suitable for broiler performance data for both univariate and bivariate models.

Keywords: Broiler chicken; Bivariate nonlinear mixed models; Variance components; Growing Model; Repeated measurements

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1 INTRODUCTION

Chicken meat plays an important role in the world animal protein market, and it is as among the fastest growing sources of animal protein in Brazil and the world (ABPA - Associação Brasileira de Proteína Animal). There is great interest in further optimizing the production process of broiler meat, one of the aspects explored for this purpose is the study of the performance variables of poultry. In this context, knowledge of the growth pattern of birds provides significant information to assist in the production process and to facilitate understanding of the needs of each growth phase until the age of slaughter.

Nonlinear growth models such as Gompertz (GOMPERTZ, 1825; WINSOR, 1932), von Bertalanffy (VON BERTALANFFY, 1957), Richards (RICHARDS, 1959) and logistic (NELDER, 1961) are commonly used in these studies. Despite the frequent use of these models, it is not common to include random effects in their parameters, and thus, the consequences of using such effects in these models are little explored.

Data observed in performance studies repeatedly evaluated in the same experimental units have inherent characteristics that contradict assumptions of error independence and homogeneity of variance, which are common in fixed nonlinear regression models. For example, when we study the body weight of broilers, it is natural to increase the variability between weights over time. Besides, we expect that measurements taken sequentially on the same birds in near times will be more highly correlated than measurements farther in time (LITTELL et al., 2000). Thus, to model performance data, it is necessary a model that includes the different variations over time with the possibility of including correlations between the measures taken in the same individual. Mixed models have great flexibility in data modeling and allow the inclusion of different structures of variances and correlations. Additionally, mixed models allow the joint modeling of multiple response variables.

The data used in this work come from a performance experiment of broiler chickens (FZEA/USP), with 1080 Ross broiler chickens, in a randomized block design with a factorial treatment structure with three nutritional densities and two sexes. In chapter 2, we worked with the Gompertz model, which is one of the most used to model growth data (NARINÇ et al., 2017). We compared Gompertz models with fixed effects and Gompertz with random effects on their parameters in the study of body weight of broiler chickens. In Chapter 3, we adjusted and compared the Gompertz, four-parameter logistic, von Bertalanffy, and Richards mixed-effect models applied to body weight data. In Chapter 4, we perform the joint modeling of body weight and feed consumption using the Gompertz and four-parameter logistic mixed models. For comparisons made in chapters 2, 3, and 4, we used the likelihood ratio test for nested models, and the Akaike corrected information criterion - AICc (HURVICH; TSAI, 1989) and the Bayesian information criterion - BIC (SCHWARZ, 1978). For statistical modelling, we use the free software R (CORE TEAM, 2019).

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2 MIXED GOMPERTZ MODEL IN STUDY OF BROILER CHICKENS WEIGHT PERFORMANCE

Abstract

Brazil plays a prominent role in world poultry farming, according to the Brazilian Association of Animal Protein, as the largest exporter and second-largest producer of chicken meat. There is great interest in research aimed at further improving the efficiency of chicken meat production. In this context, the study performance from broiler chickens, as well as the knowledge of the growth curve, helps in the process of optimizing meat production and facilitates the understanding of the needs of each growth phase until the age of slaughter. Among the most used models to describe the growth pattern of broiler chickens is the Gompertz model, however, in this model is not common to include random effects. In this work, the Gompertz models with fixed effects and random effects in the model parameters were compared to describe the growth curve of 1080 Ross broiler chickens, which were weighed from 3 to 56 days of age. The data come from an experiment (FZEA/USP) in a randomized block design with a factorial treatment structure with three nutritional densities and two sexes. Comparisons were made between the two models using the corrected Akaike information criterion (AICc), the Bayesian information criterion (BIC), and the likelihood ratio test. The results indicated the Gompertz mixed model as the most appropriate to performance data from broiler chickens.

Keywords: Nonlinear model; Variance components; Growth models; Variance heterogeneity.

2.1 Introduction

Chicken meat is the fastest-growing source of animal protein in Brazil and worldwide, with Brazil currently the largest exporter and second-largest producer, standing out as a reference in the world poultry sector (ABPA - Associação Brasileira de Proteína Animal).

Models to study broiler performance have been developed to assist the process of optimizing meat production and to facilitate the understanding of the needs of each growth phase until the age of poultry slaughter. Growth models use nonlinear functions, and most of them have a sigmoidal structure, although the course of the growth curve may vary from model to model. Historical reviews of growth models used in bird species have been published by Darmani Kuhi et al. (2003) and Narinç et al. (2017).

In a survey of Thomson Reuters in the "Web of Science" databases covering the years 1970 to 2016, it was reported that the Gompertz growth model was the most widely used in publications in four different study categories (agriculture dairy animal science, veterinary science, agriculture multidisciplinary, and computational mathematical

biology), followed by Logistic, Richards and von Bertalanffy models (NARINÇ et al., 2017).

Topal and Bolukbasi (2008), Mendeş (2009), Masoudi and Azarfar (2017) compared several models to describe the growth pattern of Ross broiler chickens and concluded that the Gompertz growth model was the most suitable to describe the body weight growth of broilers. Despite the preference for the Gompertz model to describe the growth pattern of birds, it is not common to include random effects in the model. In the development of broiler chickens, it is natural to increase the variability of some characteristics between experimental units over time, for example, in the early days, the weight of broilers has a small variability, but over time this variability between weights tends to increase. Besides, measurements taken sequentially on the same birds in near times are expected to be more highly correlated than measurements further away in time (LITTELL et al., 2000). These characteristics inherent in growth data repeatedly evaluated in the same experimental units over time contradict the assumptions of error independence and homogeneity of variances common in fixed nonlinear regression models. Data with these aspects present at least two sources of variation in observations, one between individuals and one within individuals (WANG; ZUIDHOF, 2004), which can be modeled using mixed nonlinear models with random effects included in the curve parameters, that allow great flexibility in the construction of variance and covariance structures and an adequate explanation of the mean response. In this work, body weight data of Ross broiler chickens were modeled using two Gompertz growth models, the first with fixed effects and the second with random effects on their parameters. In the search for the model that best fits the data, we used the likelihood ratio test, the Akaike corrected information criterion - AICc (HURVICH; TSAI, 1989) and the Bayesian information criterion (SCHWARZ, 1978).

2.2 Material and Methods

The dataset that motivated this work is from a study by Silva (2018) to evaluate the productive performance of broiler chickens. The procedures performed in the experiment were approved by the Animal Use Ethics Committee (Protocol No. 1484110915) of the School of Zootechnics and Food Engineering of the University of São Paulo (FZEA / USP), Pirassununga, Brazil. We used 1080 Ross broilers, with an initial weight of 45.69 ± 0.33 grams, distributed in 36 boxes, with 30 birds each, using a randomized block design to control the temperature differences in the shed. Six treatments were studied in a factorial scheme (3×2), being three nutritional densities (Low, Moderate, and High) and two sexes (Male and Female), with the following combination of levels: Males with High (HighM), Moderate (ModM) and Low (LowM), Females with High (HighF), Moderate (ModF) and Low (LowF), with six repetitions (blocks). The experimental diets were formulated based on corn and soybean meal in a three-phase feeding program: initial (1 to 10 days), growth (11 to 22 days), and final (23 to 56 days). The experiment followed the growth of birds

from 3 to 56 days of age, and the average body weight (in grams) of each box was collected in 19 measurements at times: 3, 7, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 41, 44, 47, 51, 54 and 56 days.

In the literature, different mixed nonlinear models have been proposed, as in Lindstrom and Bates (1990), Vonesh and Carter (1992), Wakefield et al. (1994), Vonesh and Chinchilli (1997) among others. For data analysis, the mixed nonlinear model (NLMM) was used, as described in Lindstrom and Bates (1990). In its first stage NLMM can be written as:

$$y_{ij} = f(\boldsymbol{\phi}_{ij}, \boldsymbol{x}_{ij}) + \varepsilon_{ij}, \quad i = 1, \ldots, M; j = 1, \ldots, n_i \tag{2.1}$$

where y_{ij} is the jth observation in individual i, M is the number of samples in the group, n_i is the number of observations in the individual i, f is a nonlinear function of the parameter vector $\boldsymbol{\phi}_{ij}$ with a covariate vector $\boldsymbol{x}_{ij}$ and ε_{ij} is a commonly distributed error term.

In the second stage the parameters of specific groups are modeled as

$$\boldsymbol{\phi}_{ij} = \boldsymbol{A}_{ij}\boldsymbol{\beta} + \boldsymbol{B}_{ij}\boldsymbol{b}_i \tag{2.2}$$

where $\boldsymbol{\beta}$ is a vector of unknown fixed parameters and common to all individuals, $\boldsymbol{b}_i$ is a unknown random effects vector for the ith individual, $\boldsymbol{A}_{ij}$ and $\boldsymbol{B}_{ij}$ are design matrices for the fixed and random effects, respectively, that may depend on the values of some covariates in the jth observation.

A general expression for NLMM can be written to individual i as

$$\boldsymbol{y}_i = f(\boldsymbol{\beta}, \boldsymbol{b}_i, \boldsymbol{X}_i) + \boldsymbol{\varepsilon}_i \tag{2.3}$$

where $\boldsymbol{y}_i = [y_{i1}, y_{i2}, \ldots, y_{in_i}]^T$ is a vector of measurements on the individual i, $\boldsymbol{X}_i$ is a known matrix of covariates and $\boldsymbol{\varepsilon}_i = [\varepsilon_{i1}, \varepsilon_{i2}, \ldots, \varepsilon_{in_i},]^T$ is a vector of intra-individual errors, $\boldsymbol{b}_i$ and $\boldsymbol{\varepsilon}_i$ are usually assumed to be independent and normally distributed with zero mean and matrix of variance $\boldsymbol{G}$ and $\boldsymbol{R}$, respectively, that is $\boldsymbol{b}_i \sim N(\boldsymbol{0}, \boldsymbol{G})$ and $\boldsymbol{\varepsilon}_i \sim N(\boldsymbol{0}, \boldsymbol{R})$.

Two models were used for broiler body weight data:

(1) Gompertz Fixed Model

$$y_{ijk} = \beta_{1k}\exp[-\beta_{2k}\exp(-\beta_{3k}t_{ij})] + \varepsilon_{ijk} \tag{2.4}$$

with $i = 1, \ldots, 6$, $j = 1, \ldots, 19$ and $k = 1, \ldots, 6$ where y_{ijk} is the body weight observed at time t_{ij} in the ith box, that received the kth treatment on the jth day of the experimental period. The coefficient β_{1k} represents the maximum body weight of broiler that received treatment k (superior asymptote), β_{2k} is a scale parameter related to the initial weight of broiler that received treatment k, β_{3k} represents the maturity index expressed as a propor-

tion of maximum growth percentage in relation to the adult weight of broiler and ε_{ijk} is the experimental error associated with the observation y_{ijk}. We assume that ε_{ijk} errors are normally distributed with mean 0 and constant variance σ^2_ε.

(2) Gompertz Mixed Model

$$y_{ijk} = (\beta_{1k} + b_{1i})\exp[-\beta_{2k}\exp((-\beta_{3k} + b_{3i})t_{ij})] + \varepsilon_{ijk} \tag{2.5}$$

where β_{1k}, β_{2k} and β_{3k} have the same interpretations of model (2.4) and b_{1i} and b_{3i} are random effects associated with the model coefficients, β_{1k} and β_{3k}, respectively. We assume that,

$$\begin{bmatrix} b_{1i} \\ b_{3i} \end{bmatrix} \sim N(\mathbf{0}, \boldsymbol{G}) \text{ and } \varepsilon_{ijk} \sim N(\mathbf{0}, \boldsymbol{R})$$

where $\boldsymbol{G} = \begin{bmatrix} \sigma^2_{b_1} & \sigma_{b_1 b_3} \\ \sigma_{b_3 b_1} & \sigma^2_{b_3} \end{bmatrix}$ and $\boldsymbol{R} = \begin{bmatrix} \boldsymbol{D}_1 & \mathbf{0}_{36} & \dots & \mathbf{0}_{36} \\ \mathbf{0}_{36} & \boldsymbol{D}_2 & \dots & \mathbf{0}_{36} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{0}_{36} & \mathbf{0}_{36} & \dots & \boldsymbol{D}_{19} \end{bmatrix}$,

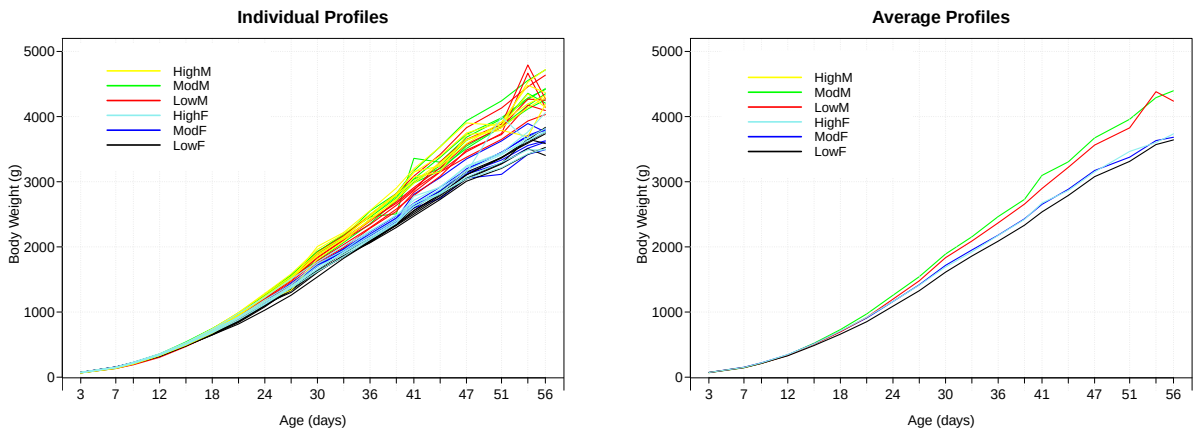
$\boldsymbol{D}_j = \boldsymbol{I}_3 \otimes \text{diag}\left(\sigma^2_{M_j}, \sigma^2_{F_j}\right) \otimes \boldsymbol{I}_6$ with $j = 1, 2, \dots, 19$, $\boldsymbol{I}_3$ and $\boldsymbol{I}_6$ are 3×3 and 6×6 order identity matrices, respectively, and $\mathbf{0}_{36}$ is a 36×36 null matrix. The component σ^2_ε corresponds to the residual variance, $\sigma^2_{M_1}$, $\sigma^2_{M_2}$, ..., $\sigma^2_{M_{19}}$ are the variance components for male broilers in each of the 19 time measurements and $\sigma^2_{F_1}$, $\sigma^2_{F_2}$, ..., $\sigma^2_{F_{19}}$ are the components of variance for female broilers in each of the 19 time measurements. This Gompertz mixed model was chosen in a preliminary model selection study.

Different methods have been proposed to estimate NLMM parameters, see Vonesh and Carter (1992), Ramos and Pantula (1995), Davidian and Giltinam (1995). In this work, we use the maximum likelihood method that requires, in the case of NLMM, numerical optimization procedures. The numerical procedure used was the algorithm described by Lindstrom and Bates (1990), which alternates between two steps, one step that uses penalized nonlinear least squares (PNLS) and the other step that uses the linear mixed model.

The models were adjusted using the `R` (R CORE TEAM, 2019) software and compared using the likelihood ratio test and the AICc and BIC information criteria. The block effect was not considered in this work, but the study for its inclusion is in progress. The quality of fit was assessed based on observation of residual versus adjusted value (fixed model) or conditional residual versus adjusted value (mixed model) plots, as well as the half-normal plot with simulation envelope using the `hnp()` function (MORAL et al., 2017) of the free statistical software `R`. The models were adjusted by the maximum likelihood method using the functions `gnls()` for the fixed effects model and `nlme()` (PINHEIRO et al., 2019) for the random-effects model.

2.3 Results and Discussion

The graph of individual body weight profiles over time (Figure 2.1) shows a similarity in the growth pattern of broiler chickens per box. It is also noted that weight variability among individuals increases over time and that this variability is greater among males than females. For all nutritional densities, from the broiler growth stage (11 to 22 days), the weight of males was higher than females.



(a) (b)

Figure 2.1 – Individual profiles (a) and average profiles (b) of broiler chickens body weight by treatment

Table 2.1 shows that the average weights per treatment of male chickens are numerically higher than the average weights of females for all nutritional densities, from day 15 of the experimental period. This distinction observed between male and female weights is in line with the work done by Havenstein et al. (2003), Sakomura et al. (2005), and Marcato et al. (2008), who evaluated the growth potential of males and females from Ross broiler chickens and concluded that males have a higher growth potential than females. According to Salim et al. (2012), the performance of each sex is related to chicken genetics: males consume more ration, use nutrients better, and grow faster than females. It is also observed in Table 2.1 that the standard error, in general, followed the increase that occurred in the average weight of the chickens over time. The mean standard error is calculated by $SD/\sqrt{n}$, where SD is the standard deviation, and n is the number of different samples from each treatment at a specific time ($n = 6$ blocks). Since n is a fixed number, in this case, the increase in standard error is due to the increase in standard deviation, which suggests variances heterogeneity within the individual, because as the age of the broiler chickens increases the variance of body weights also increases. This feature points to the need for a model that supports the increase of this variability over time.

Table 2.1 – Means and standard errors (s.e.) of broiler chickens body weight (g) by treatment over time

Age	**ModM**		**ModF**		**LowM**		**LowF**		**HighM**		**HighF**	
(Days)	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.
3	69.1	1.1	72.1	0.5	70.3	0.8	72.4	0.7	69.1	0.8	72.1	0.9
7	144.4	2.7	152.5	1.6	146.3	2.6	148.3	1.8	144.1	2.1	150.0	1.6
9	211.4	3.4	220.5	2.0	212.0	4.5	213.3	2.3	212.2	2.9	219.7	2.6
12	339.7	5.0	344.4	2.8	333.8	6.4	329.2	3.3	342.9	4.0	347.5	3.1
15	521.6	7.9	512.5	3.9	504.6	7.8	486.6	3.5	512.7	5.5	510.6	4.8
18	730.2	6.5	701.7	3.8	696.4	8.6	660.3	4.6	722.9	10.2	708.9	9.1
21	970.5	5.4	908.7	4.3	917.5	7.7	851.1	8.3	958.8	12.8	920.7	14.0
24	1257.5	5.9	1161.7	10.0	1197.7	11.7	1089.5	13.4	1238.6	16.7	1162.0	16.6
27	1542.8	8.5	1418.3	6.4	1479.3	12.7	1327.4	16.7	1499.8	34.9	1412.3	20.5
30	1890.8	21.4	1717.1	5.9	1834.9	24.0	1612.1	15.3	1904.6	29.0	1691.8	22.3
33	2154.6	19.4	1952.4	7.0	2089.5	26.3	1859.6	10.6	2154.0	20.4	1922.2	23.4
36	2465.5	25.9	2179.8	14.9	2368.8	30.7	2087.6	10.0	2473.0	21.7	2175.8	22.6
39	2729.0	47.1	2430.3	12.4	2656.7	39.0	2332.6	7.4	2794.6	26.9	2421.7	22.4
41	3097.4	58.9	2653.2	32.9	2896.0	41.6	2536.7	18.8	3093.0	35.9	2673.8	25.7
44	3305.2	55.0	2884.2	42.9	3221.5	49.8	2789.5	16.6	3313.6	54.7	2865.3	19.2
47	3673.0	62.0	3172.0	41.2	3562.6	65.8	3078.0	20.9	3706.6	46.0	3150.9	33.2
51	3959.2	61.4	3377.4	71.3	3827.4	69.5	3312.6	28.1	3861.5	20.0	3465.5	111.6
54	4290.8	63.2	3631.4	69.0	4382.3	130.7	3570.5	36.6	4231.1	124.4	3601.7	50.0
56	4396.2	73.4	3683.0	51.7	4237.3	88.0	3642.0	66.8	4339.0	83.8	3734.9	87.0

ModM and ModF: Moderate nutritional density for Male and Female; LowM and LowF: Low nutritional density for Male and Female; HighM and HighF: High nutritional density for Male and Female.

Table 2.2 presents the results of the comparison between the fixed effect Gompertz model (FG) and the random effect Gompertz (MG) model in the coefficients related to the upper asymptote (β_1) and the bird maturity index (β_3). Note that the MG model presented the lowest AICc and BIC values compared to the FG model, which indicates a better agreement of the MG model to the data. Additionally, the likelihood ratio test also favored the MG model ($p < 0.0001$). The matrix of variance and covariance of the random effects ($\boldsymbol{G}$) of the MG model has a structure with different variances for the random effects, b_1 and b_3, with the correlation between them.

Table 2.2 – Selection criteria (AICc and BIC) and likelihood ratio test for the Gompertz model with fixed (FG) and mixed (MG) effects

Mod.	RE	$\boldsymbol{G}$	$\boldsymbol{R}$	npar	$-2logL$	AICc	BIC	p-value
FG	-	-	VC	19	8116.60	8155.74	8240.62	-
MG	b_1,b_3	UN	VCH(Age∗Sex)	59	6668.48	6797.82	7053.62	$< .0001$

RE: Random effect; $\boldsymbol{G}$: Variance-covariance matrix for the random effects; $\boldsymbol{R}$: Variance-covariance matrix intra-individual; npar: number of model parameters; $-2logL$: -2(logarithm of the likelihood); UN: Unstructured; VC: variance component; VCH(Age∗Sex): Heterogeneous variance components for interaction age and sex.

The matrix of variances and covariance intra-individual ($\boldsymbol{R}$) has a structure with null correlations and different variances for the interaction Time and Sex. Although

the matrix $\boldsymbol{R}$ is diagonal (assuming the assumption of independent errors), the variance and covariance matrix of the response variable, $\boldsymbol{y} = [y_1, y_2, \ldots, y_{684}]^T$ has nonzero elements outside the main diagonal because matrix $\boldsymbol{G}$, which allows the modeling of the correlation between repeated measurements made on the same individual. According to Zuur et al. (2009), this feature is called induced correlation and is a consequence of the inclusion of random effects in the model.

The quality of the adjustments of the FG and MG models can be evaluated in Figure 2.2.

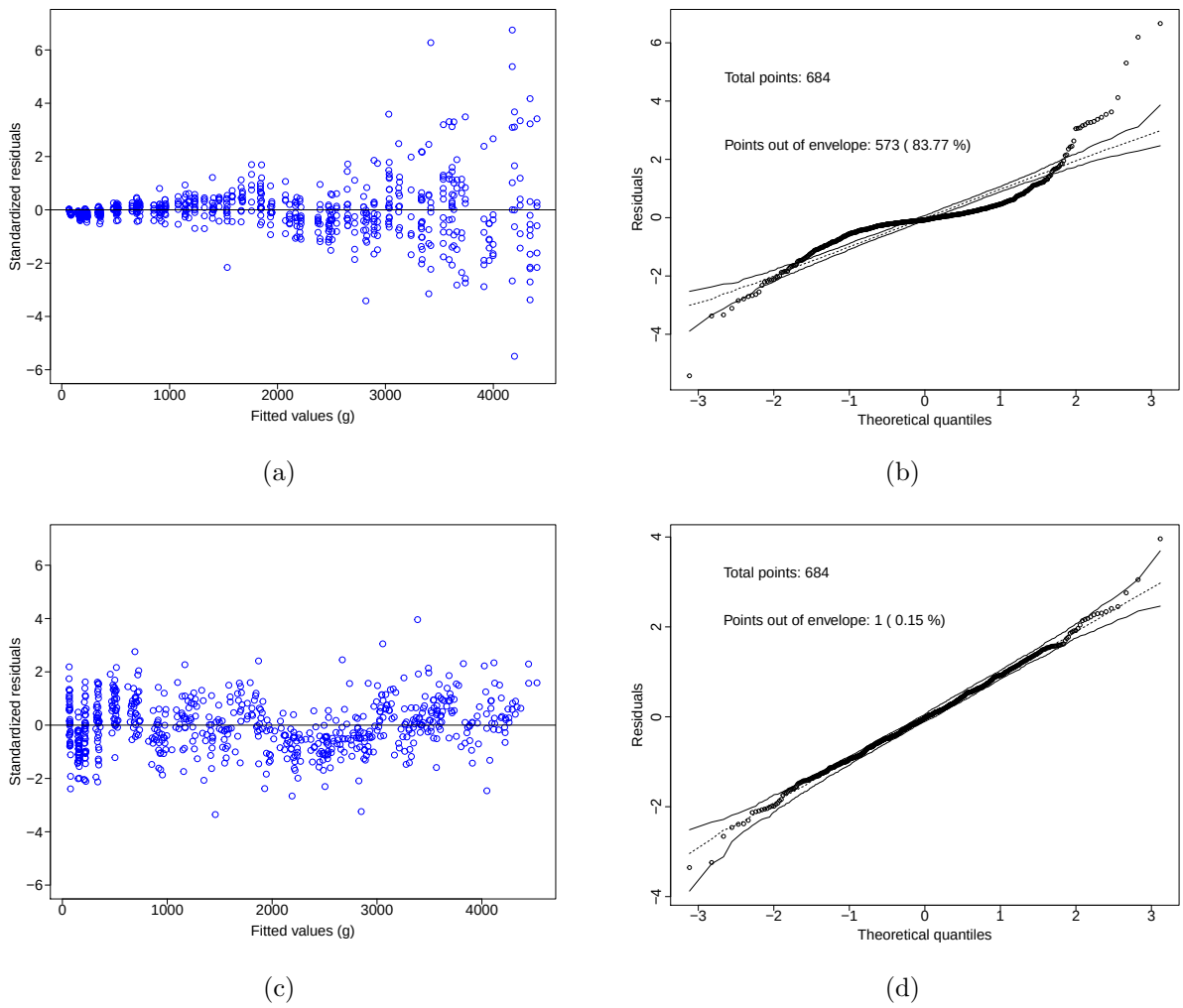


Figure 2.2 – Graph of standardized residuals versus adjusted values and half-normal simulated envelope graphs for the models Gomperz with fixed effects (FG), items (a) and (b), and Gompertz with random effects (MG) items (c) and (d)

In Figure 2.2 (c and d), we observe that the mixed Gompertz model (MG) was better fitted to body weight data of broiler chickens than the fixed Gompertz model (FG).

Table 2.3 shows that the estimates of the coefficients β_1, β_2 and β_3 were different in the FG and MG models.

Table 2.3 – Coefficients estimates of the fixed and mixed Gompertz models with the respective standard errors for each treatment and residual variance estimates for each model

	Fixed model (FG)			**Mixed model (MG)**		
Treatment	$\hat{\beta}_{11}$	$\hat{\beta}_{21}$	$\hat{\beta}_{31}$	$\hat{\beta}_{12}$	$\hat{\beta}_{22}$	$\hat{\beta}_{32}$
HighM	6006 ± 397	5.19 ± 0.34	0.049 ± 0.0042	5853 ± 380	5.19 ± 0.04	0.0503 ± 0.0024
ModM	6363 ± 430	5.04 ± 0.32	0.047 ± 0.0042	5805 ± 379	5.21 ± 0.04	0.0511 ± 0.0024
LowM	6601 ± 477	4.98 ± 0.31	0.044 ± 0.0042	5884 ± 383	5.15 ± 0.04	0.0488 ± 0.0024
HighF	5234 ± 286	4.72 ± 0.23	0.047 ± 0.0031	4842 ± 262	4.89 ± 0.02	0.0515 ± 0.0017
ModF	5057 ± 387	4.78 ± 0.33	0.049 ± 0.0045	4879 ± 371	4.91 ± 0.03	0.0512 ± 0.0024
LowF	5290 ± 429	4.77 ± 0.33	0.046 ± 0.0045	5061 ± 375	4.88 ± 0.03	0.0481 ± 0.0024
$\hat{\sigma}^2_\epsilon$		8562.55			15.17	

ModM and ModF: Moderate nutritional density for Male and Female; LowM and LowF: Low nutritional density for Male and Female; HighM and HighF: High nutritional density for Male and Female.

Estimates of the MG model presented lower standard errors than the FG model, thus, there is greater precision in the estimates of Gompertz mixed model than in the fixed Gompertz model. In the MG model, there was also a considerable reduction in residual variance, a result also reported by Wang and Zuidhof (2004), who used the mixed-effect Gompertz model to analyze data from six commercial broiler strains and concluded that the use of the mixed model reduced the residual variance by more than 55%.

The estimated of the random effects variances-covariances matrix b_1 and b_3 is given by:

$$\boldsymbol{G} = \begin{bmatrix} 96590.42 & -0.58 \\ -0.58 & 0.000004 \end{bmatrix}$$

Table 2.4 presents the estimates of the variance components of the intra-individual matrix, $\boldsymbol{R}$.

Table 2.4 – Intra-individual matrix variance component estimates ($\boldsymbol{R}$) of the model MG

	Variance components									
Sex	$\hat{\sigma}^2_1$	$\hat{\sigma}^2_2$	$\hat{\sigma}^2_3$	$\hat{\sigma}^2_4$	$\hat{\sigma}^2_5$	$\hat{\sigma}^2_6$	$\hat{\sigma}^2_7$	$\hat{\sigma}^2_8$	$\hat{\sigma}^2_9$	$\hat{\sigma}^2_{10}$
Male	1.0	4.4	3.0	4.3	9.9	5.7	4.9	3.8	86.0	210.4
Female	1.0	4.7	1.4	2.1	12.3	17.6	4.3	16.8	34.3	47.1
	$\hat{\sigma}^2_{11}$	$\hat{\sigma}^2_{12}$	$\hat{\sigma}^2_{13}$	$\hat{\sigma}^2_{14}$	$\hat{\sigma}^2_{15}$	$\hat{\sigma}^2_{16}$	$\hat{\sigma}^2_{17}$	$\hat{\sigma}^2_{18}$	$\hat{\sigma}^2_{19}$	
Male	138.2	276.2	738.1	655.5	354.8	881.3	376.8	5516.8	954.7	
Female	72.8	238.7	365.0	129.4	106.0	182.3	1547.4	388.2	685.8	

Note that the mixed model (MG) satisfactorily captured the fact that intra-individual variance increased over time and the distinction between male and female variations.

2.4 Conclusions

The mixed Gompertz model fitted best to data of body weight of broiler chickens than the fixed Gompertz model. The coefficient estimates were more accurate for the mixed model because there was a reduction in the residual variance and standard error of each estimate. The use of the mixed model allowed us to satisfactorily model the increase in intra-individual variation over time and the distinction between male and female variations, and also allowed the modeling of correlations in measurements made on the same individual over time.

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3 NONLINEAR MIXED MODELS FOR GROWTH CURVES OF BROILER CHICKENS

Abstract

In the performance study of broiler chickens, it is common to use nonlinear models to describe the growth patterns of birds. Among the most commonly used nonlinear models to describe growth curves in birds are sigmoidal models such as Gompertz, Logistic, von Bertalanffy, and Richards. Among the various sigmoidal models that can describe growth patterns, choosing an appropriate model is often a challenge to the researcher. In addition to modeling the data, the researcher needs accurate estimates for decision making. Although the use of mixed models can reduce residual variance and provide accurate estimates, it is not common to use random effects in bird growth models. In this work, we made a selection of the Gompertz, four-parameter logistic, von Bertalanffy, and Richards models, with mixed effects, for body weight data of 1080 Ross broiler chickens from a randomized block design in the factorial scheme with three nutritional densities and two sexes. We observed that the inclusion of random effects considerably reduced the residual variance in all models studied compared to the fixed effect model. According to the selection criteria used (correlation between the values observed and predicted by the model, residual variance, AICc, and BIC), we came to the following ranking of the models that best fit the broiler chicken data: 1st four-parameter logistic, 2nd von Bertalanffy, 3rd Gompertz, and 4th Richards. For the four growth models studied, we observed differences between the growth potential of males and females. Regarding the diets, we found that diets with high and moderate nutritional density provided a higher weight of broiler chickens than the diet with low nutritional density within each sex, considering the entire experimental period.

Keywords: Nonlinear model; Variance components; growth models; mixed models; Gompertz; von Bertalanffy; Richards; four-parameter logistic.

3.1 Introduction

Chicken meat is the animal protein source that grows the most in Brazil and the world. Brazil is currently the largest exporter and second-largest producer, standing out as a reference in the world poultry sector (ABPA - Associação Brasileira de Proteína Animal). The excellent performance of broiler chicken depends on several requirements that need to be adequately satisfied, such as facilities (shed), equipment, handling, sanitation, and nutrition. Feeding of broiler chickens accounts for about two-thirds of the cost of production (RIZZO, 2008), so many efforts are made to improve dietary effectiveness. Models for broiler chickens growth data have been developed over time, among the pro-

cedures used to estimate the growth curve of the animals is the use of nonlinear models such as Gompertz (GOMPERTZ, 1825; WINSOR, 1932), von Bertalanffy (VON BERTALANFFY, 1957), Richards (RICHARDS, 1959) and Logistic (NELDER, 1961).

In many types of growth data, the growth rate is not steadily decreasing but increases to the maximum before declining and reaching zero. Models that can accommodate this feature are nonlinear sigmoidal models. Such models include parameters with biological interpretations that add recognizable characteristics to the curve, for example, initial body weight, growth velocity, and adult weight. The point of inflection of this type of model is precisely the point at which the growth rate is maximum. It is common to use these models to describe the growth pattern of broiler chickens (see TZENG; BECKER, 1981; ROUSH et al., 2006; MARCATO et al., 2008; DEMUNER et al., 2017). However, it is not common to include random effects in these models.

In broiler chickens development data, it is natural the growing variability between the experimental units over time. For example, when studying the weight variable, in the initial days, the broiler chickens weights have a small variability, but over time this variability among the weights tends to grow, which indicates, in modeling, the need to include a covariance structure that supports the heterogeneity of variances over time. Moreover, the correlations between measurements made in time should not be ignored in the modeling, since measurements in the same experimental unit in the near time are expected to be more correlated than measures taken in more distant times. Both the heterogeneity of variances and the correlations in the time can be modeled using the mixed models, which allow great flexibility in the construction of the variance and covariance structures and an adequate explanation of the mean response. The Gompertz, four-parameter logistic, von Bertalanffy, and Richards models with mixed effects were adjusted to the data of body weight, of 1080 broiler chickens of the strain Ross, to investigate and to choose the model that best fits the data.

3.2 Case-study

The data that motivated this work is from a study conducted by Silva (2018) to evaluate the productive performance of broiler chickens, at the School of Animal Science and Food Engineering of the University of São Paulo (FZEA/USP) Brazil. A total of 1080 Ross broiler chickens were used, with a initial body weight of 45.69 ± 0.33 grams, allocated in 36 boxes, with 30 birds each. The broiler chickens were distributed in a randomized block design to control temperature differences throughout the shed. Six treatments were studied in the factorial scheme (3×2) being three nutritional densities (low, moderate, and high) and two sexes (male and female) (Table 3.1) with six replicates (Blocks). The experimental diets were formulated based on corn and soybean meal in a three-phase feeding program: initial (1 to 10 days), growth (11 to 22 days), and final (23 to 56 days). The experiment

was carried out in the period from 3 to 56 days, was collected in grams the body weight, totaling 19 measures at the times: 3, 7, 9, 12, 15, 18, 21 , 24, 27, 30, 33, 36, 39, 41, 44, 47, 51, 54 and 56 days.

Table 3.1 – Description of treatments

Treatment	**Nutrition**	**Sex**
ModM	Moderate	Male
ModF	Moderate	Female
LowM	Low	Male
LowF	Low	Female
HighM	High	Male
HighF	High	Female

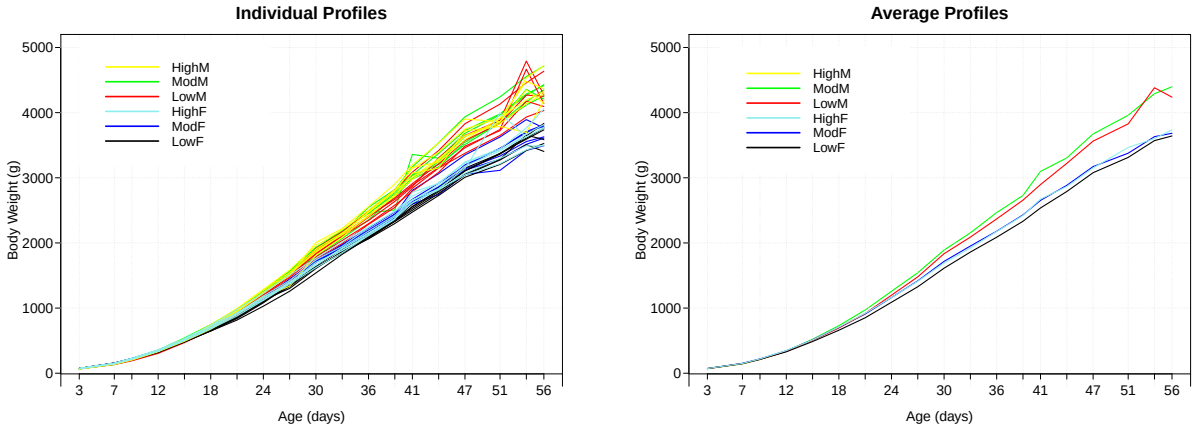
The mean values by treatment, in grams, of the body weight and their sample standard errors (s.e.) are shown in Table 3.2. In Appendix A1, we present the variances, covariances, and sample correlations over time for broiler chicken body weight.

Table 3.2 – Means and standard errors (s.e.) of body weight (g) of broiler chickens by treatment over time

Age	**ModM**		**ModF**		**LowM**		**LowF**		**HighM**		**HighF**	
(Days)	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.
3	69.1	1.1	72.1	0.5	70.3	0.8	72.4	0.7	69.1	0.8	72.1	0.9
7	144.4	2.7	152.5	1.6	146.3	2.6	148.3	1.8	144.1	2.1	150.0	1.6
9	211.4	3.4	220.5	2.0	212.0	4.5	213.3	2.3	212.2	2.9	219.7	2.6
12	339.7	5.0	344.4	2.8	333.8	6.4	329.2	3.3	342.9	4.0	347.5	3.1
15	521.6	7.9	512.5	3.9	504.6	7.8	486.6	3.5	512.7	5.5	510.6	4.8
18	730.2	6.5	701.7	3.8	696.4	8.6	660.3	4.6	722.9	10.2	708.9	9.1
21	970.5	5.4	908.7	4.3	917.5	7.7	851.1	8.3	958.8	12.8	920.7	14.0
24	1257.5	5.9	1161.7	10.0	1197.7	11.7	1089.5	13.4	1238.6	16.7	1162.0	16.6
27	1542.8	8.5	1418.3	6.4	1479.3	12.7	1327.4	16.7	1499.8	34.9	1412.3	20.5
30	1890.8	21.4	1717.1	5.9	1834.9	24.0	1612.1	15.3	1904.6	29.0	1691.8	22.3
33	2154.6	19.4	1952.4	7.0	2089.5	26.3	1859.6	10.6	2154.0	20.4	1922.2	23.4
36	2465.5	25.9	2179.8	14.9	2368.8	30.7	2087.6	10.0	2473.0	21.7	2175.8	22.6
39	2729.0	47.1	2430.3	12.4	2656.7	39.0	2332.6	7.4	2794.6	26.9	2421.7	22.4
41	3097.4	58.9	2653.2	32.9	2896.0	41.6	2536.7	18.8	3093.0	35.9	2673.8	25.7
44	3305.2	55.0	2884.2	42.9	3221.5	49.8	2789.5	16.6	3313.6	54.7	2865.3	19.2
47	3673.0	62.0	3172.0	41.2	3562.6	65.8	3078.0	20.9	3706.6	46.0	3150.9	33.2
51	3959.2	61.4	3377.4	71.3	3827.4	69.5	3312.6	28.1	3861.5	20.0	3465.5	111.6
54	4290.8	63.2	3631.4	69.0	4382.3	130.7	3570.5	36.6	4231.1	124.4	3601.7	50.0
56	4396.2	73.4	3683.0	51.7	4237.3	88.0	3642.0	66.8	4339.0	83.8	3734.9	87.0

ModM and ModF: Moderate nutritional density for Male and Female; LowM and LowF: Low nutritional density for Male and Female; HighM and HighF: High nutritional density for Male and Female.

The individual profiles and mean profiles by treatments, of the body weight variable, depending on the age of the broiler chickens, are shown in Figure 3.1. In Appendix A2 we present the individual profiles separated by treatments.



(a) (b)

Figure 3.1 – Individual profiles (a) and average profiles (b) of broiler chickens body weight by treatment

3.3 Modelling

3.3.1 Nonlinear mixed-effects model

The nonlinear mixed models are used to describe the nonlinear relationship of the response variable with the parameters and covariates. It allows an interpretation of its parameters and an explanation of the possible variations according to a classification factor. In the literature, different nonlinear mixed models have been proposed, see Lindstrom and Bates (1990), Vonesh and Carter (1992), Wakefield et al. (1994), among others.

As described in Lindstrom and Bates (1990), in the 1st stage, the jth observation in the ith group is given by

$$y_{ij} = f(\boldsymbol{\phi}_{ij}, \boldsymbol{x}_{ij}) + \varepsilon_{ij}, \qquad i = 1, \ldots, M, \quad j = 1, \ldots, n_i$$

where f is a nonlinear function of the vector of parameters $\boldsymbol{\phi}_{ij}$ with a vector of covariates $\boldsymbol{x}_{ij}$, ε_{ij} is a normally distributed error term, M is the total number of groups, and n_i is the number of observations in the ith group.

In the 2nd stage the parameters of specific groups are modeled as

$$\boldsymbol{\phi}_{ij} = \boldsymbol{A}_{ij}\boldsymbol{\beta} + \boldsymbol{B}_{ij}\boldsymbol{b}_i$$

where $\boldsymbol{\beta}$ is a fixed effects vector; $\boldsymbol{b}_i$ is a random effects vector (varying with i but not with j), which are assumed to be independently distributed as $N(\boldsymbol{0}, \boldsymbol{G})$. $\boldsymbol{A}_{ij}$ and $\boldsymbol{B}_{ij}$ are design matrices for the fixed and random effects, respectively, which may depend of the values of some covariates in the jth observation. Furthermore, it is assumed that $\boldsymbol{b}_i$ are independent of $\boldsymbol{\varepsilon}_{ij}$.

The assumptions about random effects and error terms within the group can

be summarized in the following expressions, $\boldsymbol{b}_i \sim N(\mathbf{0}, \boldsymbol{G})$ and $\boldsymbol{\varepsilon}_i \sim N(\mathbf{0}, \boldsymbol{R})$, respectively.

3.3.1.1 Modelling the variance heterogeneity

The assumption of homogeneous variances is often violated in practice. Davidian and Giltinan (1995) mention that growth data often exhibit a constant coefficient of variation instead of constant variance, that is, variance proportional to the square of the mean response. In this case, as mentioned by the authors, a more appropriate assumption would be

$$\mathrm{E}(\mathbf{Y}_i) = f(x_i, \boldsymbol{\beta}), \quad \mathrm{Var}(\mathbf{Y}_i) = \sigma^2[f(x_i, \boldsymbol{\beta})]^2, \tag{3.1}$$

where the scale parameter σ is the coefficient of variation.

Davidian and Giltinan (1995) propose to model heteroscedasticity using the variance function, whose general formulation of the model for errors within the group (individual), also presented by Pinheiro and Bates (2000), is defined as

$$\mathrm{Var}(\epsilon_{ij}|\mathbf{b}_i) = \sigma^2 g^2(\mu_{ij}, \boldsymbol{\nu}_{ij}, \boldsymbol{\delta}), \quad i = 1, \ldots, N, \quad j = 1, \ldots, n_i, \tag{3.2}$$

where $\mu_{ij} = \mathrm{E}[Y_{ij}|\mathbf{b}_i]$, $\boldsymbol{\nu}_{ij}$ is a covariates vector for variance, $\boldsymbol{\delta}$ is a parameter vector for variance and $g(.)$ is the variance function, assumed to be continuous in $\boldsymbol{\delta}$.

3.3.2 Growth Models

Models for growth data have been developed over time. According to Draper and Smith (1998), in general, growth models are mechanistic instead of empirical. The mechanistic model arises as a result of assumptions made from differential equations, related to the type of growth studied. The empirical model is an approximation of an unknown mechanistic model, and, distinctly, it is a polynomial model of some proper order.

In many types of growth data, the growth rate is not steadily decreasing but increases to the maximum before declining and reaching zero. Models that can accommodate this feature are nonlinear sigmoidal models. Such models add another recognizable characteristic to the curve, with the inflection point that is precisely the point at which the growth rate is maximal. Many studies have been conducted to determine the best growth models in different bird species. For example, Şengül and Kiraz (2005) concluded that the Gompertz, three-parameter logistic, and Richards models are adequate to explain the growth of large white turkeys. Nahashon et al. (2006) found that the Gompertz model was better than the three-parameter logistic to describe the growth patterns of French guinea fowl. Balcioğlu et al. (2009) used the models Gompertz, von Bertalanffy, and three-parameter logistic to estimate the growth curve of the chukar partridges and reported that the Gompertz model was the most appropriate to describe the growth pattern of birds.

Narinc et al. (2010) compared ten nonlinear models for Japanese quail growth data, among these models they used the Gompertz, Richards and von Bertalanffy and reported that the Gompertz model is the most appropriate, followed by Richards. Rizzi et al. (2013) used linear and nonlinear models (Gompertz, three-parameter logistic, and Richards) to describe broiler chicken growth patterns. Mohammed (2015) used the models Gompertz, von Bertalanffy, and three-parameter logistic to estimate the growth curve of Ross broiler chickens.

Finke et al. (1987), Finke et al. (1989), and Gahl et al. (1991) used the four-parameter logistic curve to describe the growth pattern in rats. According to Magis (2013), the four-parameter logistic model has been reconsidered in the literature due to the improvement in computational power and resources, together with the development of more accurate statistical modeling software. The expressions of the models used to describe the growth of broiler chickens in this work are presented in Table 3.3.

Table 3.3 – Growth curve model expressions

Model	**Expression**	**Source**
Gompertz	$y = \phi_1 \exp\left[-\phi_2 \exp\left(-\phi_3 t\right)\right]$	Draper and Smith (1998)
Four-parameter logistic	$y = \phi_5 + \dfrac{\phi_1 - \phi_5}{\left\{1 + \exp\left[\phi_4\left(\phi_3 - \log t\right)\right]\right\}}$	Ratkowsky and Reedy (1986)
von Bertalanffy	$y = \left[\phi_1^{(1-\phi_6)} - \phi_2 \exp\left(-\phi_3 t\right)\right]^{1/(1-\phi_6)}$	Draper and Smith (1998)
Richards	$y = \phi_1 / \left[1 + \phi_2 \exp\left(-\phi_3 t\right)\right]^{1/\phi_6}$	Bates and Watts (1988)

y is the response variable; t is the age of the broiler chickens; ϕ_1 is the maximum response of growth; ϕ_2 is a scale parameter related to initial response; ϕ_3 is a intrinsic growth rate; ϕ_4 is the predicted value at the response halfway between the two asymptotes (upper and lower); ϕ_5 is the lower asymptote; ϕ_6 is the parameter related to shape of the curve; exp: exponential function; log: natural logarithm.

For a better understanding of the interpretation of the coefficients, were plotted curves for each growth model studied, assigning different values for each of the coefficients referring to the fixed part of the models. These curves were presented in Appendix A3.

3.3.3 Estimation

There are different methods of estimation of the parameters of the nonlinear mixed-effects models, see Vonesh and Carter (1992), Ramos and Pantula (1995), Davidian and Giltinan (1995). In this work, we use the maximum likelihood method. Since random effects are unobserved quantities, the maximum likelihood estimation is based on the marginal density of the responses y, which is calculated as follows

$$p(\boldsymbol{y}|\boldsymbol{\beta}, \sigma^2, \boldsymbol{G}) = \int p(\boldsymbol{y}|\boldsymbol{b}, \boldsymbol{\beta}, \sigma^2) p(\boldsymbol{b}|\boldsymbol{G}) d\boldsymbol{b}, \tag{3.3}$$

where $p(\boldsymbol{y}|\boldsymbol{\beta}, \sigma^2, \boldsymbol{G})$ is the marginal density of $\boldsymbol{y}$, $p(\boldsymbol{y}|\boldsymbol{b}, \boldsymbol{\beta}, \sigma^2)$ is the conditional density of $\boldsymbol{y}$ given the random effects, $\boldsymbol{b}$, and $p(\boldsymbol{b}|\boldsymbol{G})$ is the marginal distribution of $\boldsymbol{b}$. In nonlinear mixed models, the random effects can enter the model in a nonlinear way, then the integral of the expression (3.3) is usually does not closed-form. Thus numerical optimization procedures are required to obtain the parameter estimates. Different methods to approximate the integral of the expression (3.3) have been proposed, some of these methods are based on the first-order Taylor expansion (SHEINER; BEAL, 1980; LINDSTROM; BATES, 1990). Other methods use the Gaussian quadrature rules (DAVIDIAN; GALLANT, 1992) or the Laplace approximation. The latter is often used in Bayesian inference (TIERNEY; KADANE, 1986; LEONARD et al., 1989), but it can be used to approximate the likelihood function of nonlinear mixed models. We also have the adaptive Gaussian quadrature rule method, which improves the Laplace approximation method (PINHEIRO; BATES, 2000).

We use in this work the algorithm described by Lindstrom and Bates (1990), that algorithm alternates between two steps, one step consisting of penalized nonlinear least squares (PNLS) and the other using mixed linear effects (LME).

In the PNLS step, conditional estimates of β fixed effects are obtained by minimizing the penalized nonlinear least-squares objective function

$$\sum_{i=1}^{M}[\|\mathbf{y} - f_i(\beta, b_i)\|^2 + \|\boldsymbol{\Delta} b_i\|^2].$$

where $\boldsymbol{\Delta}$ is used for computational convenience and corresponds to the precision factor related to the variance and covariance matrix that satisfies

$$\frac{\mathbf{G}^{-1}}{1/\sigma^2} = \boldsymbol{\Delta}^T \boldsymbol{\Delta}.$$

If $\mathbf{G}$ is positively-defined, then $\boldsymbol{\Delta}$ will exist, but may not be unique. The step where we use the linear random effects (LME) is based on Taylor's first-order expansion of the f function around the corresponding β value and the conditional form of the random effects b_i to update the $\boldsymbol{\Delta}$ estimate. The algorithm alternates between PNLS and LME steps until a convergence criterion is met. According to Pinheiro and Bates (2000), higher efficiency of the algorithm is achieved when variance component estimates ($\boldsymbol{\Delta}$) are not strongly correlated with fixed effects estimates β.

3.3.4 Initial value

To fit the models, we need the initial values for each parameter that will be estimated. The specification of the initial values is one of the most challenging problems found in the process of estimating the parameters of nonlinear models (DRAPER; SMITH, 1998). Incorrect initial values result in many iterations, longer convergence time, or even non-convergence of iterations (FEKEDULEGN et al., 1999). The proper understanding of

the definition of each parameter in the context of the data that will be modeled facilitates the specification of the initial values.

There is no general method for obtaining the initial values, but some procedures may be useful to get them. A graphic procedure was used to obtain the initial values for each of the models studied. As the parameters of the growth models used have a practical interpretation, the graphic exploration of the dispersion of observations over time gives us indications for possible initial estimates of the parameters. Figure 3.2 shows the dispersion of the weights of the broiler chickens throughout the experimental period with a curve plotted on the mean values at each point in the time, called the average profile. The possible values of the horizontal asymptotes inferior and superior are easily visualized in Figure 3.2. The dashed lines in the figure, related to the values 50 and 5000, represent the initial values considered for the lower (ϕ_5) and upper (ϕ_1) asymptotes, respectively, in the models studied. After obtaining the initial values for the asymptotes, the procedure consisted of assigning values for the other parameters (ϕ_2, ϕ_3, ϕ_4, or ϕ_6) and observe the approximation of the curve of the model to the average profile. Then different values were successively assigned to the coefficients of the curve, and the proximity of the curve to the average profile was visualized. When the curve of the model was close to the mean values at each experimental time, then we assume these values of the coefficients of the curve as initial values for the iterative process.

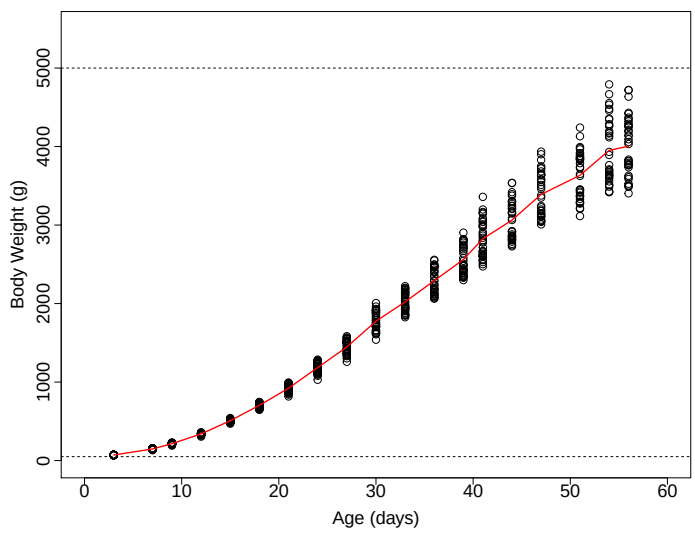


Figure 3.2 – Scatter plot of weight observations over time with the mean curve

3.3.5 Selection of models

In the selection stage of the appropriate model, we try to choose a model that is rich enough to explain the behavior and variation of the response variable. But it must also be a parsimonious model concerning the number of parameters, that is, it must be a model simple enough to interpret, understand, explain to others, and use. The selection of

models is used when there is no particular clear choice between the many possible different models. In the search process is necessary to take into account information about what is planned to be done or what is expected of the research, the type of sampling or experimental design used, the prior knowledge about the explanatory variables relevant and the variability of the sample units. In selecting one model, we must keep in mind that in most situations we will not be able to determine the "correct" or "true" model because the model that generated the collected data can be very complex or unknown. Several methods of model selection depart from the perspective that all models are wrong, but some are useful (CLAESKENS; HJORT, 2008). Several criteria for selecting models are presented in the literature, in this work we will use the Likelihood Ratio Test (LRT), the Akaike Information Criterion - AIC (AKAIKE, 1974; SAKAMOTO et al., 1986), the Akaike's Information Corrected Criterion - AICc (HURVICH; TSAI, 1989), and Bayesian information criterion - BIC (SCHWARZ, 1978).

3.3.5.1 Likelihood Ratio Test

The likelihood ratio test (LRT) is a general method used to compare nested models adjusted for maximum likelihood (ML) or restricted maximum likelihood (REML). The alternative hypothesis of the test, H_1, represents the reference model with the highest number of parameters, while the null hypothesis, H_0, represents the restricted model with the lowest number of parameters. The test statistic is given by:

$$\Lambda = 2\log\left(\frac{L_2}{L_1}\right) = 2\left[\log(L_2) - \log(L_1)\right]$$

where L_2 is the likelihood of the reference model and L_1 is the likelihood of the restricted model. If k_i is the number of parameters to be estimated in the model i, then the asymptotic distribution of the LRT statistic under the null hypothesis follows a distribution χ^2 with $k_2 - k_1$ degrees of freedom, on what k_2 is the number of parameters of the reference model and k_1 is the number of parameters of the restricted model. Then, to test H_0 *versus* H_1, with significance level α, we compare Λ to a $\chi^2_{k_2-k_1}$. When $\Lambda \geq \chi^2_{(k_2-k_1,\alpha)}$ we reject H_0 in favor of H_1.

3.3.5.2 Information criteria

Information criteria are rules made to comparing models adjusted by maximum likelihood methods. The AIC and BIC information criteria have played a significant role in model selection in many areas of study. These criteria are used to compare two or more models for the same dataset, and these models can be nested or non-nested. The fundamental idea of these criteria is to penalize the maximum value of log-likelihood as the number

of parameters increases. The expressions for the calculation of AIC and BIC are:

$$AIC = -2l(\hat{\boldsymbol{\beta}}, \hat{\boldsymbol{\theta}}, \hat{\sigma}) + 2k \tag{3.4}$$

$$BIC = -2l(\hat{\boldsymbol{\beta}}, \hat{\boldsymbol{\theta}}, \hat{\sigma}) + k\log(n) \tag{3.5}$$

where $l(\hat{\boldsymbol{\beta}}, \hat{\boldsymbol{\theta}}, \hat{\sigma})$ is the value of the logarithm of the likelihood function of the calculated model with the estimates obtained in the maximization process, k represents the total number of model parameters, considering the parameters of the fixed part together with the parameters of the covariance structure, and n is the number of observations used in the estimation of the model under study. The model with the lowest AIC or BIC value is selected as the most appropriate.

In the calculation of the AIC, as more parameters are added in the model, the first term on the right side of the expression (3.4) ($-2l(\hat{\boldsymbol{\beta}}, \hat{\boldsymbol{\theta}}, \hat{\sigma})$) tends to decrease, while the second term ($2k$) always increases with the number of parameters, this causes a balance between super-parametrized and sub-parametrized models (BURNHAM; ANDERSON, 2002). When the number of parameters (k) is high relative to the sample size (say, $n/k < 40$) a correction is recommended in the AIC (BURNHAM; ANDERSON, 2002; POSADA; BUCKLEY, 2004), then the expression for the calculation of the corrected AIC is given by:

$$AIC_C = AIC + \frac{2k(k+1)}{n-k-1}$$

Verbeke and Molenberghs (2000) emphasize that the information criteria provide only practical rules to discriminate some model among several statistical models, and should never be used or interpreted as formal statistical tests of significance.

3.3.6 Diagnostic

Performing model diagnostics makes it possible to verify the distribution assumptions for the residuals and the model's sensitivity to unusual observations. Diagnostic tools for classical linear models are well established in the literature, details of development and applications can be seen in Cook (1977), Hoglin and Welsch (1978), Welsch and Kuh (1977), Belsley et al. (1980), Atkinson (1985) among others. In mixed models, the workload in this area is relatively smaller because of complexity, generally mixed models require iterative optimization, have more components, different types of residues, conditional and marginal distributions and are most often applied to data with grouped structures (LITTELL et al., 2006).

Hilden-Minton (1995) and Nobre and Singer (2007) defined three types of residuals in mixed linear models,

(i) Marginal residuals: $\hat{\boldsymbol{\xi}} = \mathbf{y} - \mathbf{X}\hat{\boldsymbol{\beta}}$;

(ii) Conditional residuals: $\hat{\boldsymbol{\epsilon}} = \mathbf{y} - \mathbf{X}\hat{\boldsymbol{\beta}} - \mathbf{Z}\hat{\mathbf{b}}$;

(iii) EBLUP: $\mathbf{Z}\hat{\mathbf{b}}$, which predicts the random effects $\mathbf{Zb} = \mathrm{E}[\mathbf{Y}|\mathbf{b}] - \mathrm{E}[\mathbf{Y}]$.

The authors make recommendations regarding the use of each type of residue to evaluate some assumptions of the mixed model. For example, Hilden-Minton (1995) suggests using the marginal residuals ($\hat{\boldsymbol{\xi}}$) to assess the assumption of linearity of the relationship between $\mathrm{E}[\mathbf{Y}]$ and the $\mathbf{X}$ covariates, and their use in evaluating the validity of the covariance structure. Pinheiro and Bates (2000) suggest the use of conditional residuals to verify the hypothesis of normality and homoscedasticity of the conditional error. This type of residue can also be used to identify discrepant observations. EBLUP can be used to detect possible discrepant experimental units, to assess the assumption of normality of random effects, as well as to verify their structure of variance and covariance.

According to Pinheiro and Bates (2000), construction strategies and diagnostics of mixed linear models can be applied to mixed nonlinear models.

3.3.7 Adjustment of models

The Gompertz, four-parameter logistic, von Bertalanffy, and Richards models were adjusted for broiler chicken body weight data. We selected the variance and covariance structure that best described the data for each of the growth models. Initially, we used simpler structures to reduce convergence problems. We were sequentially adding random effects to the model parameters, following the suggestion of the 95% confidence intervals graphs presented in Appendix A4. In this selection, we used the likelihood ratio test and the information criteria, AIC, AICc, and BIC. The block effect was not considered in this work, but the study for its inclusion is in progress. The quality of the fit was verified by observing the chart of the standardized conditional residuals versus the adjusted values, we also saw the half-normal plot with simulated envelope using the hnp() function of the hnp package (MORAL et al., 2017) of the R statistical software (R CORE TEAM, 2019). The models were adjusted by the maximum likelihood method using the nlme() function of the nlme package (PINHEIRO et al., 2019). After the model selection step, a comparison between the growth models was made using, besides the information criteria, the residual variance estimate and the correlation between the observed values and values adjusted by the model. The selection of the models consisted, firstly, in choosing random effects for the coefficients and, later, in selecting the variance-covariance structure. Part of the programming used in this work is in Appendix A5.

3.4 Results

In this section, we present the results of the selection procedures of the Gompertz, four-parameter logistic, von Bertalanffy, and Richards growth models. After

the selection of growth models, comparisons were made between the four selected models. The number of curves that best describe the growth of broiler chickens in relation to treatments was also selected.

3.4.1 Mixed Gompertz growth model

Results corresponding to the model selection procedure for the Gompertz mixed-effects growth model are presented in this section. Table 3.4 shows the results of the model selection step indicating the parameters with random effects (RE), the respective variance and covariance structures ($\boldsymbol{G}$ and $\boldsymbol{R}$) of the compared models, the information criteria values (AICc and BIC) and the likelihood ratio test result (p-value). The number of parameters in the model is indicated in the npar column, where the GF model has 18 parameters corresponding to the coefficients of the Gompertz curve for each of the six treatments plus the residual variance parameter. From the G1 model, there are 18 parameters referring to the three coefficients of the Gompertz growth curve for each of the six treatments in the fixed part, plus the parameters corresponding to the variance components. The GF model corresponds to the Gompertz model without random effects with homogeneous covariance structure. From model G1 to G9, random effects were selected by changing the structure of matrix $\boldsymbol{G}$. After selecting random effects, we modified the structure of the covariance matrix, $\boldsymbol{R}$, in this step we worked with models G10, G11, and G12.

Table 3.4 – Selection of Gompertz models with mixed effects

Mod.	RE	$\boldsymbol{G}$	$\boldsymbol{R}$	npar	$-2logL$	AICc	BIC	Comp.	p-value
GF	-	-	VC	19	8116.60	8155.74	8240.62	-	-
G1	ϕ_1	-	VC	20	7839.32	7880.58	7969.87	GF *vs* G1	$< .0001$
G2	ϕ_1, ϕ_2	UN	VC	22	7782.42	7827.96	7926.04	G1 *vs* G2	$< .0001$
G3	ϕ_2	-	VC	20	8019.22	8060.49	8149.79	G2 *vs* G3	$< .0001$
G4	ϕ_1, ϕ_2, ϕ_3	UN	VC	25	7773.16	7825.13	7936.35	G2 *vs* G4	0.0258
G5	ϕ_1, ϕ_3	UN	VC	22	7773.16	7818.68	7916.77	G4 *vs* G5	1
G6	ϕ_2, ϕ_3	UN	VC	22	7834.70	7880.23	7978.32	G5 *vs* G6	-
G7	ϕ_3	-	VC	20	7916.10	7957.36	8046.65	G5 *vs* G7	$< .0001$
G8	ϕ_1,ϕ_3	VC	VC	20	7916.10	7957.36	8046.65	G5 *vs* G8	$< .0001$
G9	ϕ_1,ϕ_3	VCH	VC	21	7839.32	7882.71	7976.40	G5 *vs* G9	$< .0001$
G10	ϕ_1,ϕ_3	UN	VCH(Sex)	23	7703.18	7750.85	7853.32	G5 *vs* G10	$< .0001$
G11	ϕ_1,ϕ_3	UN	VCH(Age)	40	6762.16	6847.26	7023.28	G10 *vs* G11	$< .0001$
G12	ϕ_1,ϕ_3	UN	VCH(Age∗Sex)	59	6668.48	6797.82	7053.62	G11 *vs* G12	$< .0001$

RE: Random effect; $\boldsymbol{G}$: Variance-covariance matrix for the random effects; $\boldsymbol{R}$: Variance-covariance matrix intra-individual; npar: number of model parameters; $-2logL$: -2(logarithm of the likelihood); UN: Unstructured; VC: Variance Components; VCH(Age): Heterogeneous variance components for age ; VCH(Sex): Heterogeneous variance components for sex; VCH(Age∗Sex): Heterogeneous variance components for interaction age and sex.

According to the information criteria and the likelihood ratio test, the most appropriate model for the data was the G12. This model has random effects on the parameters ϕ_1 and ϕ_3 with a correlation between them and a heterogeneous intra-individual covariance structure with different variance components for the Age and Sex interaction. We can observe the quality of fit of model G12 in Figure 3.3 in items (c) and (d), where are the graphs of standardized residuals versus adjusted values and the half-normal plot with simulation envelope, respectively. In this same figure are the charts of the residuals of the fixed model, GF, in items (a) and (b). We observed in Figure 3.3 the need to include random effects in the Gompertz model for a better description of broiler chicken weight data.

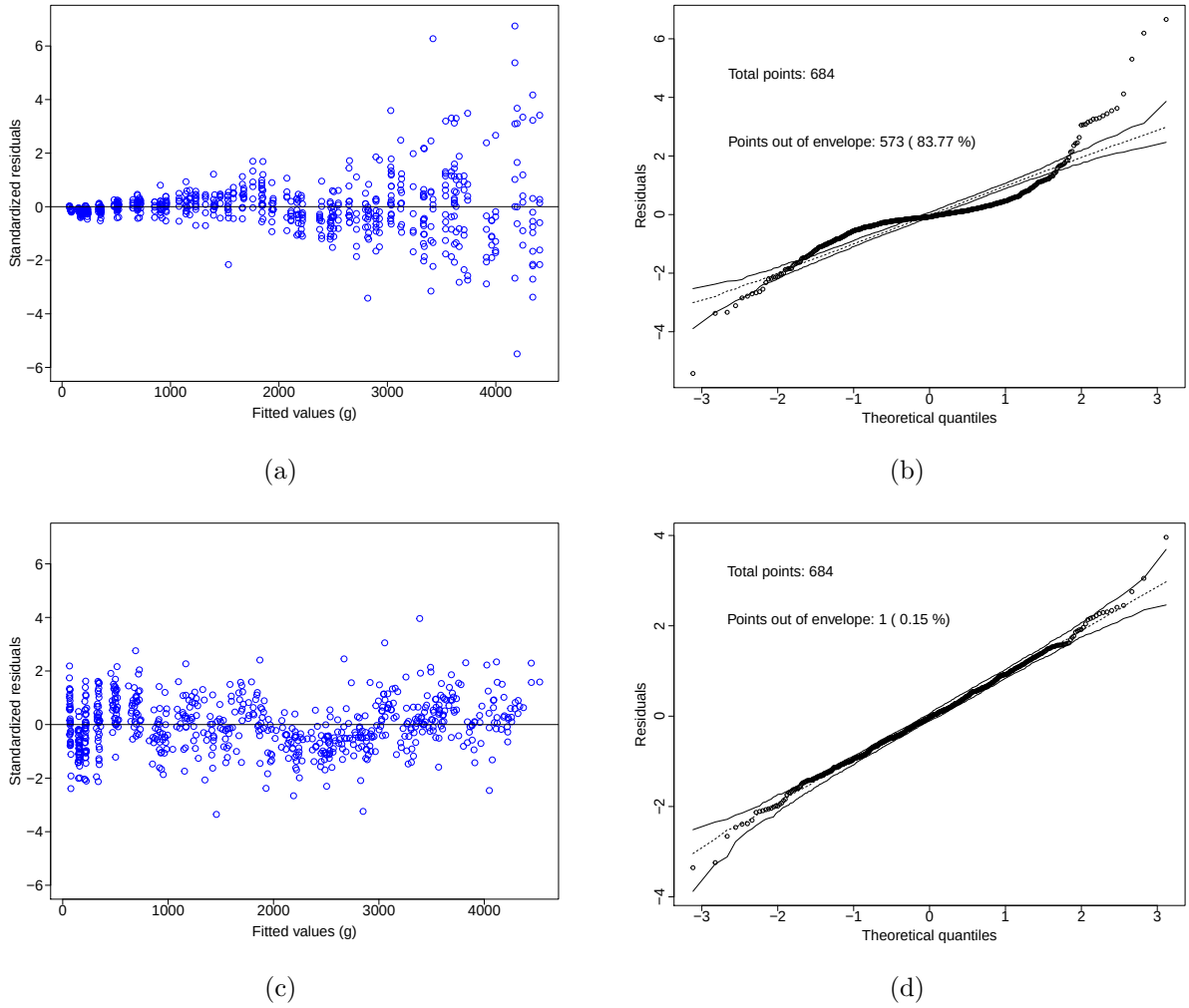


Figure 3.3 – Graph of standardized residuals versus adjusted values and half-normal simulated envelope graphs for the models Gomperz with fixed effects (GF), items (a) and (b), and Gompertz with random effects (G12) items (c) and (d)

3.4.2 Mixed four-parameter logistic growth model

In the procedure for the selection of the four-parameter logistic model, the ϕ_5 coefficient was not statistically significant concerning the treatment effect. Thus the treatment factor effect of this coefficient was removed (see Appendix A6). Table 3.5 presents the results of the steps for model selection. The LF model corresponds to the four-parameter logistic model without random effects, with a homogeneous covariance structure. Thus, the LF model has 19 parameters corresponding to the logistic curve coefficients for each of the six treatments plus the residual variance parameter. From the L1 model, the fixed part contains 19 parameters referring to the four growth curve coefficients, being ϕ_1, ϕ_3, and ϕ_4 for each of the six treatments and ϕ_5 only in the intercept. Already in the random part, we have the parameters corresponding to the variance components according to the covariance structure evaluated. From model L1 to L9, random effects were selected by changing the structure of matrix $\boldsymbol{G}$. After selecting random effects, we modified the structure of the covariance matrix, $\boldsymbol{R}$, in this step we worked with models L10, L11, and L12.

Table 3.5 – Selection of four-parameter logistic models with mixed effects

Mod.	RE	$\boldsymbol{G}$	$\boldsymbol{R}$	npar	$-2logL$	AICc	BIC	Comp.	p-value
LF	-	-	VC	20	8111.10	8152.37	8241.66	-	-
L1	ϕ_1	-	VC	21	7826.78	7870.17	7963.86	LF *vs* L1	$< .0001$
L2	ϕ_1, ϕ_3	UN	VC	23	7766.80	7814.48	7916.95	L1 *vs* L2	$< .0001$
L3	ϕ_3	-	VC	21	7894.78	7938.18	8031.87	L2 *vs* L3	$< .0001$
L4	ϕ_1, ϕ_4	UN	VC	23	7767.50	7815.17	7917.64	L2 *vs* L4	-
L5	ϕ_1, ϕ_5	UN	VC	23	7808.58	7856.25	7958.72	L2 *vs* L5	-
L6	ϕ_1, ϕ_3, ϕ_4	UN	VC	26	7766.80	7820.94	7936.53	L2 *vs* L6	0,9999
L7	ϕ_1, ϕ_3, ϕ_5	VCH	VC	23	7826.76	7874.44	7976.91	L2 *vs* L7	-
L8	ϕ_1, ϕ_3, ϕ_4, ϕ_5	VCH	VC	24	7798.08	7847.90	7954.75	L2 *vs* L8	$< .0001$
L9	ϕ_1, ϕ_3, ϕ_4, ϕ_5	VC	VC	21	7872.76	7916.16	8009.85	L8 *vs* L9	$< .0001$
L10	ϕ_1, ϕ_3, ϕ_4, ϕ_5	VCH	VCH(Sex)	25	7745.54	7797.52	7908.74	L8 *vs* L10	$< .0001$
L11	ϕ_1, ϕ_3, ϕ_4, ϕ_5	VCH	VCH(age)	42	6461.80	6551.44	6735.98	L10 *vs* L11	$< .0001$
L12	ϕ_1, ϕ_3, ϕ_4, ϕ_5	VCH	VCH(Sex∗Age)	61	6411.38	6545.53	6809.58	L11 *vs* L12	$< .0001$

RE: Random effect; $\boldsymbol{G}$: Variance-covariance matrix for the random effects; $\boldsymbol{R}$: Variance-covariance matrix intra-individual; npar: number of model parameters; $-2logL$: -2(logarithm of the likelihood); UN: Unstructured; VC: Variance Components; VCH(Age): Heterogeneous variance components for age ; VCH(Sex): Heterogeneous variance components for sex; VCH(Age∗Sex): Heterogeneous variance components for interaction age and sex.

The most appropriate model for the data was the L12, with a random effect on the four growth model coefficients and null correlations, and a heterogeneous intra-individual covariance structure with different variance components for the Age and Sex interaction. We can observe the quality of fit of model L12 in Figure 3.4 in items (c) and (d), where are the graphs of standardized residuals versus adjusted values and the half-normal plot with simulation envelope, respectively. In this same figure are the charts of the residuals of the fixed model, LF, in items (a) and (b). We observed in Figure 3.4 the need

to include random effects in the four-parameter logistic model for a better description of broiler chicken weight data.

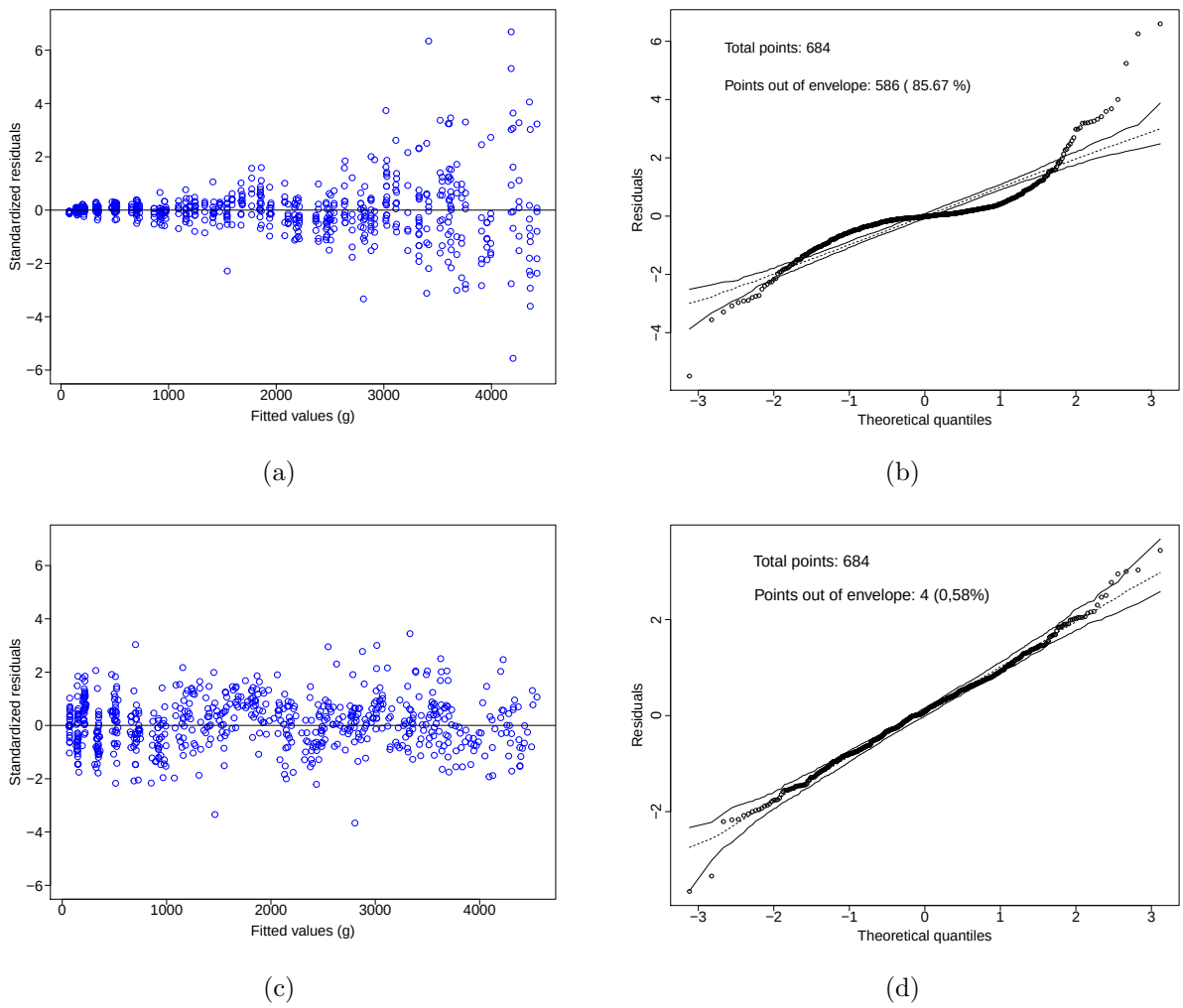


Figure 3.4 – Graph of standardized residuals versus adjusted values and half-normal simulated envelope graphs for the models four-parameter logistic with fixed effects (LF), items (a) and (b), and four-parameter logistic with random effects (L12) items (c) and (d)

3.4.3 Mixed von Bertalanffy growth model

Results corresponding to the selection steps for the von Bertalanffy mixed-effect growth model are presented in Table 3.6. There was no statistical significance of treatments in coefficient ϕ_6, so was disregarded the treatment factor for this coefficient (see Appendix A6). The VF model corresponds to the fixed model with homogeneous covariance structure. This model has 19 parameters corresponding to the coefficients of the von Bertalanffy curve for each of the six treatments plus the residual variance parameter. From the V1 model, the fixed part has 19 parameters referring to the four growth curve coefficients, being ϕ_1, ϕ_2, and ϕ_3 for each of the six treatments and ϕ_6 only in the intercept. Already in the random part, we have the parameters corresponding to the variance components according to the covariance structure evaluated. From model V1 to V8, random effects

were selected by changing the structure of matrix $\boldsymbol{G}$. After selecting random effects, we modified the structure of the covariance matrix, $\boldsymbol{R}$, in this step we worked with models V9, V10, and V11.

Table 3.6 – Selection of von Bertalanffy models with mixed effects

Mod.	RE	$\boldsymbol{G}$	$\boldsymbol{R}$	npar	$-2logL$	AICc	BIC	Comp.	p-value
VF	-	-	VC	20	8110.62	8151.88	8241.17	-	-
V1	ϕ_1	-	VC	21	7838.22	7881.61	7975.30	VF *vs* V1	$< .0001$
V2	ϕ_1, ϕ_3	UN	VC	23	7770.18	7817.85	7920.32	V1 *vs* V2	$< .0001$
V3	ϕ_3	-	VC	21	7901.04	7944.44	8038.13	V2 *vs* V3	$< .0001$
V4	ϕ_1, ϕ_6	UN	VC	23	7838.22	7885.89	7988.36	V2 *vs* V4	-
V5	ϕ_1, ϕ_2, ϕ_3	UN	VC	26	7770.18	7824.32	7939.91	V2 *vs* V5	0.999
V6	ϕ_1, ϕ_3, ϕ_6	VCH	VC	23	7838.22	7885.89	7988.36	V2 *vs* V6	-
V7	ϕ_1, ϕ_3	VC	VC	21	7901.04	7944.44	8038.13	V2 *vs* V7	$< .0001$
V8	ϕ_1, ϕ_3	VCH	VC	22	7838.22	7883.75	7981.83	V2 *vs* V8	$< .0001$
V9	ϕ_1, ϕ_3	UN	VCH(Sex)	24	7698.18	7748.00	7854.85	V2 *vs* V9	$< .0001$
V10	ϕ_1, ϕ_3	UN	VCH(Age)	24	6915.50	6965.31	7072.16	V9 *vs* V10	-
V11	ϕ_1, ϕ_3	UN	VCH(Sex$*$Age)	60	6657.56	6789.31	7049.23	V10 *vs* V11	$< .0001$

RE: Random effect; $\boldsymbol{G}$: Variance-covariance matrix for the random effects; $\boldsymbol{R}$: Variance-covariance matrix intra-individual; npar: number of model parameters; $-2logL$: -2(logarithm of the likelihood); UN: Unstructured; VC: Variance Components; VCH(Age): Heterogeneous variance components for age; VCH(Sex): Heterogeneous variance components for sex; VCH(Age$*$Sex): Heterogeneous variance components for interaction age and sex.

Based on the information criteria and the likelihood ratio test, the selected model was the V11. This model has a random effect on parameters ϕ_1 and ϕ_3, with correlations between them and covariance structure intra-individual heterogeneous with different variance components for the interaction Age and Sex. We can observe the quality of fit of model V11 in Figure 3.5 in items (c) and (d), where are the graphs of standardized residuals versus adjusted values and the half-normal plot with simulation envelope, respectively. In this same figure are the charts of the residuals of the fixed model, VF, in items (a) and (b). We observed in Figure 3.5 the need to include random effects in the von Bertalanffy model for a better description of broiler chicken weight data.

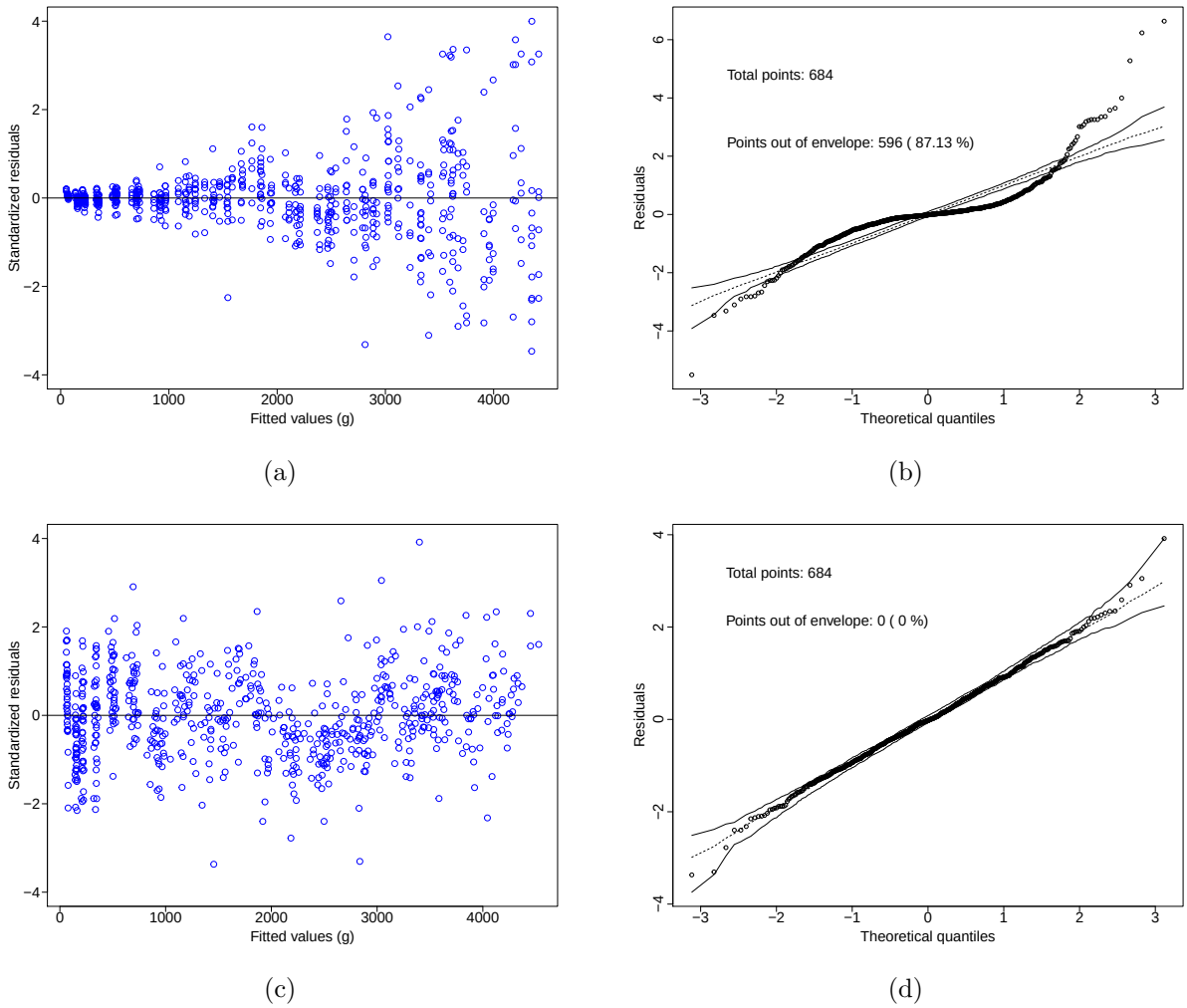


Figure 3.5 – Graph of standardized residuals versus adjusted values and half-normal simulated envelope graphs for the models von Bertalanffy with fixed effects (VF), items (a) and (b), and von Bertalanffy with random effects (V11) items (c) and (d)

3.4.4 Mixed Richards growth model

Results corresponding to the selection steps for the Richards mixed-effects growth model are presented in Table 3.7. The RF model corresponds to the model without random effects, with a homogeneous covariance structure. This model has 24 parameters corresponding to the Richards curve coefficients for each of the six treatments plus the residual variance parameter. From the R1 model, the fixed part has 24 parameters referring to the four growth curve coefficients for each of the six treatments. Already in the random part, we have the parameters corresponding to the variance components according to the covariance structure evaluated. From model R1 to R6, random effects were selected by changing the structure of matrix $\boldsymbol{G}$. After selecting random effects, we modified the structure of the covariance matrix, $\boldsymbol{R}$, in this step we worked with models R7, R8, and R9.

Table 3.7 – Selection of Richards models with mixed effects

Mod.	RE	$\boldsymbol{G}$	$\boldsymbol{R}$	npar	$-2logL$	AICc	BIC	Comp.	p-value
RF	-	-	VC	25	8108.42	8160.41	8271.63	-	-
R1	ϕ_1	-	VC	26	7826.32	7880.45	7996.04	RF *vs* R1	$< .0001$
R2	ϕ_1, ϕ_3	VCH	VC	27	7826.32	7882.62	8002.57	R1 *vs* R2	0.9802
R3	ϕ_2, ϕ_3	VCH	VC	27	7897.46	7953.77	8073.72	R1 *vs* R3	$< .0001$
R4	ϕ_2, ϕ_3, ϕ_6	VCH	VC	28	7897.50	7955.97	8080.28	R3 *vs* R4	0.8629
R5	ϕ_1, ϕ_2, ϕ_3, ϕ_6	VC	VC	26	7924.00	7978.13	8093.72	R3 *vs* R5	$< .0001$
R6	ϕ_2, ϕ_3	VC	VC	26	7897.48	7951.63	8067.22	R3 *vs* R6	0.8740
R7	ϕ_2, ϕ_3	VC	VCH(Sex)	27	7878.04	7934.35	8054.30	R3 *vs* R7	$< .0001$
R8	ϕ_2, ϕ_3	VC	VCH(age)	44	6722.46	6816.66	7009.69	R7 *vs* R8	$< .0001$
R9	ϕ_2, ϕ_3	VC	VCH(Sex∗Age)	63	6662.78	6801.78	7074.03	R8 *vs* R9	$< .0001$

RE: Random effect; $\boldsymbol{G}$: Variance-covariance matrix for the random effects; $\boldsymbol{R}$: Variance-covariance matrix intra-individual; npar: number of model parameters; $-2logL$: -2(logarithm of the likelihood); UN: Unstructured; VC: Variance Components; VCH(Age): Heterogeneous variance components for age; VCH(Sex): Heterogeneous variance components for sex; VCH(Age∗Sex): Heterogeneous variance components for interaction age and sex.

Through the information criteria and the likelihood ratio test the most appropriate model for the data was the R9, with random effect on the ϕ_2 and ϕ_3 with homogeneous variances and null correlations and a heterogeneous intra-individual covariance structure with different variance components for the Age and Sex interaction. We can observe the quality of fit of model R9 in Figure 3.6 in items (c) and (d), where are the graphs of standardized residuals versus adjusted values and the half-normal plot with simulation envelope, respectively. In this same figure are the graphs of the residuals of the fixed model, RF, in items (a) and (b). We observed in Figure 3.6 the need to include random effects in the Richards model for a better description of broiler chicken weight data.

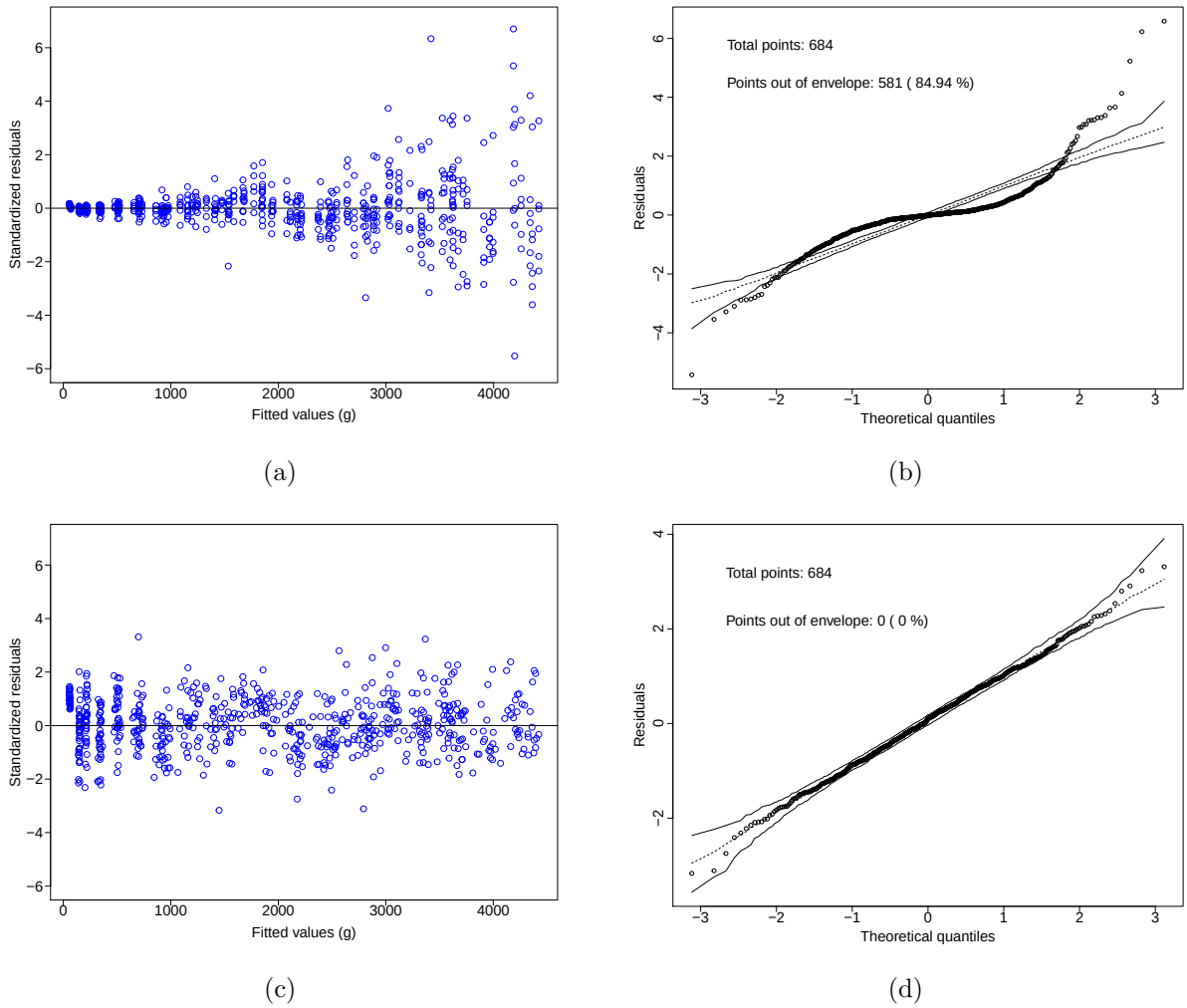


Figure 3.6 – Graph of standardized residuals versus adjusted values and half-normal simulated envelope graphs for the models Richard with fixed effects (RF), items (a) and (b), and Richard with random effects (R9) items (c) and (d)

3.4.5 Comparison between growth models

In this section, we compare some characteristics of the growth models (G12, L12, V11, and R9) selected in the previous sections. Figure 3.7 shows the graphs of the adjusted mean curves of the different growth models for each of the treatments. In this figure, it is possible to see that the adjustment of the curves of the four models was similar for the initial phase (1 to 10 days) and growth phase (11 to 22 days) of broiler chickens, but in the final phase (23 to 56 days) there was a divergence between the curves of the adjusted models. Individual adjusted curves for the different growth models are in Appendix A7.

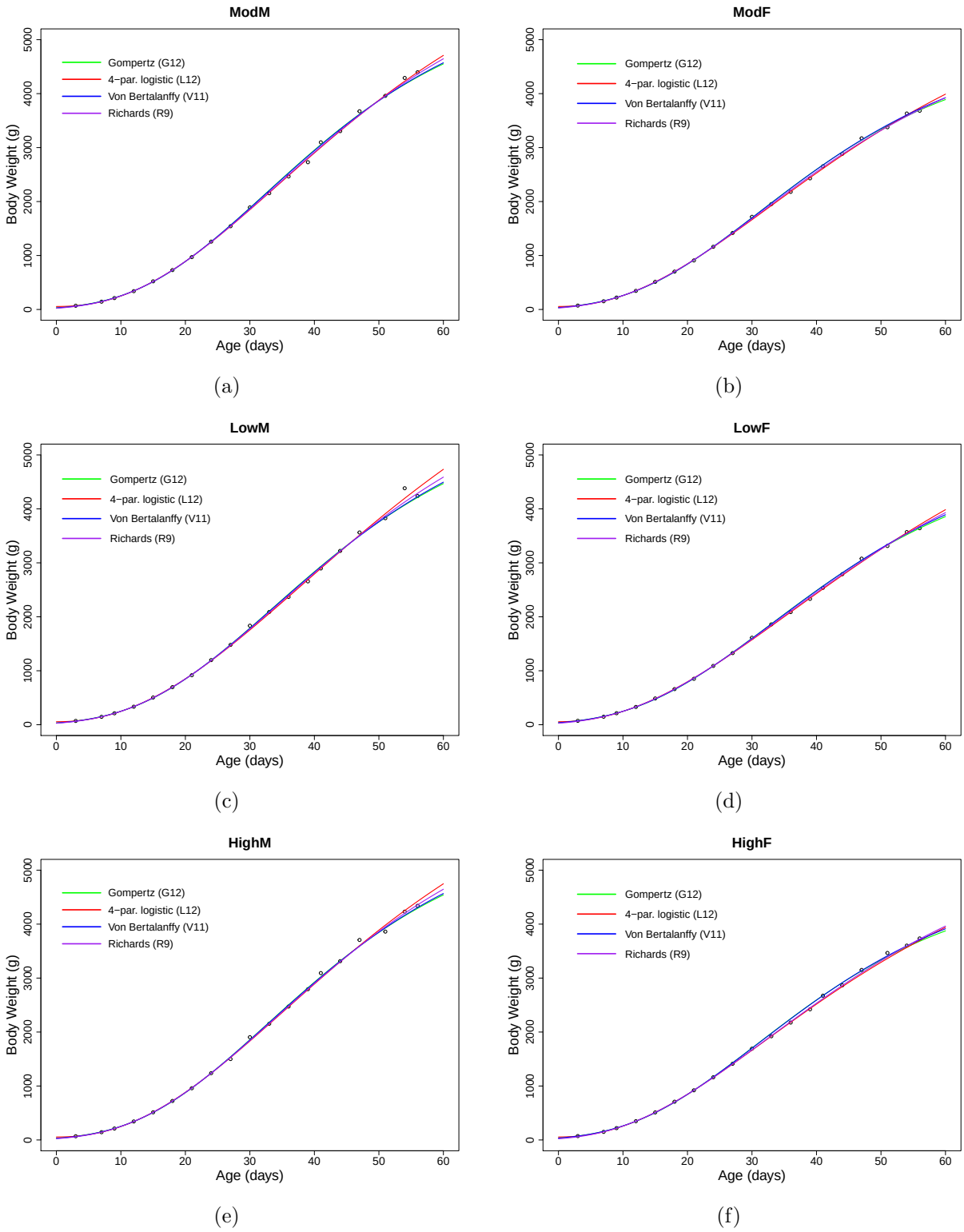


Figure 3.7 – Adjusted mean curves of the different growth models for each treatment

Table 3.8 presents the estimates of the coefficients with the respective confidence interval for each of the models studied. The logistic model showed asymptote estimates values more elevated than the asymptote values of the other models, but as we saw in Figure 3.7, the logistic curve had a similar adjustment to the other models within

the study period. The estimates of the coefficients β_5 of the logistic model and β_6 of the von Bertalanffy model were obtained considering only the intercept in the model, that is, the same value for all treatments.

Table 3.8 – Estimates of the coefficients with the respective 95% confidence interval for the models studied

		Gompertz (G12)		
Treatment	$\hat{\beta}_1$	$\hat{\beta}_2$	$\hat{\beta}_3$	
ModM	5805.00 ± 379.01	5.21 ± 0.04	0.0511 ± 0.0024	
ModF	4879.27 ± 371.14	4.91 ± 0.03	0.0512 ± 0.0024	
LowM	5883.74 ± 382.86	5.15 ± 0.04	0.0488 ± 0.0024	
LowF	5061.24 ± 374.74	4.88 ± 0.03	0.0481 ± 0.0024	
HighM	5853.44 ± 380.29	5.19 ± 0.04	0.0503 ± 0.0024	
HighF	4841.94 ± 262.35	4.89 ± 0.02	0.0515 ± 0.0017	
		Four-parameter logistic (L12)		
Treatment	$\hat{\beta}_1$	$\hat{\beta}_3$	$\hat{\beta}_4$	$\hat{\beta}_5$
ModM	8270.16 ± 473.33	3.97 ± 0.04	2.23 ± 0.04	55.47 ± 0.5
ModF	7105.65 ± 477.58	3.98 ± 0.05	2.1 ± 0.04	55.47 ± 0.5
LowM	9644.49 ± 600.81	4.12 ± 0.05	2.14 ± 0.04	55.47 ± 0.5
LowF	7977.83 ± 585.29	4.1 ± 0.06	2.05 ± 0.04	55.47 ± 0.5
HighM	8619.16 ± 497.1	4.01 ± 0.04	2.21 ± 0.04	55.47 ± 0.5
HighF	6843.03 ± 329.11	3.96 ± 0.03	2.11 ± 0.03	55.47 ± 0.5
		von Bertalanffy (V11)		
Treatment	$\hat{\beta}_1$	$\hat{\beta}_2$	$\hat{\beta}_3$	$\hat{\beta}_6$
ModM	5955.92 ± 411.25	0.2290 ± 0.0086	0.0486 ± 0.0025	0.97 ± 0.02
ModF	5039.14 ± 400.75	0.2145 ± 0.0015	0.0485 ± 0.0025	0.97 ± 0.02
LowM	6072.26 ± 417.11	0.2261 ± 0.0072	0.0462 ± 0.0025	0.97 ± 0.02
LowF	5252.92 ± 404.99	0.2136 ± 0.0014	0.0454 ± 0.0025	0.97 ± 0.02
HighM	6025.06 ± 413.24	0.2281 ± 0.0082	0.0478 ± 0.0025	0.97 ± 0.02
HighF	5014.16 ± 291.18	0.2138 ± 0.1166	0.0486 ± 0.0021	0.97 ± 0.02
		Richards (R9)		
Treatment	$\hat{\beta}_1$	$\hat{\beta}_2$	$\hat{\beta}_3$	$\hat{\beta}_6$
ModM	6553.29 ± 645.33	-0.5150 ± 0.1590	0.0414 ± 0.0053	-0.1277 ± 0.061
ModF	5335.24 ± 566.80	-0.4964 ± 0.1574	0.0423 ± 0.0052	-0.1298 ± 0.0617
LowM	6701.70 ± 700.03	-0.4548 ± 0.1764	0.0402 ± 0.0055	-0.1102 ± 0.0636
LowF	5859.24 ± 667.10	-0.5780 ± 0.1495	0.0371 ± 0.0053	-0.1609 ± 0.0636
HighM	6581.03 ± 650.39	-0.4829 ± 0.1651	0.0415 ± 0.0053	-0.1176 ± 0.0614
HighF	5743.31 ± 439.65	-0.6690 ± 0.0914	0.0374 ± 0.0036	-0.199 ± 0.0429

ModM and ModF: Moderate nutritional density for Male and Female; LowM and LowF: Low nutritional density for Male and Female; HighM and HighF: High nutritional density for Male and Female.

Table 3.9 shows the number of parameters for fixed effects factors (npf) and the number of parameters for variance components (npr). The correlation between the observed and predicted values (corr), the residual variance estimate for the fixed effect model ($\hat{\sigma}_f^2$), the residual variance estimate for the mixed model ($\hat{\sigma}_r^2$), the AICc and BIC information criteria, and the logarithm of the likelihood for each of the models studied are also presented. According to the comparison criteria shown in Table 3.9, the four-parameter

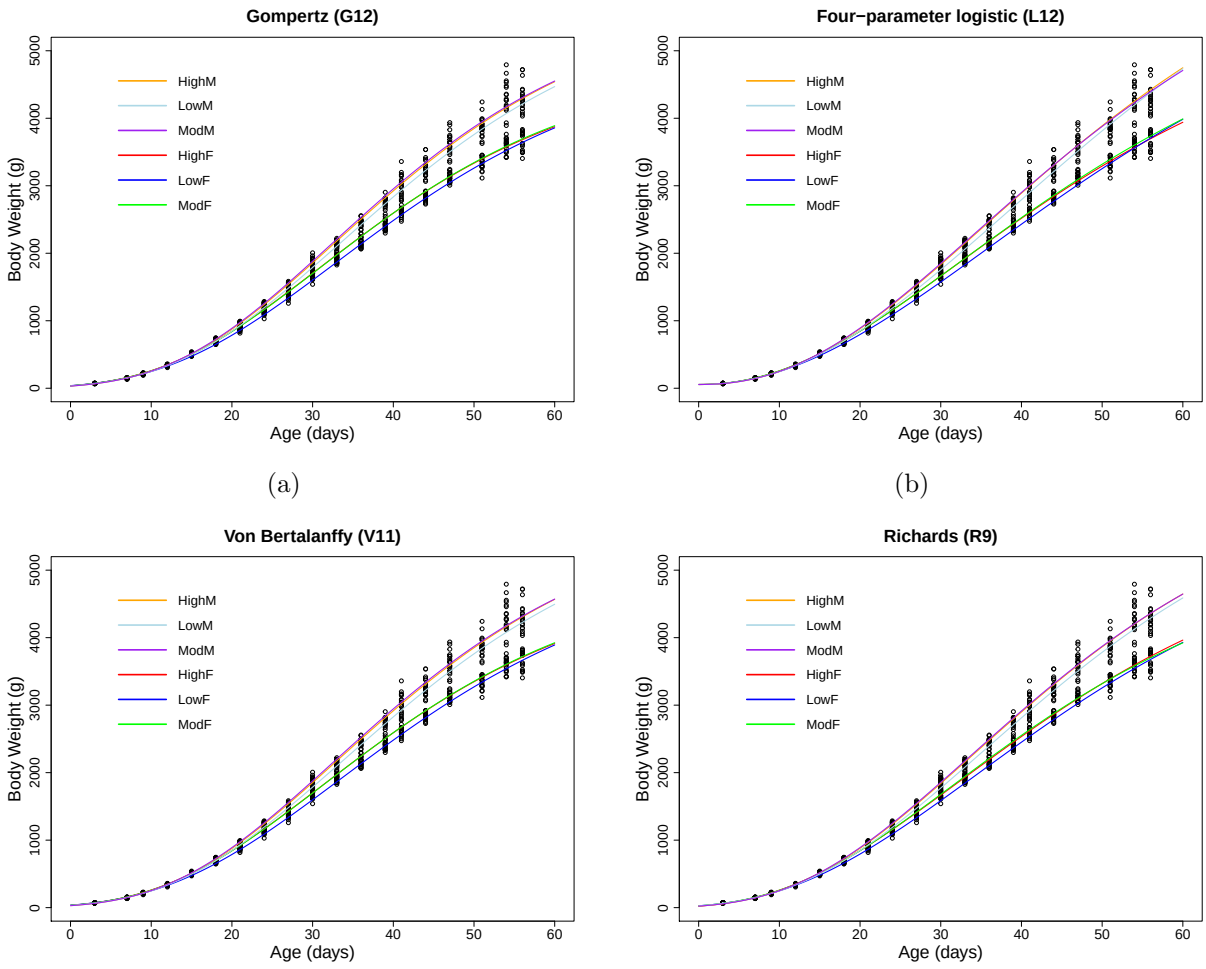
logistic model was considered the most appropriate for the chicken data, as compared to the other models it presented the lowest values for $\hat{\sigma}^2$ (0.51), AICc (6545.53), BIC (6809.58) and $-2logL$ (6411.37).

Table 3.9 – Results of information criterion and statistics of the growth models for broiler chicken weight data.

Model	npf	npr	$\hat{\sigma}^2_f$	$\hat{\sigma}^2_r$	Corr	AICc	BIC	$-2logL$
Gompertz (G12)	18	41	8562.55	15.17	0.9986	6786.47	7053.62	6668.47
4-par logistic (L12)	19	42	8506.88	0.51	0.9982	6545.53	6809.58	6411.37
von Bertalanffy (V11)	19	41	8500.76	20.43	0.9986	6789.31	7049.23	6657.56
Richards (R9)	24	39	8537.90	110.18	0.9979	6801.78	7074.03	6662.77

npf: number of parameters related to fixed-effect factors; npr: number of parameters corresponding to variance components; corr: correlation between observed values and predicted values; $\hat{\sigma}^2_f$: residual variance estimate for the fixed effect model; $\hat{\sigma}^2_r$: residual variance estimate for the mixed model; $-2logL$: -2(logarithm of the likelihood).

Figure 3.8 shows the graphs of the adjusted mean curves of growth models with the dispersion of observations. For each of the treatments, an average growth curve was adjusted.



(a) (b) (c) (d)

Figure 3.8 – Mean curves adjusted for each treatment for the different models studied

We observed that there is a greater distance between the curves of males and females. For diets, within each sex, we observed that the behavior of the adjusted average curves of the Moderate and High diets were close to each other, while the Low diet curve was slightly lower than the other two diets. Thus, considering the same random structure of the previously selected models (G12, L12, V11, R9), based on the observation of the curves of the Figure 3.8 the following models were proposed:

- G12.4, L12.4, V11.4 and R9.4: Models with four distinct curves, one for males on Moderate and High (ModHighM) diets, one for females on Moderate and High (ModHighF) diets, one for males on Low (LowM), and one for females on the Low (LowF) diet.
- G12.3M, L12.3M, V11.3M and R9.3M: Models with three distinct curves, one for males with Moderate, High, and Low (ModHighLowM) diets, another for females with Moderate and High (ModHighF) diets, and one for females with Low (LowF) diets.
- G12.3F, L12.3F, V11.3F and R9.3F: Models with three distinct curves, one for males with the Moderate and High (ModHighM) diets, another for males with the Low (LowM) diet, and one for females with the Moderate, High, and Low (ModHighLowF) diets.
- G12.2, L12.2, V11.2 and R9.2: Models with two distinct curves, one for males with Moderate, High, and Low (ModHighLowM) diets and one for females with Moderate, High, and Low (ModHighLowF) diets.

The adjusted mean curves of the four-parameter logistic models L12.4, L12.3M, L12.3F, and L12.2 can be seen in Figure 3.9 items (a), (b), (c), and (d), respectively. The graphs with the adjusted mean curves for the Gompertz, Von Bertalanffy, and Richards models with four curves, three curves, and two curves are similar to those of the four-parameter logistic model.

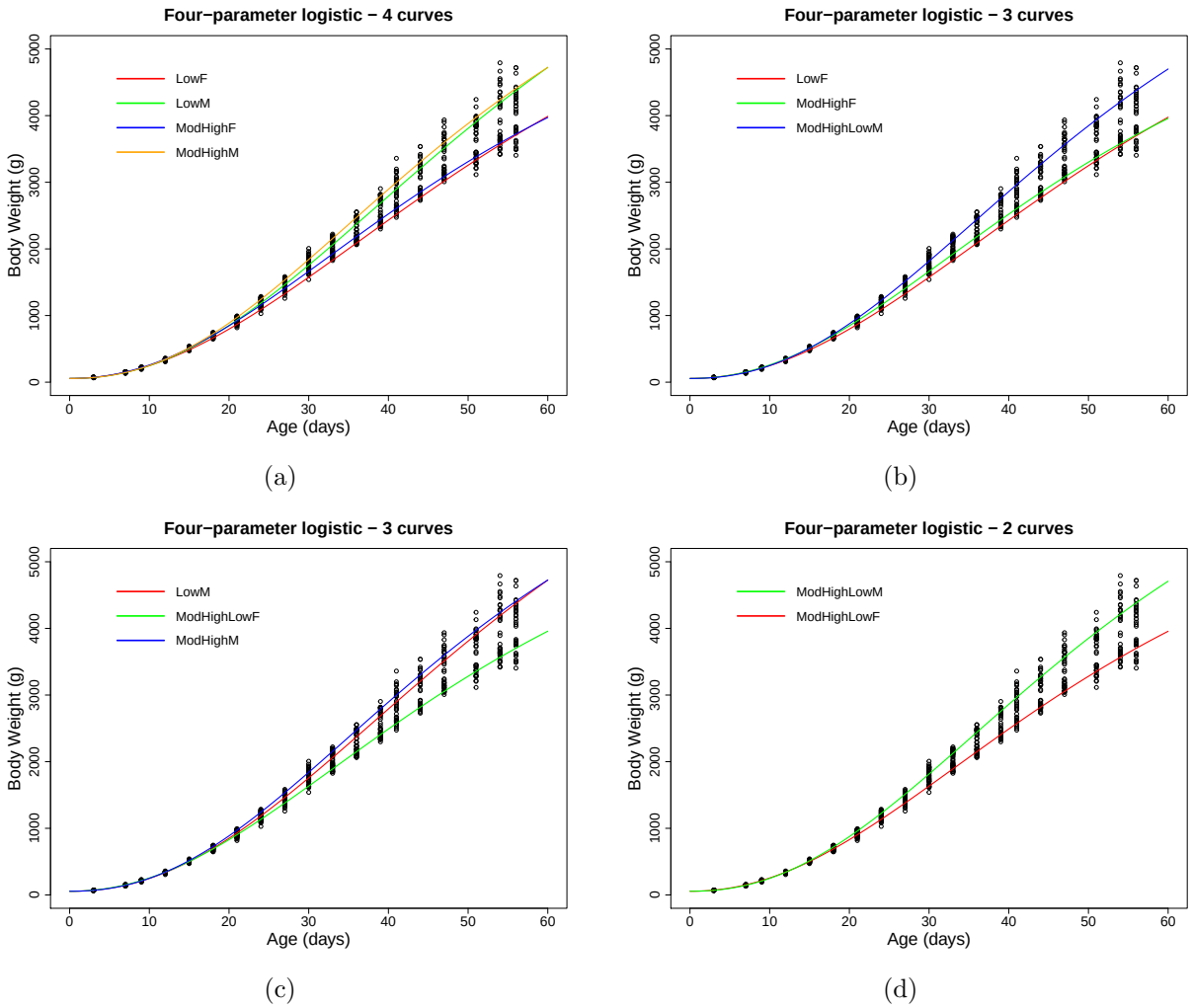


Figure 3.9 – Adjusted curves for models L12.4 (a), L12.3M (b), L12.3F (c), and L12.2 (d)

Table 3.10 presents the results of the selection of models with six, four, three, and two curves for treatments of different growth models. By the likelihood ratio test and AICc, the four curve model (G12.4, L12.4, V11.4, and R9.4) was selected for all growth models (Gompertz, four-parameter logistic, von Bertalanffy, and Richards).

Table 3.10 – Results of selecting models with different curve numbers

			Gompertz			
Model	npar	$-2logL$	AICc	BIC	Comparison	p-value
G12	59	6668.48	6797.82	7053.62	-	-
G12.4	53	6670.40	6785.49	7016.39	G12 *vs* G12.4	0.9259
G12.3M	50	6686.50	6794.56	7012.91	G12.4 *vs* G12.3M	0.0011
G12.3F	50	6692.78	6800.84	7019.18	G12.4 *vs* G12.3F	$< .0001$
G12.2	47	6705.62	6806.71	7012.42	G12.4 *vs* G12.2	$< .0001$
			Four-parameter logistic			
Model	npar	$-2logL$	AICc	BIC	Comparison	p-value
L12	61	6411.38	6545.53	6809.58	-	-
L12.4	55	6415.44	6535.25	6774.48	L12 *vs* L12.4	0.6666
L12.3M	52	6461.26	6573.99	6800.71	L12.4 *vs* L12.3M	$< .0001$
L12.3F	52	6454.56	6567.30	6794.02	L12.4 *vs* L12.3F	$< .0001$
L12.2	49	6489.46	6595.18	6809.33	L12.4 *vs* L12.2	$< .0001$
			von Bertalanffy			
Model	npar	$-2logL$	AICc	BIC	Comparison	p-value
V11	60	6657.56	6789.31	7049.23	-	-
V11.4	54	6659.76	6777.20	7012.27	V11 *vs* V11.4	0.9002
V11.3M	51	6699.42	6809.81	7032.34	V11.4 *vs* V11.3M	$< .0001$
V11.3F	51	6680.36	6790.76	7013.30	V11.4 *vs* V11.3F	$< .0001$
V11.2	48	6693.32	6796.72	7006.66	V11.4 *vs* V11.2	$< .0001$
			Richards			
Model	npar	$-2logL$	AICc	BIC	Comparison	p-value
R9	63	6662.78	6801.78	7074.03	-	-
R9.4	55	6671.18	6790.98	7030.21	R9 *vs* R9.4	0.3954
R9.3M	51	6699.86	6810.25	7032.79	R9.4 *vs* R9.3M	$< .0001$
R9.3F	51	6699.86	6810.25	7032.79	R9.4 *vs* R9.3F	$< .0001$
R9.2	47	6759.36	6860.46	7066.18	R9.4 *vs* R9.2	$< .0001$

npar: number of model parameters; $-2logL$: -2(logarithm of the likelihood).

Estimates of the coefficients of selected models with four curves and the respective intervals with 95% confidence are on the Table 3.11.

Table 3.11 – Estimates of the coefficients with the respective 95% confidence interval for four-curve models (G12.4, L12.4, V11.4, and R9.4)

		Gompertz (G12.4)		
Treatment	$\hat{\beta}_1$	$\hat{\beta}_2$	$\hat{\beta}_3$	
LowM	5889.14 ± 385.77	5.15 ± 0.04	0.048781 ± 0.002414	
LowF	5059.89 ± 266.64	4.88 ± 0.02	0.048154 ± 0.001705	
ModHighM	5834.04 ± 329.67	5.20 ± 0.03	0.050657 ± 0.002088	
ModHighF	4859.97 ± 324.48	4.90 ± 0.03	0.051385 ± 0.002087	
		Four-parameter logistic (L12.4)		
Treatment	$\hat{\beta}_1$	$\hat{\beta}_3$	$\hat{\beta}_4$	$\hat{\beta}_5$
LowM	9577.37 ± 697.58	4.11 ± 0.06	2.14 ± 0.04	55.48 ± 0.5
LowF	7993.25 ± 495.00	4.10 ± 0.04	2.05 ± 0.03	55.48 ± 0.5
ModHighM	8418.13 ± 551.74	3.99 ± 0.05	2.22 ± 0.03	55.48 ± 0.5
ModHighF	6999.64 ± 545.82	3.97 ± 0.05	2.10 ± 0.03	55.48 ± 0.5
		von Bertalanffy (V11.4)		
Treatment	$\hat{\beta}_1$	$\hat{\beta}_2$	$\hat{\beta}_3$	$\hat{\beta}_6$
LowM	6077.63 ± 419.50	0.2248 ± 0.0071	0.0462 ± 0.0025	0.97 ± 0.02
LowF	5249.43 ± 299.10	0.2124 ± 0.1164	0.0455 ± 0.0021	0.97 ± 0.02
ModHighM	5994.86 ± 357.20	0.2272 ± 0.0083	0.0482 ± 0.0022	0.97 ± 0.02
ModHighF	5024.02 ± 350.72	0.2129 ± 0.0012	0.0486 ± 0.0022	0.97 ± 0.02
		Richards (R9.4)		
Treatment	$\hat{\beta}_1$	$\hat{\beta}_2$	$\hat{\beta}_3$	$\hat{\beta}_6$
LowM	6698.20 ± 753.31	-0.4543 ± 0.1902	0.0402 ± 0.0057	-0.1100 ± 0.0668
LowF	5918.03 ± 522.29	-0.5971 ± 0.1158	0.0366 ± 0.0040	-0.1687 ± 0.0476
ModHighM	6562.89 ± 620.51	-0.4981 ± 0.1496	0.0415 ± 0.0048	-0.1223 ± 0.0567
ModHighF	5549.72 ± 595.47	-0.5974 ± 0.1390	0.0396 ± 0.0048	-0.1678 ± 0.0570

LowM and LowF: Low nutritional density for Male and Female; ModHighM and ModHighF: Moderate and high nutritional density for Male and Female.

In Table 3.12, we present the information criteria (AICc and BIC) and some statistics (Corr and R) for the four-curve models. Note that the four-parameter logistic model presented the lowest values of AICc, BIC, and residual variance, this model is the most appropriate model to data compared to other growth models.

Table 3.12 – Results of information criterion and statistics of the growth models for broiler chicken weight data.

Model	npf	npr	$\hat{\sigma}_f^2$	$\hat{\sigma}_r^2$	Corr	AICc	BIC	$-2logL$
Gompertz (G12.4)	12	41	8546.36	15.05	0.9986	6785.49	7016.39	6670.40
4-par logistic (L12.4)	13	42	8497.50	0.47	0.9983	6535.25	6774.48	6415.45
von Bertalanffy (V11.4)	13	41	8483.87	20.23	0.9986	6777.20	7012.27	6659.76
Richard (R9.4)	16	39	8510.58	109.37	0.9979	6790.98	7030.21	6671.17

npf: number of parameters related to fixed-effect factors; npr: number of parameters corresponding to variance components; corr: correlation between observed values and predicted values; $\hat{\sigma}_f^2$: residual variance estimate for the fixed effect model; $\hat{\sigma}_r^2$: residual variance estimate for the mixed model; $-2logL$: -2(logarithm of the likelihood).

3.5 Discussion

Gompertz, Logistic, von Bertalanffy, and Richards models are widely used to describe the growth pattern of different bird species. Narinç et al. (2017) reviewed existing approaches to modeling growth curves. Tzeng and Becker (1981) analyzed growth data of male chickens using the Gompertz, three-parameter logistic, and von Bertalanffy functions and reported that the Gompertz was the most appropriate model. Yakupoglu and Atil (2001) compared Gompertz and von Bertalanffy models adjusted for broiler chicken data and stated that the Gompertz model provides a better description of the growth curve, which differs from our results, where the von Bertalanffy model had a better fit to the data than the Gompertz model, although we have used random effects in both models, effects not used by the authors.

Darmani Kuhi et al. (2003) used the Gompertz, three-parameter logistic, Lopez, Richards, France, and von Bertalanffy models to model growth data for chicken meat and egg strains reported that the Richards model was better than the others. Norris et al. (2007) compared the Gompertz, three-parameter logistic, and Richards models to model the live weight of indigenous chickens and reported that the Gompertz model was the most suitable for modeling chicken growth. Rizzi et al. (2013) compared linear and nonlinear models (Gompertz, three-parameter logistic, and Richards) to describe broiler chicken growth patterns and concluded that the Richards model was the most appropriate. Mohammed (2015) used the models Gompertz, von Bertalanffy, and three-parameter logistic to estimate the growth curve of Ross broiler chickens and reported that the Gompertz model was the most appropriate. While in our study, the four-parameter logistic model and von Bertalanffy, both with random effects, were better adjusted than Gompertz to describe the growth pattern of broiler chickens. Demuner et al. (2017) compared the Gompertz, three-parameter logistic, von Bertalanffy, and Richards models to model broiler chickens data. The authors report that the Richards and Gompertz models obtained the best adjustments.

We used mixed nonlinear models (Gompertz, four-parameter logistic, von Bertalanffy, and Richards) and got suitable adjustments of these models to broiler chicken data. We note that by including random effects in these models and selecting an appropriate variance and covariance structure, there was a considerable improvement in the fit of the models. Much of the residual variation that was present in the fixed effect model was modeled by the variance and covariance structures of the mixed effect model, which considerably reduced the residual variance. These results are in agreement with the work of Wang and Zuidhof (2004), who used a mixed Gompertz growth model to analyze data from a commercial broiler chicken strain crosses experiment and concluded that the use of the mixed model decreases by over 55% of the residual variance. They indicated that the mixed model has several advantages over the fixed effects model, recommending the use of mixed models for the analysis of longitudinal growth data. Some authors indicate

a significant decrease in residual variance estimation using nonlinear models mixed with growth data from other species, such as Aggrey (2009) and Karaman et al. (2013), who reported a decrease of 72% and 65%, respectively, in Japanese quail growth data.

Galeano-Vasco et al. (2014) compared mixed nonlinear models (von Bertalanffy, Richards, Gompertz, Brody, and three-parameter logistic) for the ability to estimate the growth curve in commercial laying hens. They concluded that the Gompertz model had a better fit for the data, followed by Richards and then von Bertalanffy. In our work, for broiler chicken data, we obtained that the von Bertalanffy model was better adjusted than the Gompertz, followed by Richards. These same authors reported that the models Brody and three-parameter logistic did not fit the data. We had a similar problem regarding the adjustment of the three-parameter logistic model that did not fit well with broiler chicken data (see Appendix A8).

For the four growth models studied (Gompertz, four-parameter logistic, von Bertalanffy, and Richards), we observed the difference between the growth of male and female chickens. Which is in agreement with the works of Havenstein et al. (2003), Sakomura et al. (2005), and Marcato et al. (2008), who evaluated the male and female growth potential of Ross broiler chickens and concluded that males have higher growth potential than females. According to Salim et al. (2012), the performance of each sex is related to genetics. Male broiler chickens consume more feed, use nutrients better, and grow faster than females.

According to the comparison criteria used in this work (correlation between observed values and predicted values, estimated residual variance, AICc, and BIC), we had the following classification of the models for the best fit to the data: 1st four-parameter logistic, 2nd von Bertalanffy, 3rd Gompertz, and 4th Richards.

3.6 Conclusion

In the selection of Gompertz, four-parameter logistic, von Bertalanffy, and Richards models, it was possible to observe a considerable improvement in the adjustment of each of the four models after the inclusion of random effects. According to the comparison criteria used in this work, we had the following classification of the models according to the best fit to the data: 1st four-parameter logistic, 2nd von Bertalanffy, 3rd Gompertz, and 4th Richards. For the four growth models studied (Gompertz, four-parameter logistic, von Bertalanffy, and Richards), in the selection of curves for the treatments, we observed differences between the growth potential of males and females. Regarding the diets, we found that diets with high and moderate nutritional density provided a higher weight of broiler chickens than the diet with low nutritional density within each sex, considering the entire experimental period.

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4 AN APPROACH TO MULTIVARIATE LONGITUDINAL DATA ANALYSIS USING NONLINEAR MIXED MODELS

Abstract

In broiler performance studies, it is common to observe multiple responses repeatedly taken over time in a single experiment, in the same experimental units. Usually, the analysis of these data is performed using univariate techniques; however, these techniques disregard the possible correlations between the variables and do not allow joint interpretations of them. One possible way to jointly analyze multiple response longitudinal data is by using mixed models. The data used in this work come from an experiment (FZEA/USP), with 1080 Ross broiler chickens, in a randomized block design with a factorial treatment structure with three nutritional densities and two sexes. We sought to model the variables body weight responses and feed consumption, in grams, using bivariate Gompertz mixed model and bivariate four-parameter logistic mixed model. Additionally, we compared these models using the Akaike's information corrected criterion (AICc) and Bayesian information criterion (BIC). The results indicated that the four-parameter logistic mixed bivariate model better explained the behavior of the mean responses over time.

Keywords: Broiler chickens; Bivariate nonlinear mixed models; Repeated measurements; Variance components; Growth models.

4.1 Introduction

In scientific research, researchers are often faced with studies that have multiple outcomes and that are observed over the levels of a longitudinal factor, and these outcomes are commonly admitted to be correlated. Data are considered longitudinal when a measurement is made for each study subject repeatedly over a longitudinal factor, such as time. In a study with longitudinal data, the clustered nature of the data has to take into account, i.e., allow measurements within subjects to be correlated, while observations from different subjects are independent (VERBEKE et al., 2014).

Many authors have proposed models for longitudinal data in the statistical literature, for example, Verbeke and Molenberghs (2000), Diggle et al. (2002) and Molenberghs and Verbeke (2005). However, most attention is given to the univariate analysis for longitudinal data, although it is very common to find tests with more than one variable response measured over time, not necessarily with the same number of observations or the same number of occasions over time (VERBEKE et al., 2014). In addition, variables can be qualitative, discrete or continuous and have a linear or non-linear behavior.

A flexible way to analyze data with these characteristics is through the use

of mixed models, where the choice of a model depends on the type of response (continuous, ordinal or categorical) and also how the variables and covariates are related to the model (linear, generalized linear or non-linear) (WEISS, 2005; FIEUWS, 2006). Some approaches to modeling multivariate longitudinal data have been proposed in the statistical literature, such as Lambert and Vandenhende (2002), Ferrer McArdle (2003), Beckett et al. (2004) and Fieuws et al. (2008).

While some questions can be answered by modeling the variables separately, others are only answered by taking into account the joint nature of the variables involved. The purpose of this work was to compare the bivariate mixed Gompertz and four-parameter logistic mixed models applied to broiler performance data. The variables used in this study are body weight and feed consumption, in grams, from an experiment with 1080 Ross broiler chickens.

4.2 Case-study

The data that motivated this work is from a study conducted by Silva (2018) to evaluate the productive performance of broiler chickens, at the School of Animal Science and Food Engineering of the University of São Paulo (FZEA/USP) Brazil. A total of 1080 Ross broiler chickens were used, with a initial bodyweight of 45.69 ± 0.33 grams, allocated in 36 boxes, with 30 birds each. The broiler chickens were distributed in a randomized block design to control temperature differences throughout the shed. Six treatments were studied in the factorial scheme (3×2) being three nutritional densities (low, moderate, and high) and two sexes (male and female)(Table 4.1) with six replicates (Blocks). The experimental diets were formulated based on corn and soybean meal in a three-phase feeding program: initial (1 to 10 days), growth (11 to 22 days), and final (23 to 56 days). The experiment was carried out in the period from 3 to 56 days, was collected in grams the bodyweight and feed consumption, totaling 19 measures at the times: 3, 7, 9, 12, 15, 18, 21 , 24, 27, 30, 33, 36, 39, 41, 44, 47, 51, 54 and 56 days.

Table 4.1 – Description of treatments

Treatment	**Nutrition**	**Sex**
ModM	Moderate	Male
ModF	Moderate	Female
LowM	Low	Male
LowF	Low	Female
HighM	High	Male
HighF	High	Female

4.3 Modelling

4.3.1 Linear mixed model for multivariate longitudinal data

A mixed model is a flexible tool for joint modeling of different variables responses from longitudinal data, especially when the data collected are unbalanced (FIEUWS, 2006). Let measurement $\boldsymbol{Y}_{ij}$ be obtained on the ith individual at the jth occasion (time). The intervals between occasions do not need to be equally spaced. Here $i = 1, \ldots, N$, $j = 1, \ldots, n_i$. It is also assumed that the same number of measures on individuals and response variables is not needed. Let $\boldsymbol{Y}_i$ be the vector of all measures taken on individual i, i.e., $\boldsymbol{Y}_i^T = (y_{i1}, \ldots, y_{in_i})$. A linear mixed model for univariate longitudinal data is written as follows (LAIRD; WARE, 1982):

$$\boldsymbol{Y}_i = \boldsymbol{X}_i\boldsymbol{\beta} + \boldsymbol{Z}_i\boldsymbol{b}_i + \boldsymbol{\varepsilon}_i$$

$$\boldsymbol{b}_i \sim N_q(\boldsymbol{0}, \boldsymbol{G})$$

$$\boldsymbol{\varepsilon}_i \sim N_{n_i}(\boldsymbol{0}, \boldsymbol{R}_i)$$

with $\boldsymbol{b}_1, \ldots, \boldsymbol{b}_N$ and $\boldsymbol{\varepsilon}_1, \ldots, \boldsymbol{\varepsilon}_N$ independent, $\boldsymbol{X}_i$ and $\boldsymbol{Z}_i$ are matrices of known covariates $\boldsymbol{\beta}$ is the vector of the fixed effects parameters, $\boldsymbol{b}_i$ is the vector of the random effects, $\boldsymbol{\varepsilon}_i$ is the vector of the residual components, $\boldsymbol{G}$ is a general matrix of variances and covariances with (i, j) elements and $d_{ij} = d_{ji}$, $\boldsymbol{R}_i$ is a matrix of variances and covariances that depend on i only for n_i dimension, i.e., the unknown parameters of $\boldsymbol{R}_i$ do not depend on the individual i.

Let Y_m the different variables that were measured over time in the same individual and should be modeled together with $m = 1, 2, \ldots, r$. Therefore,

$$\boldsymbol{Y}_{i,Y_m} = \boldsymbol{X}_{i,Y_m}\boldsymbol{\beta}_{Y_m} + \boldsymbol{Z}_{i,Y_m}\boldsymbol{b}_{i,Y_m} + \boldsymbol{\varepsilon}_{i,Y_m}$$

where $\boldsymbol{\beta}_{Y_m}$ is the vector of fixed effects parameters for the Y_m variable response, $\boldsymbol{X}_{i,Y_m}$ and $\boldsymbol{Z}_{i,Y_m}$ are respectively the matrices of specification of fixed and random effects for the Y_m variable response, $\boldsymbol{b}_{i,Y_m}$ is the vector of random effects and $\boldsymbol{\varepsilon}_{i,Y_m}$ is the vector of the residual components of the variable Y_m. In terms of hierarchical models, the general linear mixed model can be rewritten as:

$$\boldsymbol{Y}_{i,Y_m}|\boldsymbol{b}_{i,Y_m} \sim N_{n_{i,Y_m}}(\boldsymbol{X}_{i,Y_m}\boldsymbol{\beta}_{Y_m} + \boldsymbol{Z}_{i,Y_m}\boldsymbol{b}_{i,Y_m}, \boldsymbol{R}_{i,Y_m})$$

where $N_{n_{i,Y_m}}$ is the normal distribution n_{i,Y_m}-dimensional.

The $\boldsymbol{R}_{i,Y_m}$ matrix can admit various covariance matrix structures, and the choice depends on the data variability and the correlation between repeated measures. According to Barbosa (2009), the structure of variances and covariances influences esti-

mation of the parameter of fixed effects factors, their standard errors as well as the fit diagnostics of the model and inferences about the population.

4.3.2 Nonlinear mixed-effects model

In the literature, different nonlinear mixed models have been proposed, as in Lindstrom and Bates (1990), Vonesh and Carter (1992), Wakefield et al. (1994), Vonesh and Chinchilli (1997) among others. For data analysis, the nonlinear mixed model (NLMM) was used, as described in Lindstrom and Bates (1990). In its first stage NLMM can be written as:

$$y_{ij} = f(\boldsymbol{\phi}_{ij}, \boldsymbol{x}_{ij}) + \varepsilon_{ij}, \quad i = 1, \ldots, N; j = 1, \ldots, n_i$$

where y_{ij} is the jth observation in individual i, N is the number of samples in the group, n_i is the number of observations in the individual i, f is a nonlinear function of the parameter vector $\boldsymbol{\phi}_{ij}$ with a covariate vector $\boldsymbol{x}_{ij}$ and ε_{ij} is a commonly distributed error term.

In the second stage the parameters of specific groups are modeled as

$$\boldsymbol{\phi}_{ij} = \boldsymbol{A}_{ij}\boldsymbol{\beta} + \boldsymbol{B}_{ij}\boldsymbol{b}_i$$

where $\boldsymbol{\beta}$ is a vector of unknown fixed parameters and common to all individuals, $\boldsymbol{b}_i$ is a unique unknown random effects vector for the ith individual, $\boldsymbol{A}_{ij}$ and $\boldsymbol{B}_{ij}$ are design matrices for the fixed and random effects, respectively, that may depend on the values of some covariates in the jth observation.

A general expression for NLMM can be written to individual i as

$$\boldsymbol{y}_i = f(\boldsymbol{\beta}, \boldsymbol{b}_i, \boldsymbol{X}_i) + \boldsymbol{\varepsilon}_i$$

where $\boldsymbol{y}_i = [y_{i1}, y_{i2}, \ldots, y_{in_i}]^T$ is a vector of measurements on the individual i, $\boldsymbol{X}_i$ is a known matrix of covariates and $\boldsymbol{\varepsilon}_i = [\varepsilon_{i1}, \varepsilon_{i2}, \ldots, \varepsilon_{in_i},]^T$ is a vector of intra-individual errors, $\boldsymbol{b}_i$ and $\boldsymbol{\varepsilon}_i$ are usually assumed to be independent and normally distributed with zero mean and matrix of variance $\boldsymbol{G}$ and $\boldsymbol{R}$, respectively, that is $\boldsymbol{b}_i \sim N(\boldsymbol{0}, \boldsymbol{G})$ and $\boldsymbol{\varepsilon}_i \sim N(\boldsymbol{0}, \boldsymbol{R})$.

4.3.3 Bivariate Gompertz mixed model

Let Y_1 and Y_2 two response variables measured for subject i at time j and in treatment k. Mixed Gompertz model for each response variable is given by:

$$y_{ijk,Y_1} = (\beta_{1k,Y_1} + b_{1i,Y_1})\exp[(-\beta_{2k,Y_1} + b_{2i,Y_1})\exp((-\beta_{3k,Y_1} + b_{3i,Y_1})t_{ij,Y_1})] + \varepsilon_{ijk,Y_1}$$

$$y_{ijk,Y_2} = (\beta_{1k,Y_2} + b_{1i,Y_2})\exp[(-\beta_{2k,Y_2} + b_{2i,Y_2})\exp((-\beta_{3k,Y_2} + b_{3i,Y_2})t_{ij,Y_2})] + \varepsilon_{ijk,Y_2}$$

with $i = 1, \ldots, 6$, $j = 1, \ldots, 19$ and $k = 1, \ldots, 6$, where Y_{ijk,Y_1} and Y_{ijk,Y_2} are body weight and feed consumption, respectively, observed at the instant t_{ij}, on the ith box, which received the kth treatment on the jth day of the experimental period. The coefficient β_{1k,Y_1} represents the maximum body weight, and β_{1k,Y_2} represents the maximum feed consumption of broilers that received the treatment k, β_{2k,Y_1} and β_{2k,Y_2} are scale parameters related to the initial weight and the initial consumption, respectively, of the birds that received the treatment k, β_{3k,Y_1} represents the maturity index expressed as a proportion of the maximum growth percentage in relation to the adult weight of the birds and β_{3k,Y_2} represents the consumption index expressed in proportion to the percentage of the maximum consumption in relation to the adult birds consumption; ε_{ijk,Y_1} and ε_{ijk,Y_2} are the experimental errors associated with observations of body weight and feed consumption, respectively; b_{1i,Y_1}, b_{2i,Y_1}, b_{3i,Y_1}, b_{1i,Y_2}, b_{2i,Y_2}, and b_{3i,Y_2} are the random effects associated with the model coefficients, β_{1k,Y_1}, β_{2k,Y_1}, β_{3k,Y_1}, β_{1k,Y_2}, β_{2k,Y_2}, and β_{3k,Y_2}, respectively. We can write a Gompertz mixed model by connecting the vectors of body weight and feed consumption observations into a single vector for individual i, resulting in:

$$\begin{bmatrix} \boldsymbol{y}_{i,Y_1} \\ \boldsymbol{y}_{i,Y_2} \end{bmatrix} = \begin{bmatrix} f_{Y_1}(\boldsymbol{\beta}_{Y_1}, \boldsymbol{b}_{i,Y_1}, \boldsymbol{t}_{ij,Y_1}) \\ f_{Y_2}(\boldsymbol{\beta}_{Y_2}, \boldsymbol{b}_{i,Y_2}, \boldsymbol{t}_{ij,Y_2}) \end{bmatrix} + \begin{bmatrix} \boldsymbol{\varepsilon}_{i,Y_1} \\ \boldsymbol{\varepsilon}_{i,Y_2} \end{bmatrix}$$

We assume that,

$$\boldsymbol{b}_i = \begin{bmatrix} b_{1i,Y_1} \\ b_{2i,Y_1} \\ b_{3i,Y_1} \\ b_{1i,Y_2} \\ b_{2i,Y_2} \\ b_{3i,Y_2} \end{bmatrix} \sim N_{q,Y_1Y_2}(\mathbf{0}, \boldsymbol{G}) \text{ and } \boldsymbol{\varepsilon}_i \sim N_{n_i,Y_1Y_2}(\mathbf{0}, \boldsymbol{R})$$

where

$$\boldsymbol{G} = \begin{bmatrix} \sigma^2_{b_1,Y_1} & \sigma_{b_1Y_1,b_2Y_1} & \sigma_{b_1Y_1,b_3Y_1} & \sigma_{b_1Y_1,b_1Y_2} & \sigma_{b_1Y_1,b_2Y_2} & \sigma_{b_1Y_1,b_3Y_2} \\ & \sigma^2_{b_2,Y_1} & \sigma_{b_2Y_1,b_3Y_1} & \sigma_{b_2Y_1,b_1Y_2} & \sigma_{b_2Y_1,b_2Y_2} & \sigma_{b_2Y_1,b_3Y_2} \\ & & \sigma^2_{b_3,Y_1} & \sigma_{b_3Y_1,b_1Y_2} & \sigma_{b_3Y_1,b_2Y_2} & \sigma_{b_3Y_1,b_3Y_2} \\ & & & \sigma^2_{b_1,Y_2} & \sigma_{b_1Y_2,b_2Y_2} & \sigma_{b_1Y_2,b_3Y_2} \\ \text{Symmetric} & & & & \sigma^2_{b_2,Y_2} & \sigma_{b_2Y_2,b_3Y_2} \\ & & & & & \sigma^2_{b_3,Y_2} \end{bmatrix}$$

In this case, the matrix structure $\boldsymbol{G}$ is called unstructured (UN) because $\boldsymbol{G}$ has different variances for random effects with nonzero correlations between them. When the correlations are null, the matrix structure $\boldsymbol{G}$ will be named heterogeneous variance components (VCH).

The matrix $\boldsymbol{R}$ is given by

$$\boldsymbol{R} = \begin{bmatrix} \sigma^2_{\varepsilon,Y_1} & 0 \\ 0 & \sigma^2_{\varepsilon,Y_2} \end{bmatrix} \otimes \begin{bmatrix} \boldsymbol{D}_1 & \mathbf{0}_{36} & \dots & \mathbf{0}_{36} \\ \mathbf{0}_{36} & \boldsymbol{D}_2 & \dots & \mathbf{0}_{36} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{0}_{36} & \mathbf{0}_{36} & \dots & \boldsymbol{D}_{19} \end{bmatrix}$$

where $\mathbf{0}_{36}$ is a 36×36 order null matrix and $\boldsymbol{D}_j$ with $j = 1, 2, \dots, 19$, is a 36×36 order diagonal matrix.

We use three possible structures for $\boldsymbol{D}_j$:

(1) Considering different variances by Sex and equal variances by Age - VCH(Sex)
$\boldsymbol{D}_j = \boldsymbol{I}_3 \otimes \text{diag}\,(\sigma^2_M, \sigma^2_F) \otimes \boldsymbol{I}_6$, where σ^2_M, and σ^2_F are variance components for male and female broilers, respectively, $\boldsymbol{I}_3$ and $\boldsymbol{I}_6$ are identity matrices of order 3×3 and 6×6, respectively.

(2) Considering different variances by Age nd equal variances by Sex - VCH(Age)
$\boldsymbol{D}_j = \boldsymbol{I}_3 \otimes \text{diag}\left(\sigma^2_j, \sigma^2_j\right) \otimes \boldsymbol{I}_6$, where $\sigma^2_1, \sigma^2_2, \dots, \sigma^2_{19}$ are the variance components for each of the 19 time measurements.

(3) Considering different variances for Age and Sex interaction - VCH(Age×Sex)
$\boldsymbol{D}_j = \boldsymbol{I}_3 \otimes \text{diag}\left(\sigma^2_{M_j}, \sigma^2_{F_j}\right) \otimes \boldsymbol{I}_6$, where $\sigma^2_{M_1}, \sigma^2_{M_2}, \dots, \sigma^2_{M_{19}}$ are the variance components for male broilers, and $\sigma^2_{F_1}, \sigma^2_{F_2}, \dots, \sigma^2_{F_{19}}$ are the variance components for female broilers in each of the 19 time measurements.

4.3.4 Bivariate four-parameters logistic mixed model

Let Y_1 and Y_2 two response variables measured for subject i at time j and in treatment k. Mixed four-parameters logistic model for each response variable is given by:

$$y_{ijk,Y_1} = (\beta_{4k,Y_1} + b_{4i,Y_1}) + \frac{(\beta_{1k,Y_1} + b_{1i,Y_1}) - (\beta_{4k,Y_1} + b_{4i,Y_1})}{1 + \exp[(\beta_{3k,Y_1} + b_{3i,Y_1})(\beta_{2k,Y_1} + b_{2i,Y_1} - \log(t_{ij,Y_1}))]} + \varepsilon_{ijk,Y_1}$$

$$y_{ijk,Y_2} = (\beta_{4k,Y_2} + b_{4i,Y_2}) + \frac{(\beta_{1k,Y_2} + b_{1i,Y_2}) - (\beta_{4k,Y_2} + b_{4i,Y_2})}{1 + \exp[(\beta_{3k,Y_2} + b_{3i,Y_2})(\beta_{2k,Y_2} + b_{2i,Y_2} - \log(t_{ij,Y_2}))]} + \varepsilon_{ijk,Y_2}$$

with $i = 1, \dots, 6$, $j = 1, \dots, 19$ and $k = 1, \dots, 6$. considering Y_1 the measurements for body weight, Y_2 the measurements for feed consumption and k the index for each treatment, we have that, Y_{ij} is the value observed at time t_{ij}, in the ith box and jth day of the experimental period. The coefficient β_1 is the upper asymptote, β_2 is the intrinsic growth rate, β_3 is the predicted value at the response halfway between the two asymptotes (upper and lower),β_4 is the lower asymptote; ε_{ij} is the experimental error associated with the observation y_{ij}, and b_{1i}, b_{2i}, b_{3i}, and b_{4i} are the random effects associated with the model coefficients, β_1,

β_2, β_3, and β_4, respectively.

We can write a four-parameters logistic mixed model by connecting the vectors of body weight and feed consumption observations into a single vector for individual i, resulting in:

$$\begin{bmatrix} \boldsymbol{y}_{i,Y_1} \\ \boldsymbol{y}_{i,Y_2} \end{bmatrix} = \begin{bmatrix} f_{Y_1}(\boldsymbol{\beta}_{Y_1}, \boldsymbol{b}_{i,Y_1}, \boldsymbol{t}_{ij,Y_1}) \\ f_{Y_2}(\boldsymbol{\beta}_{Y_2}, \boldsymbol{b}_{i,Y_2}, \boldsymbol{t}_{ij,Y_2}) \end{bmatrix} + \begin{bmatrix} \boldsymbol{\varepsilon}_{i,Y_1} \\ \boldsymbol{\varepsilon}_{i,Y_2} \end{bmatrix}$$

We assume that,

$$\boldsymbol{b}_i = \begin{bmatrix} b_{1i,Y_1} \\ b_{2i,Y_1} \\ b_{3i,Y_1} \\ b_{4i,Y_1} \\ b_{1i,Y_2} \\ b_{2i,Y_2} \\ b_{3i,Y_2} \\ b_{4i,Y_2} \end{bmatrix} \sim N_{q,Y_1Y_2}(\mathbf{0}, \boldsymbol{G}) \text{ and } \boldsymbol{\varepsilon}_i \sim N_{n_i,Y_1Y_2}(\mathbf{0}, \boldsymbol{R})$$

where

$$\boldsymbol{G} = \begin{bmatrix} \sigma^2_{b_1,Y_1} & \sigma_{b_1Y_1,b_2Y_1} & \sigma_{b_1Y_1,b_3Y_1} & \sigma_{b_1Y_1,b_4Y_1} & \sigma_{b_1Y_1,b_1Y_2} & \sigma_{b_1Y_1,b_2Y_2} & \sigma_{b_1Y_1,b_3Y_2} & \sigma_{b_1Y_1,b_4Y_2} \\ & \sigma^2_{b_2,Y_1} & \sigma_{b_2Y_1,b_3Y_1} & \sigma_{b_2Y_1,b_4Y_1} & \sigma_{b_2Y_1,b_1Y_2} & \sigma_{b_2Y_1,b_2Y_2} & \sigma_{b_2Y_1,b_3Y_2} & \sigma_{b_2Y_1,b_4Y_2} \\ & & \sigma^2_{b_3,Y_1} & \sigma_{b_3Y_1,b_4Y_1} & \sigma_{b_3Y_1,b_1Y_2} & \sigma_{b_3Y_1,b_2Y_2} & \sigma_{b_3Y_1,b_3Y_2} & \sigma_{b_3Y_1,b_4Y_2} \\ & & & \sigma^2_{b_4,Y_1} & \sigma_{b_4Y_1,b_1Y_2} & \sigma_{b_4Y_1,b_2Y_2} & \sigma_{b_4Y_1,b_3Y_2} & \sigma_{b_4Y_1,b_4Y_2} \\ & & & & \sigma^2_{b_1,Y_2} & \sigma_{b_1Y_2,b_2Y_2} & \sigma_{b_1Y_2,b_3Y_2} & \sigma_{b_1Y_2,b_4Y_2} \\ & & & & & \sigma^2_{b_2,Y_2} & \sigma_{b_2Y_2,b_3Y_2} & \sigma_{b_2Y_2,b_4Y_2} \\ \text{Symmetric} & & & & & & \sigma^2_{b_3,Y_2} & \sigma_{b_3Y_2,b_4Y_2} \\ & & & & & & & \sigma^2_{b_4,Y_2} \end{bmatrix}$$

The matrix $\boldsymbol{R}$ has the same structures presented in section section 4.3.3.

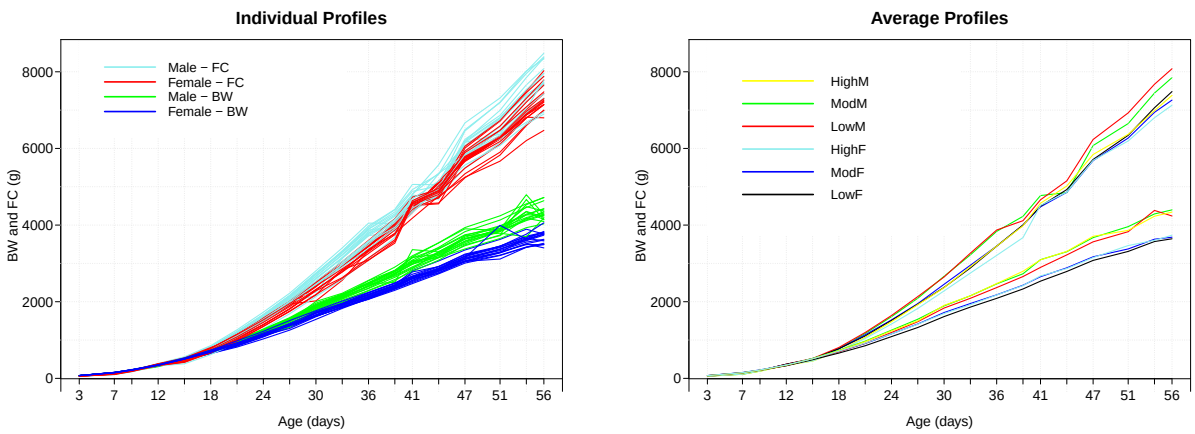
4.3.5 Adjustment of models

The variables body weight and feed consumption of broilers in grams were jointly modeled using the bivariate Gompertz mixed model and bivariate four-parameter logistic mixed model. We worked with different structures for the variance and covariance matrices $\boldsymbol{G}$ and $\boldsymbol{R}$, presented in section section 4.3.3, to select the structure that best described the data. The models were adjusted by the maximum likelihood method using nlme() function (PINHEIRO et al., 2019) of the R software (R CORE TEAM, 2019) and compared using the likelihood ratio test and the AICc (HURVICH; TSAI, 1989) and BIC (SCHWARZ, 1978) information criteria. The block effect was not considered in this work,

but the study for its inclusion is in progress. Part of the programming used in this work is in Appendix B1. The quality of fit was assessed based on the observation of conditional residuals versus adjusted values plots.

4.4 Results and Discussion

Figure 4.1 presents the individual profiles by box (a) and the average profiles by treatment (b) over time of the variables body weight and feed consumption. We note similarities in the growth pattern of the curves for each of the variables. In the first days of the period, the variability between individuals was small, over time, this variability increased as the body weight, and feed consumption increased. In general, feed consumption was higher than body weight.



(a) (b)

Figure 4.1 – Individual profiles by box and average profiles body weight and feed consumption in grams of broilers by treatment

Looking at Tables 4.2 and 4.3, we see that feed consumption exceeded body weight from the 21st day of the experimental period, for all nutritional densities, in both sexes. It can be seen from Figure 4.1 and Tables 4.2 and 4.3 that from the broiler growth phase (11 to 22 days) males consumed more ration and their body weight was higher than females, which is in agreement with Salim et al. (2012), who reported that males consume more ration, use nutrients better and grow faster than females. Regarding the nutritional densities, in general, within each sex, we observed a higher feed consumption and a lower body weight for the low nutritional density, we also noticed a lower feed consumption for the high nutritional density.

Table 4.2 – Means and standard errors (s.e.) of body weight (g) of broiler chickens by treatment over time

Age	ModM		ModF		LowM		LowF		HighM		HighF	
(Days)	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.
3	69.1	1.1	72.1	0.5	70.3	0.8	72.4	0.7	69.1	0.8	72.1	0.9
7	144.4	2.7	152.5	1.6	146.3	2.6	148.3	1.8	144.1	2.1	150.0	1.6
9	211.4	3.4	220.5	2.0	212.0	4.5	213.3	2.3	212.2	2.9	219.7	2.6
12	339.7	5.0	344.4	2.8	333.8	6.4	329.2	3.3	342.9	4.0	347.5	3.1
15	521.6	7.9	512.5	3.9	504.6	7.8	486.6	3.5	512.7	5.5	510.6	4.8
18	730.2	6.5	701.7	3.8	696.4	8.6	660.3	4.6	722.9	10.2	708.9	9.1
21	970.5	5.4	908.7	4.3	917.5	7.7	851.1	8.3	958.8	12.8	920.7	14.0
24	1257.5	5.9	1161.7	10.0	1197.7	11.7	1089.5	13.4	1238.6	16.7	1162.0	16.6
27	1542.8	8.5	1418.3	6.4	1479.3	12.7	1327.4	16.7	1499.8	34.9	1412.3	20.5
30	1890.8	21.4	1717.1	5.9	1834.9	24.0	1612.1	15.3	1904.6	29.0	1691.8	22.3
33	2154.6	19.4	1952.4	7.0	2089.5	26.3	1859.6	10.6	2154.0	20.4	1922.2	23.4
36	2465.5	25.9	2179.8	14.9	2368.8	30.7	2087.6	10.0	2473.0	21.7	2175.8	22.6
39	2729.0	47.1	2430.3	12.4	2656.7	39.0	2332.6	7.4	2794.6	26.9	2421.7	22.4
41	3097.4	58.9	2653.2	32.9	2896.0	41.6	2536.7	18.8	3093.0	35.9	2673.8	25.7
44	3305.2	55.0	2884.2	42.9	3221.5	49.8	2789.5	16.6	3313.6	54.7	2865.3	19.2
47	3673.0	62.0	3172.0	41.2	3562.6	65.8	3078.0	20.9	3706.6	46.0	3150.9	33.2
51	3959.2	61.4	3377.4	71.3	3827.4	69.5	3312.6	28.1	3861.5	20.0	3465.5	111.6
54	4290.8	63.2	3631.4	69.0	4382.3	130.7	3570.5	36.6	4231.1	124.4	3601.7	50.0
56	4396.2	73.4	3683.0	51.7	4237.3	88.0	3642.0	66.8	4339.0	83.8	3734.9	87.0

ModM and ModF: Moderate nutritional density for Male and Female; LowM and LowF: Low nutritional density for Male and Female; HighM and HighF: High nutritional density for Male and Female.

Table 4.3 – Means and standard errors (s.e.) of feed consumption (g) of broiler chickens by treatment over time

Age	ModM		ModF		LowM		LowF		HighM		HighF	
(Days)	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.	Means	s.e.
3	58.1	0.5	60.3	0.5	60.0	0.7	61.1	0.7	58.1	0.3	58.9	0.6
7	108.2	1.8	115.3	1.3	117.3	2.9	118.1	1.2	106.4	1.8	110.8	2.1
9	190.2	2.9	201.1	1.5	202.0	4.9	203.3	1.9	185.5	2.7	192.5	3.5
12	354.8	4.7	367.5	2.9	369.9	7.3	369.0	3.1	344.4	4.3	352.8	5.9
15	485.3	12.1	504.4	7.7	518.2	17.3	504.7	8.0	449.0	16.6	454.8	14.0
18	777.0	12.4	775.0	9.4	806.0	19.8	771.7	10.9	710.4	19.1	710.5	18.6
21	1172.4	13.5	1136.6	10.0	1196.5	24.7	1105.8	15.0	1071.9	28.5	1041.6	25.8
24	1609.0	13.7	1525.6	11.2	1640.1	28.1	1509.7	23.0	1479.3	38.8	1417.4	27.0
27	2090.3	16.8	1950.6	14.8	2133.7	29.4	1935.3	25.6	1923.5	48.9	1824.1	31.2
30	2662.8	19.3	2454.9	16.5	2645.3	84.3	2373.3	76.6	2365.2	70.7	2282.0	35.4
33	3222.6	29.4	2951.6	8.5	3266.3	43.8	2880.8	70.9	2911.9	68.1	2748.2	42.8
36	3835.3	36.9	3452.1	25.4	3871.0	49.6	3449.3	38.1	3450.8	70.7	3208.5	49.0
39	4227.8	58.4	3999.5	29.5	4114.0	85.7	4000.9	41.9	3981.3	74.3	3672.2	45.7
41	4770.6	75.9	4475.7	29.2	4660.2	82.9	4494.2	55.9	4569.5	70.6	4515.1	68.4
44	4847.6	66.0	4856.4	111.0	5154.1	124.4	4927.1	61.2	5019.5	78.6	4859.6	30.3
47	6075.2	136.5	5681.8	102.1	6233.2	117.5	5712.4	110.8	5841.8	76.3	5688.4	92.1
51	6649.0	155.6	6270.7	115.0	6927.4	119.2	6343.0	125.8	6367.7	98.0	6194.6	112.3
54	7444.5	155.1	6942.0	116.7	7674.3	124.0	7061.0	135.5	6984.8	133.0	6801.5	126.0
56	7847.7	164.6	7261.3	152.8	8079.5	133.5	7483.8	163.8	7384.2	174.1	7126.5	140.7

ModM and ModF: Moderate nutritional density for Male and Female; LowM and LowF: Low nutritional density for Male and Female; HighM and HighF: High nutritional density for Male and Female.

4.4.1 Bivariate Gompertz mixed model

To adjust the Gompertz bivariate mixed model for the variables body weight and feed consumption, we first plotted the individual interval graphs with 95% confidence for

each of the bivariate model coefficients. These confidence intervals are presented in Figure 4.2; through these intervals, we select the coefficients that would receive random effects. According to Pinheiro and Bates (2000), the non-overlapping of the intervals indicates the need to include random effects, so for the Gompertz bivariate mixed model, we include random effects in the coefficients β_{1,Y_1}, β_{3,Y_1}, β_{1,Y_2}, β_{2,Y_2}, and β_{3,Y_2}.

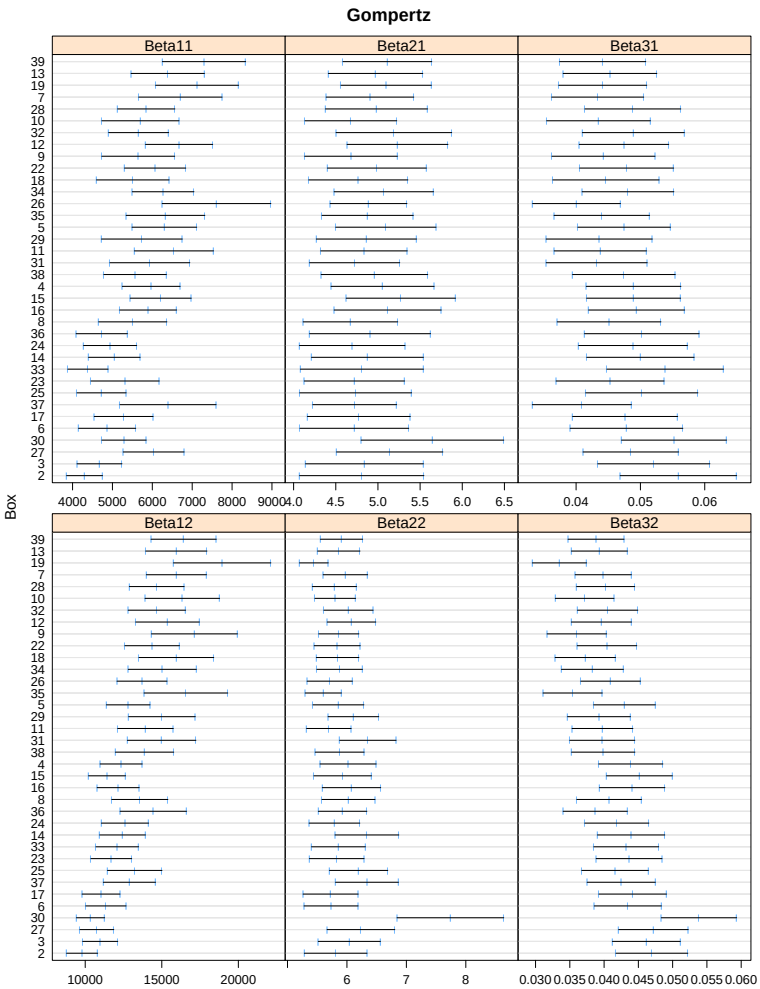


Figure 4.2 – Ninety-five percent confidence intervals on the bivariate Gompertz model parameters for each box

Table 4.4 presents the results of the selection of the bivariate Gompertz mixed model. The three models presented (G1, G2, and G3) have the same random effects b_{1,Y_1}, b_{3,Y_1}, b_{1,Y_2}, b_{2,Y_2}, and b_{3,Y_2}, and different structures of variance and covariance matrices $\boldsymbol{G}$ and $\boldsymbol{R}$. In model G1 and G2, we consider a structure for matrix $\boldsymbol{G}$ with different variances and correlations between random effects. For the intra-individual matrix ($\boldsymbol{R}$), we considered uncorrelated structures with different variances for each sex in the G1 model, different variances for each age in the G2 model, and different variances for the interaction between sex and age in the G3 model. In model G3, there was a need not to consider correlations between random effects in the matrix ($\boldsymbol{G}$), as there was no convergence to the structure

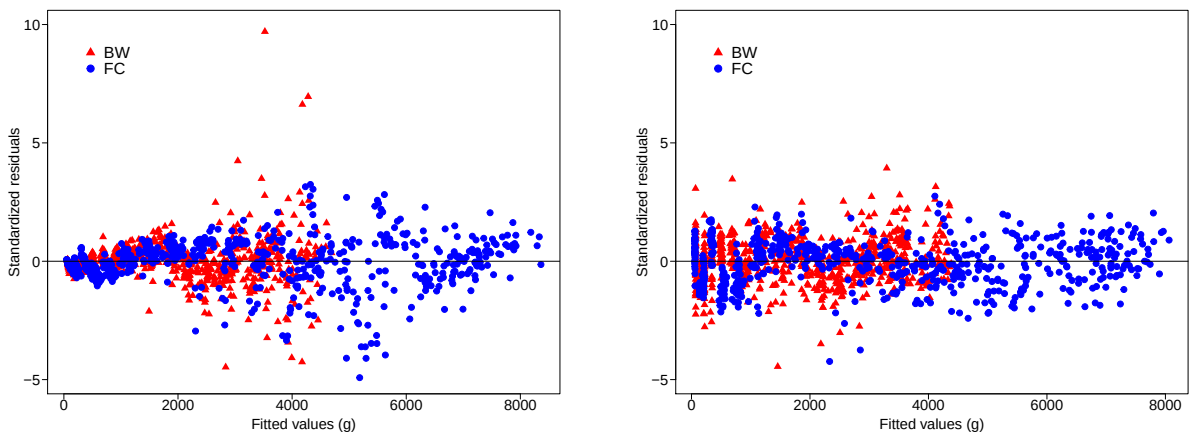
with correlations. According to the AICc, BIC, and the likelihood ratio test, the bivariate model best suited to body weight and feed consumption data was the G3 model. Through the same criteria, we verified the necessity of the permanence of the random effects in the coefficients β_{1,Y_1}, β_{3,Y_1}, β_{1,Y_2}, β_{2,Y_2}, and β_{3,Y_2} of the model G3.

Table 4.4 – Selection of bivariate Gompertz models with mixed effects

Mod.	$\boldsymbol{G}$	$\boldsymbol{R}$	npar	$-2logL$	AICc	BIC	Comp.	p-value
G1	UN	VCH(Sex)	54	16320.84	16433.37	16710.79	-	-
G2	UN	VCH(Age)	71	14632.56	14782.46	15145.27	G1 *vs* G2	$< .0001$
G3	VCH	VCH(Age∗Sex)	80	14580.86	14750.93	15158.54	G2 *vs* G3	$< .0001$

$\boldsymbol{G}$: Variance-covariance matrix for the random effects; $\boldsymbol{R}$: Variance-covariance matrix intra-individual; npar: number of model parameters; $-2logL$: -2(logarithm of the likelihood); UN: Unstructured; VCH(Age): Heterogeneous variance components for age ; VCH(Sex): Heterogeneous variance components for sex; VCH(Age∗Sex): Heterogeneous variance components for interaction age and sex.

In Figure 4.3, we present the graph of the standardized conditional residuals versus the adjusted values for the initial model G1 (a) and the selected model G3 (b). The residuals represented by the red triangles refer to the observations of the body weight variable, while the blue dots are the residuals to the observations of the feed consumption variable. We see in this figure that the G3 model was better fitted to the data than the G1 model.



(a) (b)

Figure 4.3 – Graph of conditional residuals versus adjusted values of bivariate Gompertz mixed models G1 (a) and G3 (b)

In Table 4.5, we present the estimates of the coefficients of the selected model (G3) with their respective standard errors and the estimates of the residual variance components for each of the variables. Note that a different curve was adjusted for each of the treatments, as the treatment factor was significant for each of the model coefficients (see Appendix B2).

Table 4.5 – Estimates of the coefficients of the bivariate Gompertz mixed model (G3) with the respective standard errors for each treatment and residual variance estimates for each of the variables

	Body weight			**Feed consumption**		
Treatment	$\hat{\beta}_{1,Y_1}$	$\hat{\beta}_{2,Y_1}$	$\hat{\beta}_{3,Y_1}$	$\hat{\beta}_{1,Y_2}$	$\hat{\beta}_{2,Y_2}$	$\hat{\beta}_{3,Y_2}$
HighM	5933 ± 184	5.17 ± 0.03	0.050 ± 0.0010	12480 ± 779	6.15 ± 0.06	0.044 ± 0.0014
ModM	5892 ± 182	5.18 ± 0.03	0.050 ± 0.0010	12222 ± 732	6.20 ± 0.06	0.046 ± 0.0014
LowM	6027 ± 192	5.14 ± 0.03	0.048 ± 0.0010	12653 ± 740	6.16 ± 0.06	0.046 ± 0.0014
HighF	4672 ± 119	4.88 ± 0.02	0.052 ± 0.0007	12386 ± 585	6.09 ± 0.04	0.043 ± 0.0010
ModF	4731 ± 169	4.89 ± 0.03	0.052 ± 0.0011	11387 ± 751	6.03 ± 0.06	0.045 ± 0.0014
LowF	4856 ± 180	4.87 ± 0.03	0.049 ± 0.0011	12112 ± 786	6.04 ± 0.06	0.044 ± 0.0014
$\hat{\sigma}^2_\varepsilon$		1.07			5.10	

ModM and ModF: Moderate nutritional density for Male and Female; LowM and LowF: Low nutritional density for Male and Female; HighM and HighF: High nutritional density for Male and Female.

The estimated of the random effects variances-covariances matrix b_{1,Y_1}, b_{3,Y_1}, b_{1,Y_2}, b_{2,Y_2}, and b_{3,Y_2} is given by:

$$\boldsymbol{G} = \begin{bmatrix} 4209.30 & 0 & 0 & 0 & 0 \\ 0 & 0.0000002 & 0 & 0 & 0 \\ 0 & 0 & 9.50 & 0 & 0 \\ 0 & 0 & 0 & 0.00023 & 0 \\ 0 & 0 & 0 & 0 & 0.0000004 \end{bmatrix}$$

Table 4.6 presents the estimates of the variance components of the intra-individual matrix, $\boldsymbol{R}$.

Table 4.6 – Intra-individual matrix variance component estimates ($\boldsymbol{R}$) of the model G3

	Variance components									
Sex	$\hat{\sigma}^2_1$	$\hat{\sigma}^2_2$	$\hat{\sigma}^2_3$	$\hat{\sigma}^2_4$	$\hat{\sigma}^2_5$	$\hat{\sigma}^2_6$	$\hat{\sigma}^2_7$	$\hat{\sigma}^2_8$	$\hat{\sigma}^2_9$	$\hat{\sigma}^2_{10}$
Male	1.8	121.7	43.8	50.7	493.4	303.7	41.4	154.0	670.4	3136.8
Female	1.0	84.5	8.5	92.1	217.7	177.4	187.7	346.4	378.1	1054.8
	$\hat{\sigma}^2_{11}$	$\hat{\sigma}^2_{12}$	$\hat{\sigma}^2_{13}$	$\hat{\sigma}^2_{14}$	$\hat{\sigma}^2_{15}$	$\hat{\sigma}^2_{16}$	$\hat{\sigma}^2_{17}$	$\hat{\sigma}^2_{18}$	$\hat{\sigma}^2_{19}$	
Male	1023.5	2379.9	13301.5	12897.2	28731.4	15537.7	12450.0	42446.3	22295.7	
Female	1182.1	2112.8	3899.0	6738.5	8271.7	16329.9	29538.9	27076.1	35610.0	

Note that the selected model (G3) has different variances for males and females on different days of the experimental period and also models the heterogeneity of intra-individual variances over time.

4.4.2 Bivariate four-parameter logistic mixed model

For the preliminary adjustment of the bivariate four-parameter logistic (4PL) mixed model, we found by the 95% confidence interval graph, shown in Figure 4.4, the need

to include random effects in the coefficients β_{1,Y_1}, β_{1,Y_2}, β_{2,Y_2}, β_{3,Y_2} and β_{4,Y_2} of the 4PL bivariate mixed model.

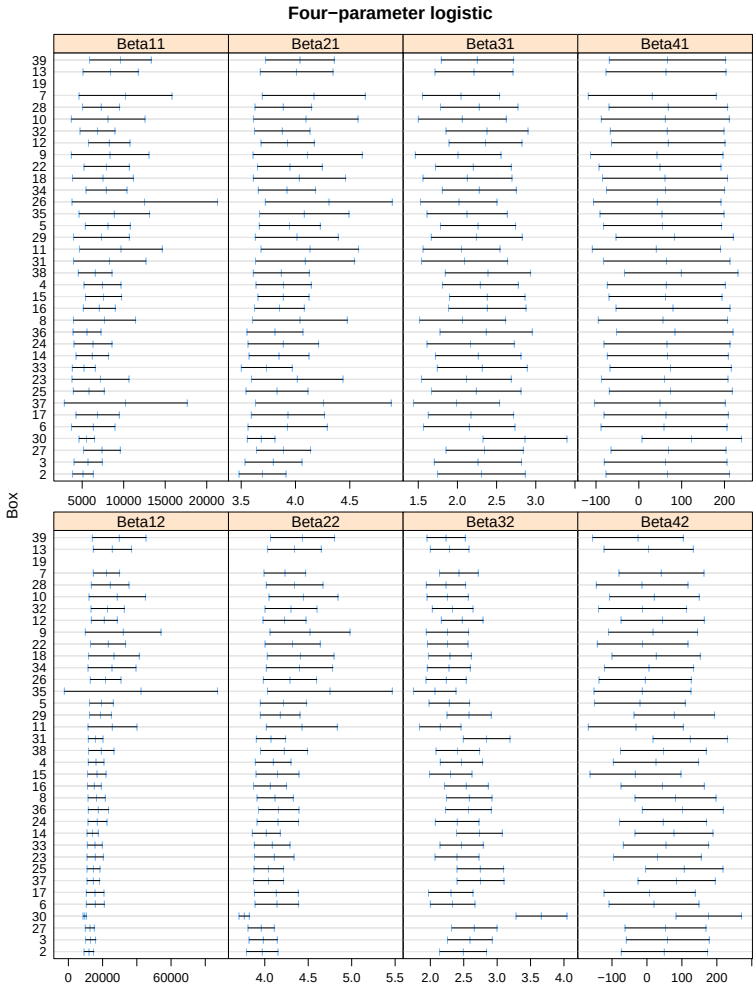


Figure 4.4 – Ninety-five percent confidence intervals on the bivariate four-parameter logistic model parameters for each box

Table 4.7 presents the results of the selection of the 4PL bivariate mixed model. The three models are shown (L1, L2, and L3) have the same random effects b_{1,Y_1}, b_{1,Y_2}, b_{2,Y_2}, b_{3,Y_2}, and b_{4,Y_2}.

Table 4.7 – Selection of bivariate four-parameter logistic models with mixed effects

Mod.	$\boldsymbol{G}$	$\boldsymbol{R}$	npar	$-2logL$	AICc	BIC	Comp.	p-value
L1	VCH	VCH(Sex)	56	16448.82	16565.68	16853.19	-	-
L2	VCH	VCH(Age)	73	14447.88	14602.23	14975.02	L1 *vs* L2	$< .0001$
L3	VCH	VCH(Age∗Sex)	92	14381.28	14578.70	15045.62	L2 *vs* L3	$< .0001$

$\boldsymbol{G}$: Variance-covariance matrix for the random effects; $\boldsymbol{R}$: Variance-covariance matrix intra-individual; npar: number of model parameters; $-2logL$: -2(logarithm of the likelihood); VCH(Age): Heterogeneous variance components for age ; VCH(Sex): Heterogeneous variance components for sex; VCH(Age∗Sex): Heterogeneous variance components for interaction age and sex.

Due to problems with the tuning process convergence of some models, struc-

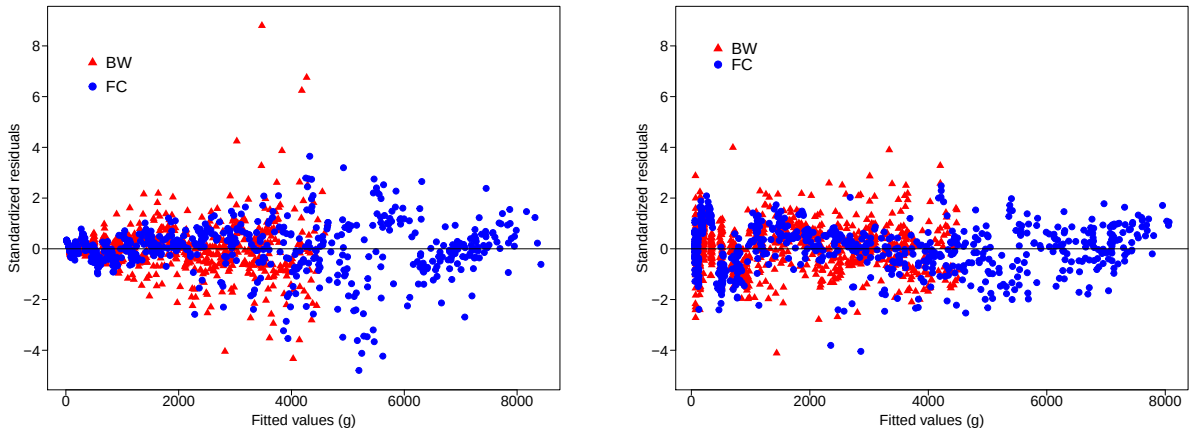
tures with heterogeneous variances and null correlations were used for the matrix of variances and covariance $\boldsymbol{G}$. For matrix $\boldsymbol{R}$, we considered structures with null correlations and different variances for each sex in the L1 model, different variances for each age in the L2 model, and different variances for the interaction between sex and age in the L3 model. According to the AICc, BIC, and the likelihood ratio test, the 4PL bivariate mixed model best suited to body weight and feed consumption data was the L3 model. After selecting the L3 model, we verified the need for random effects on the model coefficients, the results of this selection are presented in Table 4.8. In this selection procedure, we maintained the same structure of matrix $\boldsymbol{R}$ of model L3, previously selected, for all models, and modified the structure of matrix $\boldsymbol{G}$. According to the AICc, BIC, and the likelihood ratio test, the selected model was the L3.6 model. Subsequently, we verified the significance of the treatment factor in the coefficients of the model selected using ANOVA (See Appendix B2). We found the lack of significance of the treatment factor in the coefficient β_{4,Y_2}, thus removing the treatment factor of this coefficient in the L3.7 model. Therefore, the 4PL bivariate mixed model most suited to the data according to the selection procedure used was the L3.7. This model has random effects on coefficients β_{1,Y_1}, β_{1,Y_2}, and β_{3,Y_2}, with different variances and correlations between random effects in matrix $\boldsymbol{G}$. The matrix $\boldsymbol{R}$ has different variances for the interaction age and sex and null correlations.

Table 4.8 – Selection of bivariate four-parameter logistic models with mixed effects modifying the matrix $\boldsymbol{G}$

Mod.	RE	$\boldsymbol{G}$	npar	$-2logL$	AICc	BIC	Comp.	p-value
L3	$b_{1,Y_1};b_{1,Y_2};b_{2,Y_2};b_{3,Y_2};b_{4,Y_2}$	VCH	92	14381.28	14578.70	15045.62	-	-
L3.1	$b_{1,Y_1};b_{1,Y_2};b_{2,Y_2};b_{3,Y_2}$	VCH	91	14381.28	14576.40	15038.40	L3 *vs* L3.1	0.9810
L3.2	$b_{1,Y_1};b_{1,Y_2};b_{2,Y_2}$	VCH	90	14411.26	14604.09	15061.16	L3.1 *vs* L3.2	$< .0001$
L3.3	$b_{1,Y_1};b_{1,Y_2};b_{3,Y_2}$	VCH	90	14381.28	14574.10	15031.18	L3.1 *vs* L3.3	0.9877
L3.4	$b_{1,Y_1};b_{3,Y_2}$	VCH	89	14432.28	14622.82	15074.97	L3.3 *vs* L3.4	$< .0001$
L3.5	$b_{1,Y_2};b_{3,Y_2}$	VCH	89	14586.66	14777.19	15229.33	L3.3 *vs* L3.5	$< .0001$
L3.6	$b_{1,Y_1};b_{1,Y_2};b_{3,Y_2}$	UN	93	14371.70	14571.43	15043.27	L3.3 *vs* L3.6	0.0226
L3.7	$b_{1,Y_1};b_{1,Y_2};b_{3,Y_2}$	UN	88	14319.18	14507.43	14954.64	-	-

RE: Random Effect; $\boldsymbol{G}$: Variance-covariance matrix for the random effects; npar: number of model parameters; $-2logL$: -2(logarithm of the likelihood); VCH: Heterogeneous variance components; UN: Unstructured.

In Figure 4.5, we present the graph of the standardized conditional residuals versus the adjusted values for the initial model L1 (a) and the selected model L3.7 (b). The residuals represented by the red triangles refer to the observations of the body weight variable, while the blue dots are the residuals to the observations of the feed consumption variable. We observe in this figure that the L3.7 model was better adjusted to the data.



(a) (b)

Figure 4.5 – Graph of conditional residuals versus adjusted values of bivariate four-parameter logistic mixed models L1 (a) and L3.7 (b)

In Table 4.9, we present the estimates of the coefficients of the selected model (L3.7) with the respective standard errors and the estimates of the residual variance components for each of the variables.

Table 4.9 – Estimates of the coefficients of the bivariate four-parameter logistic mixed model (L3.7) with the respective standard errors for each treatment and residual variance estimates for each of the variables

	Body weight				**Feed consumption**			
Treat.	$\hat{\beta}_{1,Y_1}$	$\hat{\beta}_{2,Y_1}$	$\hat{\beta}_{3,Y_1}$	$\hat{\beta}_{4,Y_1}$	$\hat{\beta}_{1,Y_2}$	$\hat{\beta}_{2,Y_2}$	$\hat{\beta}_{3,Y_2}$	$\hat{\beta}_{4,Y_2}$
HighM	8522±649	4.00±0.06	2.2±2.1	55.6±2.1	14489±1846	4.0±0.07	2.6±0.08	52±0.9
ModM	8376±642	3.98±0.06	2.2±2.1	55.4±2.1	13307±1682	3.9±0.06	2.7±0.07	52±0.9
LowM	9031±728	4.07±0.07	2.2±2.2	56.6±2.2	15128±1776	4.0±0.06	2.6±0.07	52±0.9
HighF	6861±424	3.95±0.05	2.1±1.5	55.9±1.5	16368±1477	4.1±0.05	2.5±0.05	52±0.9
ModF	7114±625	3.98±0.07	2.1±2.2	55.8±2.2	14324±1824	4.0±0.07	2.6±0.07	52±0.9
LowF	7943±756	4.09±0.07	2.1±2.2	56.2±2.2	16488±2034	4.1±0.07	2.5±0.07	52±0.9
$\hat{\sigma}^2_\varepsilon$		1.53				5.99		

ModM and ModF: Moderate nutritional density for Male and Female; LowM and LowF: Low nutritional density for Male and Female; HighM and HighF: High nutritional density for Male and Female.

The estimated of the random effects variances-covariances matrix b_{1,Y_1}, b_{1,Y_2}, and b_{3,Y_2} is given by:

$$\boldsymbol{G} = \begin{bmatrix} 24047.81 & 28545.47 & -4.46 \\ 28545.47 & 133925.4 & 4.09 \\ -4.46 & 4.09 & 0.0017099 \end{bmatrix}$$

Table 4.10 presents the estimates of the variance components of the intra-individual matrix, $\boldsymbol{R}$.

Table 4.10 – Intra-individual matrix variance component estimates ($\boldsymbol{R}$) of the model L3.7

	Variance components									
Sex	$\hat{\sigma}^2_1$	$\hat{\sigma}^2_2$	$\hat{\sigma}^2_3$	$\hat{\sigma}^2_4$	$\hat{\sigma}^2_5$	$\hat{\sigma}^2_6$	$\hat{\sigma}^2_7$	$\hat{\sigma}^2_8$	$\hat{\sigma}^2_9$	$\hat{\sigma}^2_{10}$
Male	1.2	9.1	44.5	185.4	165.2	115.9	70.8	101.4	410.7	2950.6
Female	1.0	6.2	44.0	229.7	49.1	50.2	176.0	259.7	307.8	1268.2
	$\hat{\sigma}^2_{11}$	$\hat{\sigma}^2_{12}$	$\hat{\sigma}^2_{13}$	$\hat{\sigma}^2_{14}$	$\hat{\sigma}^2_{15}$	$\hat{\sigma}^2_{16}$	$\hat{\sigma}^2_{17}$	$\hat{\sigma}^2_{18}$	$\hat{\sigma}^2_{19}$	
Male	565.4	1137.3	9050.7	9641.5	21695.5	10982.9	8473.1	21175.0	15996.3	
Female	934.0	901.1	2009.0	5531.6	6218.9	10147.0	18328.0	12524.2	19998.3	

Note that the selected model (L3.7) has different variances for males and females on different days of the experimental period and also models the heterogeneity of intra-individual variances over time.

4.4.3 Comparison between bivariate Gompertz mixed model and bivariate four-parameter logistic mixed model

Table 4.11 presents the results of the selection criteria used to compare the two bivariate mixed models. According to the AICc, BIC, and the correlation between observed and predicted values, the most appropriate model for broiler body weight and feed consumption data was the bivariate four-parameter logistic mixed model.

Table 4.11 – Results of information criteria and statistics for the mixed bivariate models

Model	npf	npr	$\hat{\sigma}^2_{Y_1}$	$\hat{\sigma}^2_{Y_2}$	Corr	AICc	BIC	$-2logL$
Gompertz	36	44	1.07	5.10	0.9975	14750.93	15158.54	14580.86
4-par logistic	43	45	1.53	5.99	0.9981	14507.43	14954.64	14319.18

npf: number of parameters related to fixed-effect factors; npr: number of parameters corresponding to variance components; corr: correlation between observed values and predicted values; $\hat{\sigma}^2_{Y_1}$: residual variance estimate for the variable bodyweight; $\hat{\sigma}^2_{Y_2}$: residual variance estimate for the variable feed consumption; $-2logL$: -2(logarithm of the likelihood).

4.5 Conclusion

According to the comparison criteria used in this work, the four-parameter logistic mixed bivariate model was better suited to broiler body weight and feed consumption data than the Gompertz mixed bivariate model. As we increased the number of model parameters, it became more difficult to converge the iterative process in parameter estimation, so we recommend looking for other iterative procedures to evaluate a larger number of variance and covariance structure options.

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APPENDIX

Appendix A: Additional information about Chapter 3

Appendix A1: Correlation and sample variances

Table (4.12) presents the estimates of the variances (values in bold), covariance (below bold values), and the sample correlations (above bold values) in the different days of the experimental period, for broiler chicken body weight. We observed that the variances increase with time, and the correlations decrease, which suggests that a structure that admits homogeneity of variances and the non-correlation between the observations over time is inadequate.

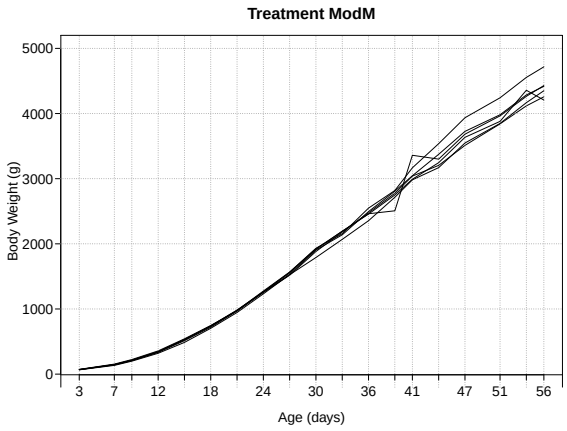
Table 4.12 – Table of variance (values in bold), covariances (below bold values), and correlations (above bold values) over time (days) for broiler chicken body weight

Days	3	7	9	12	15	18	21	24	27	30
3	**3.18**	0.87	0.78	0.71	0.73	0.68	0.55	0.39	0.38	0.15
7	6.58	**18.05**	0.95	0.90	0.86	0.78	0.64	0.48	0.44	0.14
9	8.16	23.51	**34.25**	0.97	0.85	0.76	0.69	0.56	0.47	0.15
12	10.09	30.50	44.97	**63.01**	0.88	0.78	0.66	0.55	0.43	0.10
15	14.64	41.25	55.96	78.58	**127.35**	0.77	0.67	0.57	0.48	0.18
18	17.38	47.49	64.29	89.37	125.89	**207.60**	0.78	0.68	0.63	0.35
21	17.23	47.93	71.26	92.40	133.88	197.02	**309.16**	0.92	0.78	0.56
24	18.25	53.10	86.26	114.48	168.08	256.36	425.03	**684.97**	0.77	0.66
27	23.52	65.31	96.35	120.20	191.78	319.67	478.66	707.84	**1229.97**	0.57
30	9.62	22.21	32.95	30.20	76.10	188.48	364.75	634.07	741.41	**1361.02**
33	26.86	74.82	107.83	130.42	191.91	258.65	442.33	715.28	697.22	1165.95
36	10.69	38.07	54.23	38.96	45.79	63.40	222.50	397.60	163.05	940.60
39	17.23	52.02	56.63	41.78	79.79	149.99	227.94	433.21	136.09	644.16
41	-28.64	-12.40	11.56	24.44	0.69	-180.68	43.06	165.81	-88.92	829.30
44	-49.78	-42.97	-64.50	-82.14	-97.48	-111.11	-110.82	75.69	51.29	982.56
47	-63.73	-63.13	-71.18	-80.09	-146.29	-288.91	-386.92	-266.67	-558.84	940.06
51	-66.19	13.65	-9.18	0.92	-77.48	-285.04	-424.14	-223.14	222.89	584.60
54	-25.19	105.55	119.24	176.52	381.76	599.94	517.60	1024.89	1901.30	2597.63
56	-58.14	23.83	23.42	19.62	-54.18	-170.84	-442.49	-197.20	-761.23	796.29

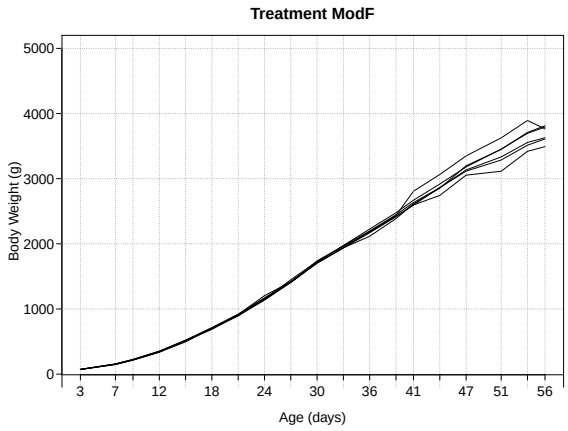
Days	33	36	39	41	44	47	51	54	56
3	0.40	0.16	0.18	-0.20	-0.34	-0.36	-0.26	-0.08	-0.20
7	0.47	0.24	0.23	-0.04	-0.12	-0.15	0.02	0.13	0.03
9	0.49	0.24	0.18	0.03	-0.14	-0.12	-0.01	0.11	0.02
12	0.44	0.13	0.10	0.04	-0.13	-0.10	0.00	0.12	0.01
15	0.45	0.11	0.13	0.00	-0.11	-0.13	-0.05	0.18	-0.03
18	0.48	0.12	0.19	-0.16	-0.10	-0.20	-0.14	0.23	-0.07
21	0.67	0.33	0.24	0.03	-0.08	-0.22	-0.17	0.16	-0.15
24	0.73	0.40	0.31	0.08	0.04	-0.10	-0.06	0.21	-0.05
27	0.53	0.12	0.07	-0.03	0.02	-0.16	0.04	0.29	-0.13
30	0.84	0.67	0.33	0.29	0.33	0.26	0.11	0.38	0.13
33	**1404.19**	0.75	0.39	0.32	0.24	0.20	0.13	0.33	0.16
36	1068.15	**1445.90**	0.66	0.46	0.50	0.50	0.34	0.23	0.42
39	775.66	1337.00	**2881.90**	-0.08	0.42	0.34	0.24	0.24	0.35
41	946.11	1365.74	-347.55	**6157.51**	0.56	0.62	0.44	0.33	0.65
44	723.65	1527.71	1816.96	3591.84	**6574.28**	0.91	0.68	0.73	0.81
47	739.83	1879.92	1812.57	4879.83	7383.03	**9969.17**	0.66	0.60	0.82
51	718.72	1893.57	1831.06	5045.03	7970.72	9471.60	**20964.51**	0.55	0.61
54	2274.76	1629.81	2393.28	4759.95	10867.82	11047.57	14636.15	**34061.30**	0.57
56	991.53	2656.37	3049.64	8356.73	10782.08	13498.85	14613.77	17448.48	**27034.37**

Appendix A2: Profiles over time of broiler chicken body weight

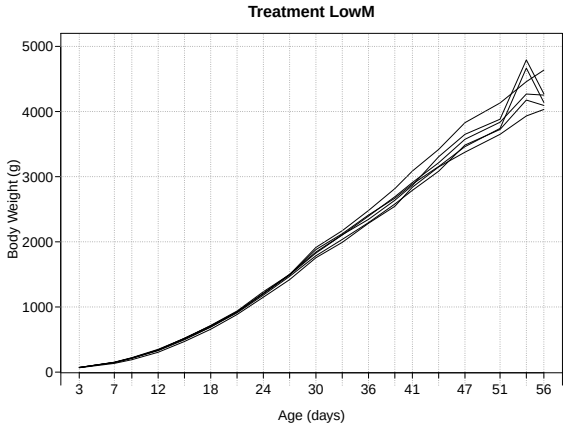
The individual profiles for each treatment for the variable body weight, depending of the age of the broiler chickens, are presented in Figure (4.6).



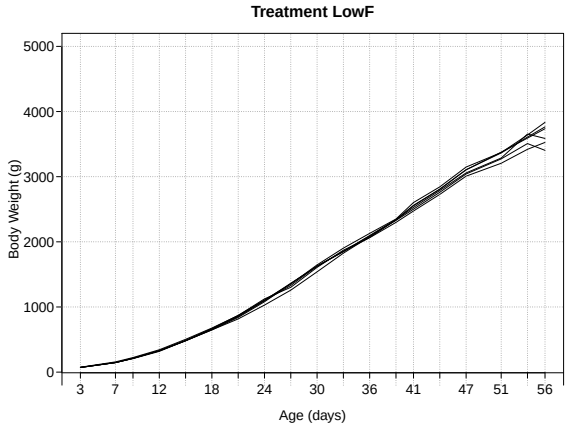
(a)



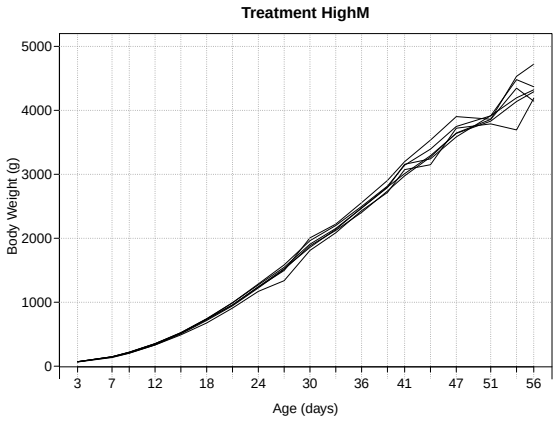
(b)



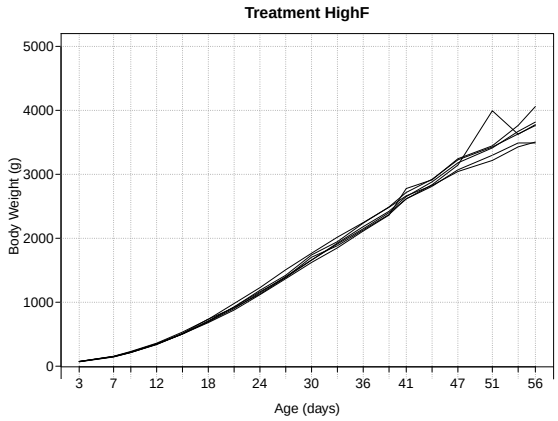
(c)



(d)



(e)



(f)

Figure 4.6 – Graph of profiles over time of total weight in grams per box for each treatment

Appendix A3: Curves for each growth model studied

For a better understanding of the interpretation of the coefficients, were plotted curves for each growth model studied, assigning different values for each of the coefficients referring to the fixed part of the models.

In these figures, the red curves were plotted with the following values:

- Gompertz: $\beta_1 = 5805$, $\beta_2 = 5.21$ and $\beta_3 = 0.0511$
- Four-parameter Logistic: $\beta_1 = 8270.16$, $\beta_3 = 3.97$, $\beta_4 = 2.23$ and $\beta_5 = 55,47$
- Von Bertalanffy: $\beta_1 = 5955.92$, $\beta_2 = 0.2290$, $\beta_3 = 0.0486$ and $\beta_6 = 0.97$
- Richards: $\beta_1 = 6553.29$, $\beta_2 = -0.5150$, $\beta_3 = 0.0414$ and $\beta_6 = -0.1277$

Note that the left graphs refer to the study time interval, while the right graphs were constructed with a more extended time interval for a better view of the entire curve, and red dashed vertical lines were drawn indicating the study interval.

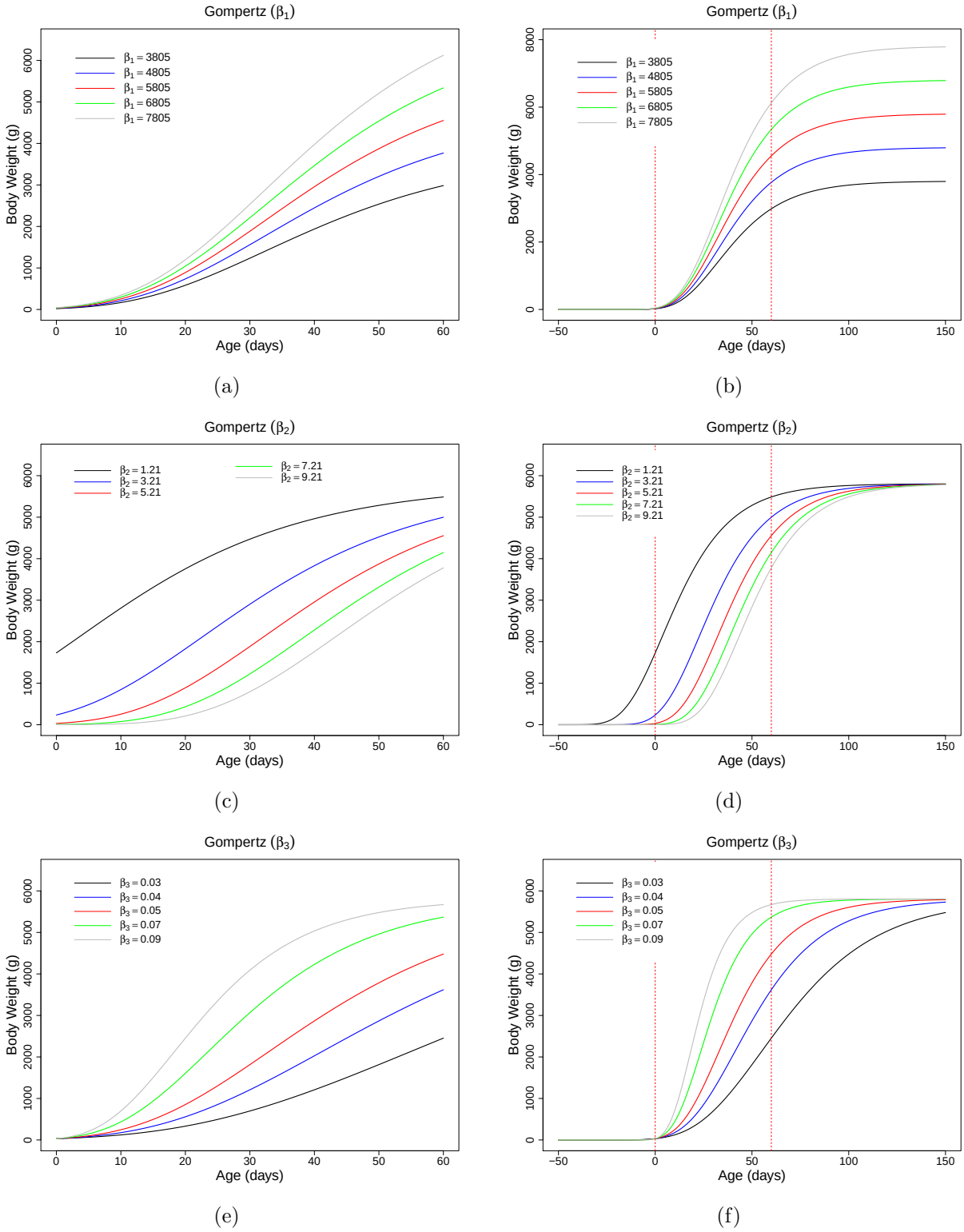


Figure 4.7 – Gompertz curves with different coefficient values

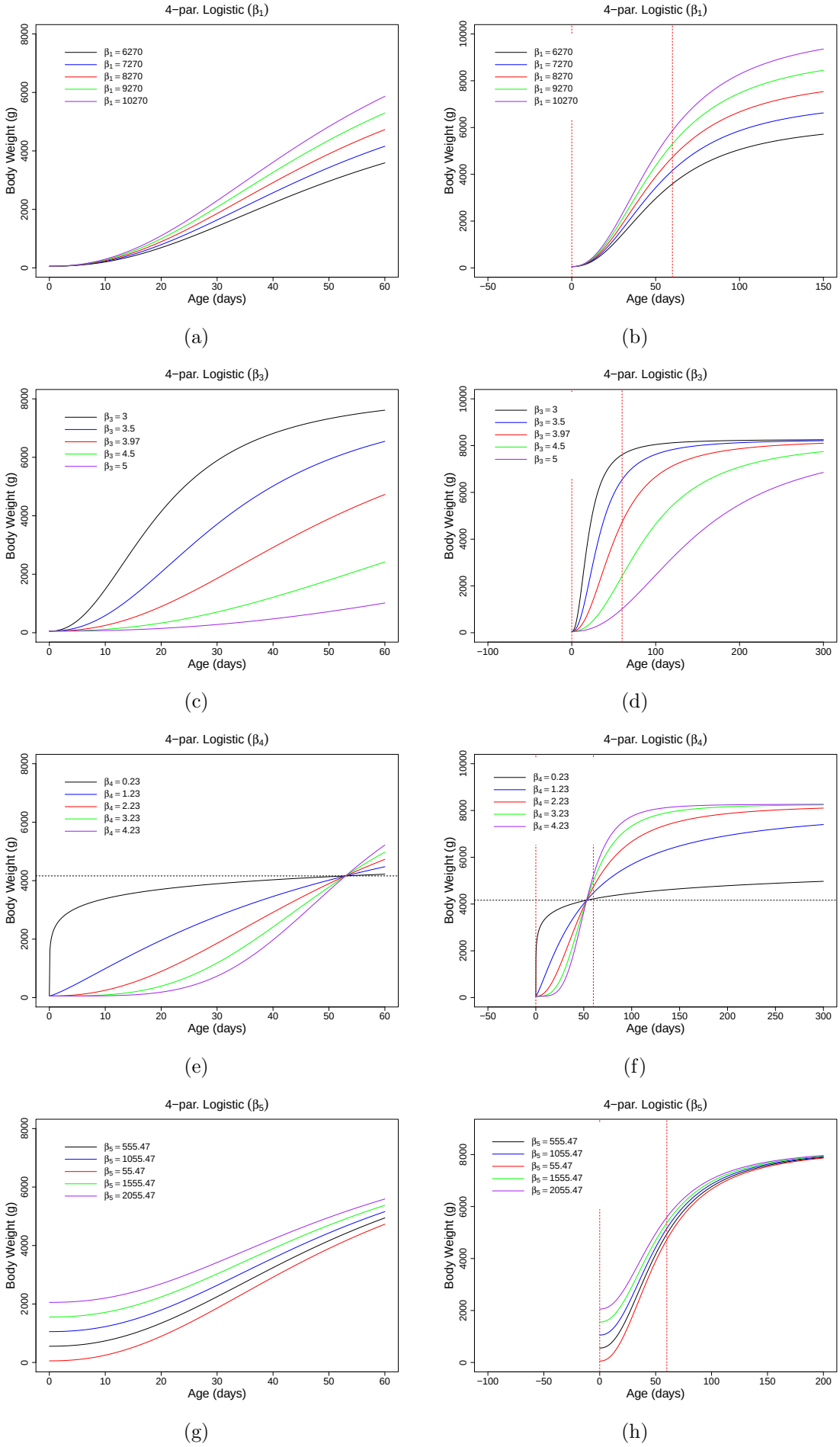


Figure 4.8 – Four-parameter logistic curves with different coefficient values

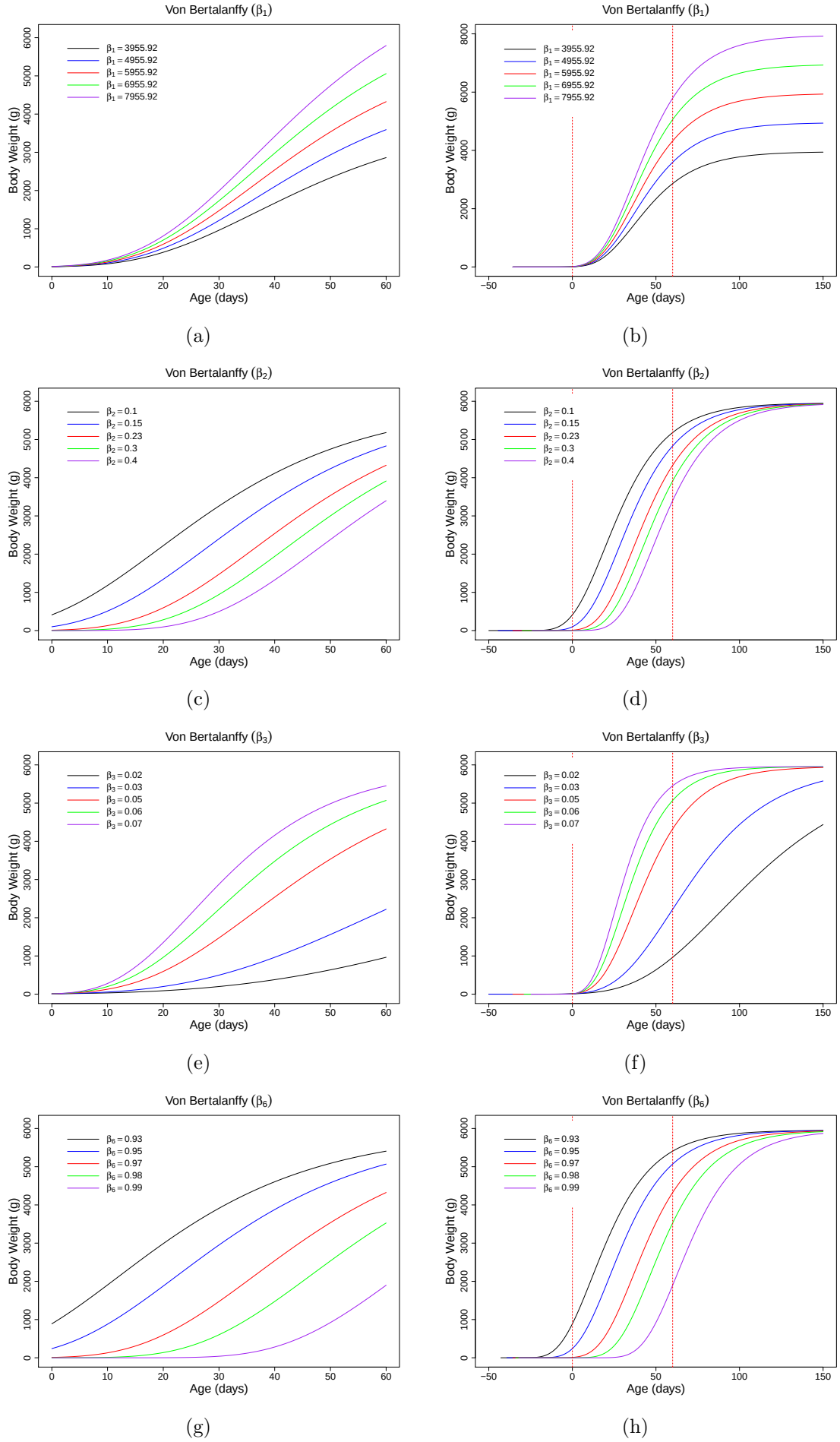


Figure 4.9 – Von Bertalanffy curves with different coefficient values

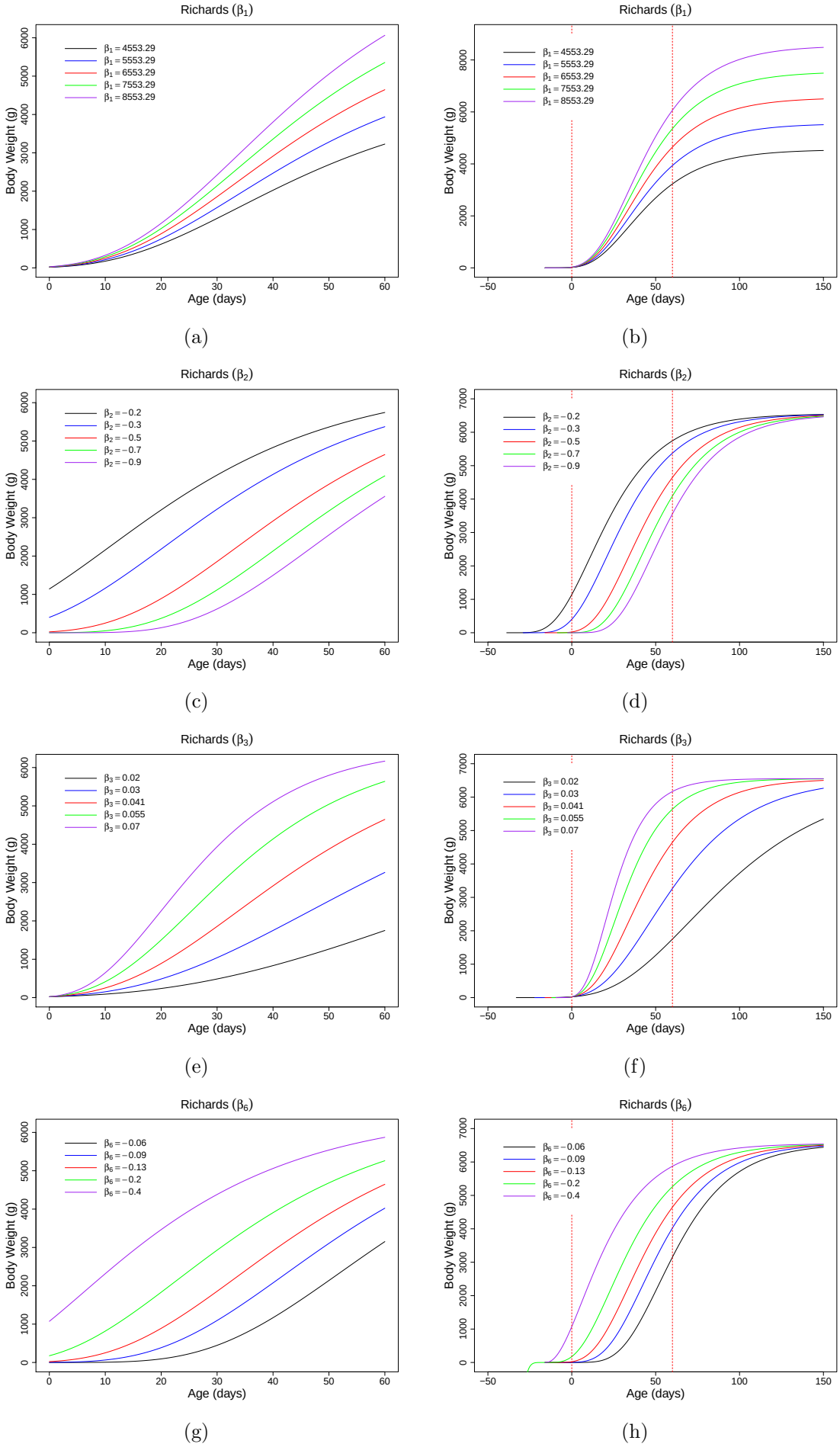


Figure 4.10 – Richards curves with different coefficient values

Appendix A4: Confidence intervals for coefficients

Confidence interval graphs for each coefficient of the model studied allow us to visualize the variation of broiler chickens weight profiles among individuals. This graph is constructed using the model adjusted by the `nlsList()` function. For the Gompertz model, for example, we have the following adjustment:

```
Coefficients:
Box   Beta1    Beta2   Beta3
25  4726.983 4.735796 0.05021185
33  4386.476 4.810472 0.05384951
2   4301.280 4.807963 0.05590498
36  4732.764 4.906873 0.05022150
6   4867.270 4.720258 0.04784039
3   4675.434 4.840197 0.05208639
24  4941.348 4.695509 0.04885686
23  5317.517 4.721149 0.04528741
18  5511.362 4.767503 0.04464600
14  5048.209 4.875836 0.05000717
29  5738.747 4.863685 0.04360113
17  5281.959 4.773968 0.04761909
9   5647.274 4.681191 0.04425823
8   5509.866 4.673800 0.04513114
10  5702.145 4.678758 0.04348872
38  5568.356 4.958440 0.04743821
31  5938.504 4.724005 0.04320770
32  5657.339 5.189211 0.04890238
```

```
Box   Beta1    Beta2   Beta3
37  6393.740 4.724523 0.04090304
35  6330.864 4.878009 0.04400203
30  5290.670 5.646084 0.05522608
28  5847.665 4.983016 0.04882548
13  6386.762 4.972140 0.04527376
16  5895.335 5.115887 0.04941160
4   5972.919 5.055132 0.04894494
27  6034.074 5.139547 0.04850581
11  6542.917 4.834760 0.04377050
22  6071.019 4.988011 0.04786292
15  6211.516 5.272180 0.04894834
5   6302.886 5.094306 0.04747635
34  6270.861 5.070001 0.04806836
19  7123.334 5.097430 0.04414809
7   6704.442 4.906021 0.04336287
39  7296.124 5.111868 0.04414061
12  6672.048 5.232264 0.04745008
26  7610.408 4.888877 0.04006993
```

In this adjustment, the 108 coefficients are used to represent the individual weight profiles. The adjusted by `nlsList` model is useful when we are interested in modeling the behavior of a particular fixed set of individuals. In this case, the interest is to estimate the average behavior of an individual in the population and the variability between and within individuals, which is precisely what mixed-effects models are designed to do. (PINHEIRO; BATES, 2000). Graphing the individual confidence intervals for the `nlsList` adjusted model coefficients provides a better idea of the variability between individuals. If the confidence intervals for each of the coefficients are not overlapping, it suggests a random effect for the coefficient. Confidence intervals for the coefficients of the Gompertz, four-parameter logistic, von Bertalanffy, and Richards models are shown in Figures 4.11, 4.12, 4.13, and 4.14. Note in the graphs that the confidence interval lengths for each coefficient are different, some individuals have a larger confidence interval than others. This is because the approximate standard errors used to produce confidence intervals in a nonlinear least squares fit depend on parameter estimates (SEBER; WILD, 2003).

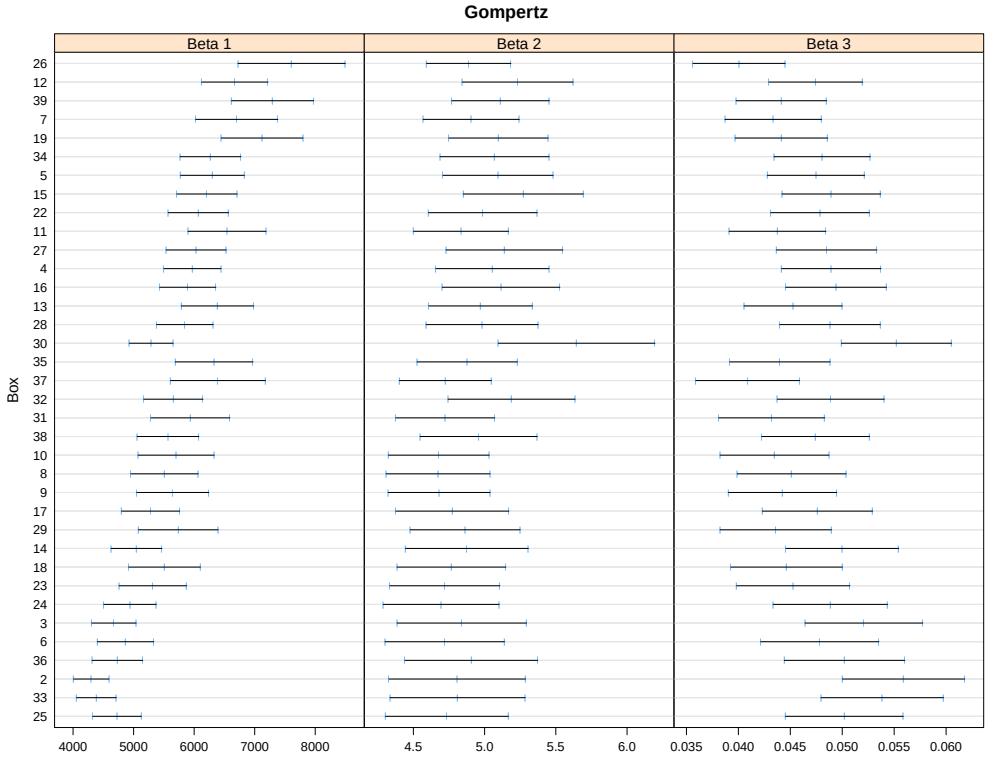


Figure 4.11 – Ninety-five percent confidence intervals on the Gompertz model coefficients for each box in the body weight data

Figure 4.12 – Ninety-five percent confidence intervals on the four-parameter logistic model coefficients for each box in the body weight data

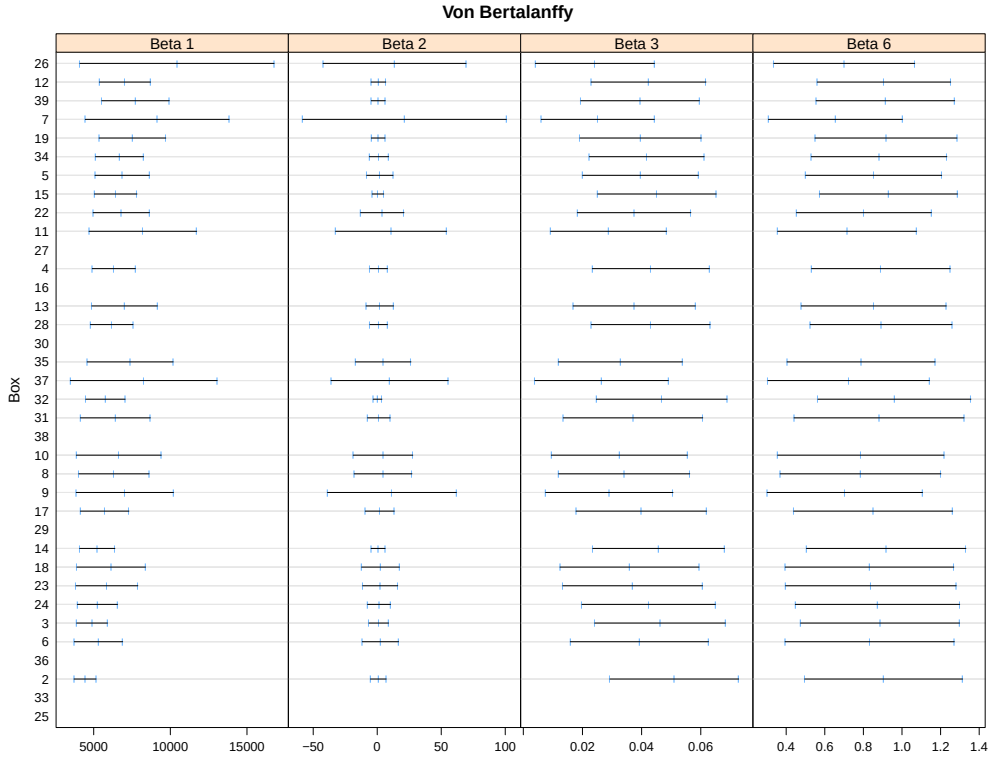


Figure 4.13 – Ninety-five percent confidence intervals on the von Bertalanffy model coefficients for each box in the body weight data

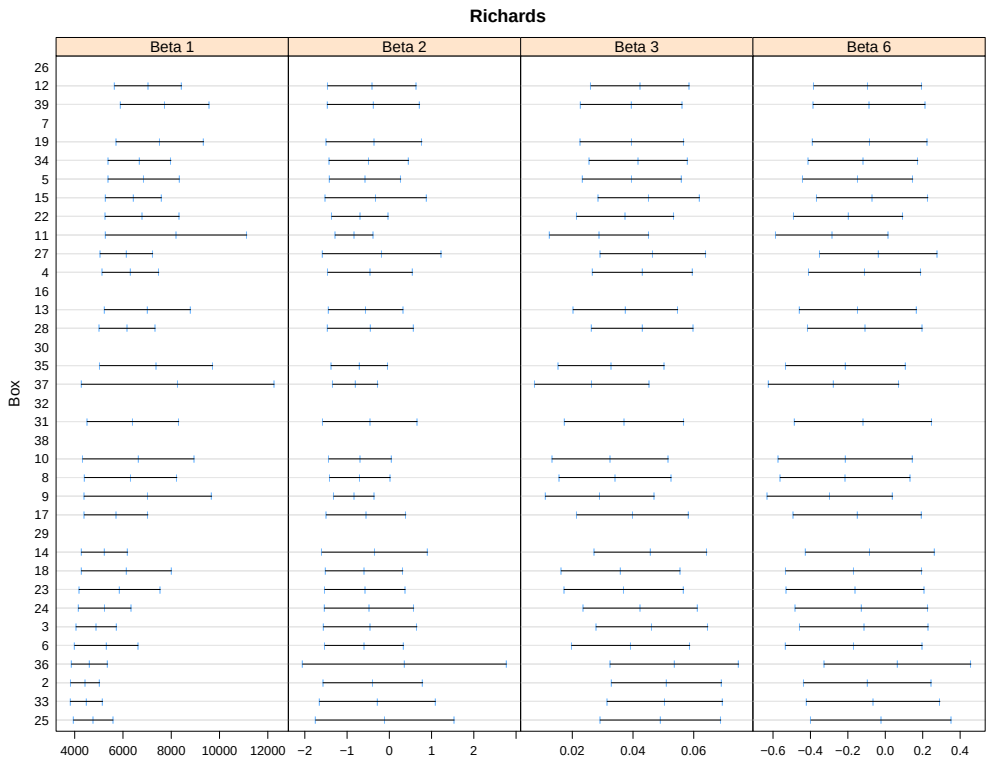


Figure 4.14 – Ninety-five percent confidence intervals on the Richards model coefficients for each box in the body weight data

Appendix A5: Code related to Chapter 3

```
#-------------------------------------------------------
# Dataset read
rm(list=ls())
data <- read.csv2("Dados_Desempenho.csv",head=T)
str(data)
data$Box <- as.factor(data$Box)
data$Block  <- as.factor(data$Block)
Box <- data$Box
Sex <- data$Sex
Nutrition <- data$Nutrition
Treatment  <- data$Treatment
Age <- data$Age
FC <- data$FC
BW <- data$BW
#-------------------------------------------------------
# Selection of Gompertz models with mixed effects
#-------------------------------------------------------
#Gompertz model
Gompertz <- function(Age,A,E,I){
A*exp(-E*exp(-I*Age))}
#A: Beta1, E: Beta2 and I: Beta3
#-------------------------------------------------------
#-------------------------------------------------------
# Charts to adjust initial values
require(nlstools)
plot(BW ~ Age, data = data, ylab = "Body weight (g)",
xlab = "Age (days)",xlim=c(0,60),ylim=c(0,5500))
curve(Gompertz(x,A=5000,E=6,I=0.06),add =TRUE,lwd=2)
#BW: Body weight
#-------------------------------------------------------
#-------------------------------------------------------
require(nlme)
data.BW <- groupedData(BW ~ Age|Box,labels=list(x="Age", y="Body Weight"),
data=data,units=list(y="(g)"))
# Model to estimate initial values
fit0 <- nlsList(BW ~ Gompertz(Age,A,E,I),start =list(A=5000,E=6,I=0.06),
data=data.BW)
```

```
ini <- fixef(fit0)
#-------------------------------------------------------
# Model with treatments, without random effects
#MG1: GF
MG1 <- gnls(BW ~ Gompertz(Age,A,E,I), params=list(A + E + I ~ Treatment),
start=c(ini[1],0,0,0,0,0,ini[2],0,0,0,0,0,ini[3],0,0,0,0,0),
control= gnlsControl(nlsTol=50, nlsMaxIter=20))
summary(MG1)
#fit1:G1
fit1 <- nlme(BW ~ Gompertz(Age,A,E,I), fixed=A + E + I ~ Treatment,
start=c(ini[1],0,0,0,0,0,ini[2],0,0,0,0,0,ini[3],0,0,0,0,0),
random=A~1, control=lmeControl(msMaxIter = 1000,maxIter = 500), data=data.BW)
anova(MG1,fit1)
#fit2:G2
fit2 <- update(fit1, random=A + E ~1)
anova(fit1,fit2)
#fit3:G3
fit3 <- update(fit2, random=E ~1)
anova(fit2,fit3)
#fit4:G4
fit4 <- update(fit2, random=A+E+I ~1)
anova(fit2,fit4)
#fit5:G5
fit5 <- update(fit4, random=A+I ~1)
anova(fit4,fit5)
#fit6:G6
fit6 <- update(fit5, random=E+I ~1)
anova(fit5,fit6)
#fit7:G7
fit7 <- update(fit5, random=I ~1)
anova(fit5,fit7)
#fit8:G8
fit8 <- update(fit5, random=pdIdent(A + I ~1))
anova(fit5,fit8)
#fit9:G9
fit9 <- update(fit5, random=pdDiag(A + I ~1))
anova(fit5,fit9)
#fit10:G10
fit10 <- update(fit5,weights=varIdent(form=~1|Sex))
```

```
anova(fit5,fit10)
#fit11:G11
fit11 <- update(fit5,weights=varIdent(form=~1|Age))
anova(fit10,fit11)
#fit12:G12
#fit12 <- update(fit5,weights=varIdent(form=~1|Sex*Age))
anova(fit11,fit12)
anova(fit12,test='Wald')

#-----------------------------------------------------------
#Four-parameter logistic model
Logistic4 <- function(Age,A,E,I,S){
S + (A-S)/(1+exp(I*(E-log(Age))))}
#A: Beta1, E: Beta3, I: Beta4 and S: Beta5
#-----------------------------------------------------------

#-----------------------------------------------------------
#von Bertalanffy model
VonBertalanffy <- function(Age,A,E,I,S){
(A^(1-S)-E*exp(-I*Age))^(1/(1-S))}
#A: Beta1, E: Beta2, I: Beta3 and S: Beta6
#-----------------------------------------------------------

#-----------------------------------------------------------
#Richards model
Richard <- function(Age,A,E,I,S){
A/(1+E*exp(-I*Age))^(1/S)}
#A: Beta1, E: Beta2, I: Beta3 and S: Beta6
#-----------------------------------------------------------
```

Appendix A6: ANOVA

We can evaluate the significance of the treatments for each of the coefficients of the studied models using the `anova()` function. The following are the ANOVA outputs for the selected growth models (G12, L12, V11, and R9). Note that in the Gompertz model, the treatment factor was significant for all coefficients, that is, we have different estimates of the specific coefficient for each of the treatment factor levels. In the four-parameter logistic and von Bertalanffy models, the treatment factor was not significant for the coefficients β_5 and β_6, respectively. Thus, the treatment factor of the β_5 coefficient in the four-parameter logistic model and the β_6 coefficient in the von Bertalanffy model was removed. Then, the `anova` function was again used to evaluate the significance of the other coefficients. The ANOVA output for the Richards model indicated the non-significance of treatments for the β_6 coefficient. However, we decided to keep the treatment factor at this coefficient because the p-value was close to 0.05.

Mixed Gompertz growth model (G12)

```
ANOVA
                    numDF denDF  F-value  p-value
Beta1.(Intercept)     1   631   104050.8  <.0001
Beta1.Treatment       5   631   260.9     <.0001
Beta2.(Intercept)     1   631   795779.9  <.0001
Beta2.Treatment       5   631   114.8     <.0001
Beta3.(Intercept)     1   631   19659.3   <.0001
Beta3.Treatment       5   631   2.5       0.0283
```

Mixed four-parameter logistic growth model (L12)

ANOVA: Model with the treatment factor in the coefficient β_5.

```
ANOVA
                    numDF denDF  F-value    p-value
Beta1.(Intercept)     1   625    2332810.7  <.0001
Beta1.Treatment       5   625    20409.2    <.0001
Beta3.(Intercept)     1   625    1268884.5  <.0001
Beta3.Treatment       5   625    864.8      <.0001
Beta4.(Intercept)     1   625    120104.2   <.0001
Beta4.Treatment       5   625    185.4      <.0001
Beta5.(Intercept)     1   625    45574.0    <.0001
Beta5.Treatment       5   625    0.1        0.9839
```

ANOVA: Model without the treatment factor in the coefficient β_5.

	numDF	denDF	F-value	p-value
Beta1.(Intercept)	1	630	334910.5	<.0001
Beta1.Treatment	5	630	6017.5	<.0001
Beta3.(Intercept)	1	630	1062162.2	<.0001
Beta3.Treatment	5	630	511.1	<.0001
Beta4.(Intercept)	1	630	101000.6	<.0001
Beta4.Treatment	5	630	16.1	<.0001
Beta5	1	630	37856.3	<.0001

Mixed Von Bertalanffy growth model (V11)

ANOVA: Model with the treatment factor in the coefficient β_6.

	numDF	denDF	F-value	p-value
Beta1.(Intercept)	1	625	114618749	<.0001
Beta1.Treatment	5	625	2414603	<.0001
Beta2.(Intercept)	1	625	289076448	<.0001
Beta2.Treatment	5	625	2331017	<.0001
Beta3.(Intercept)	1	625	31850	<.0001
Beta3.Treatment	5	625	69	<.0001
Beta6.(Intercept)	1	625	8555	<.0001
Beta6.Treatment	5	625	2	0.1765

ANOVA: Model without the treatment factor in the coefficient β_6.

	numDF	denDF	F-value	p-value
Beta1.(Intercept)	1	630	158351414	<.0001
Beta1.Treatment	5	630	19769	<.0001
Beta2.(Intercept)	1	630	1114946356	<.0001
Beta2.Treatment	5	630	223054	<.0001
Beta3.(Intercept)	1	630	5004	<.0001
Beta3.Treatment	5	630	14	<.0001
Beta6	1	630	14703	<.0001

Mixed Richard growth model (R9)

ANOVA

	numDF	denDF	F-value	p-value
Beta1.(Intercept)	1	625	387738.1	<.0001
Beta1.Treatment	5	625	923.8	<.0001
Beta2.(Intercept)	1	625	118417.6	<.0001
Beta2.Treatment	5	625	3612.6	<.0001
Beta3.(Intercept)	1	625	85654.4	<.0001
Beta3.Treatment	5	625	14.3	<.0001
Beta6.(Intercept)	1	625	224.4	<.0001
Beta6.Treatment	5	625	2.1	0.059

Appendix A7: Adjusted individual curves for growth models

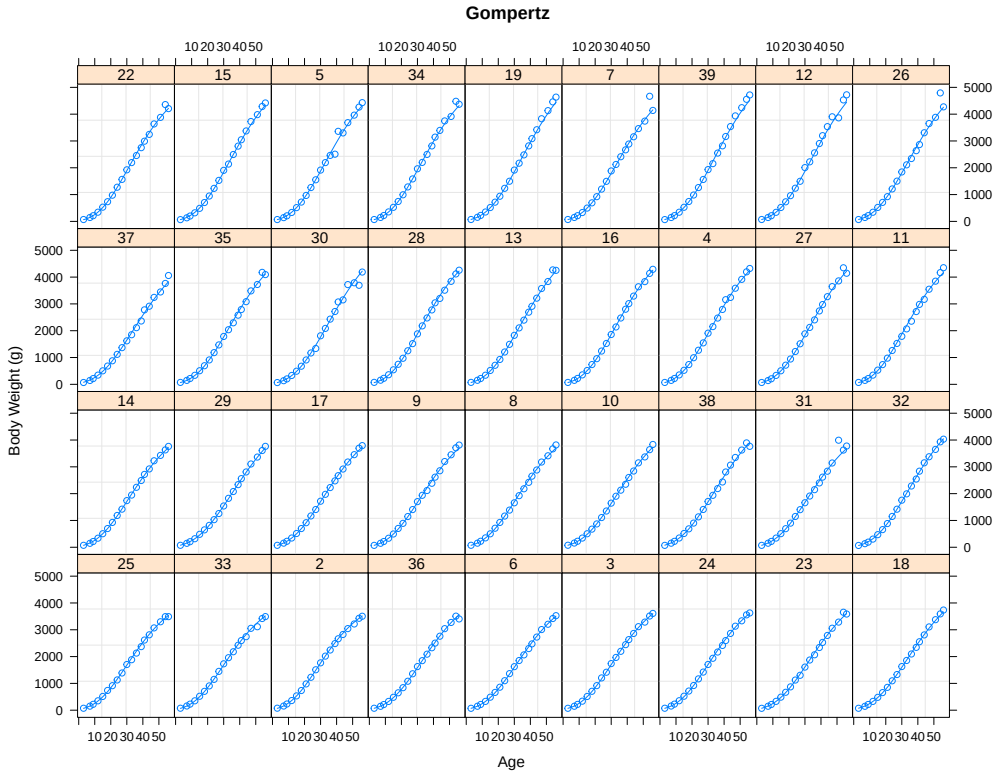


Figure 4.15 – Individual adjusted curves by Gompertz model

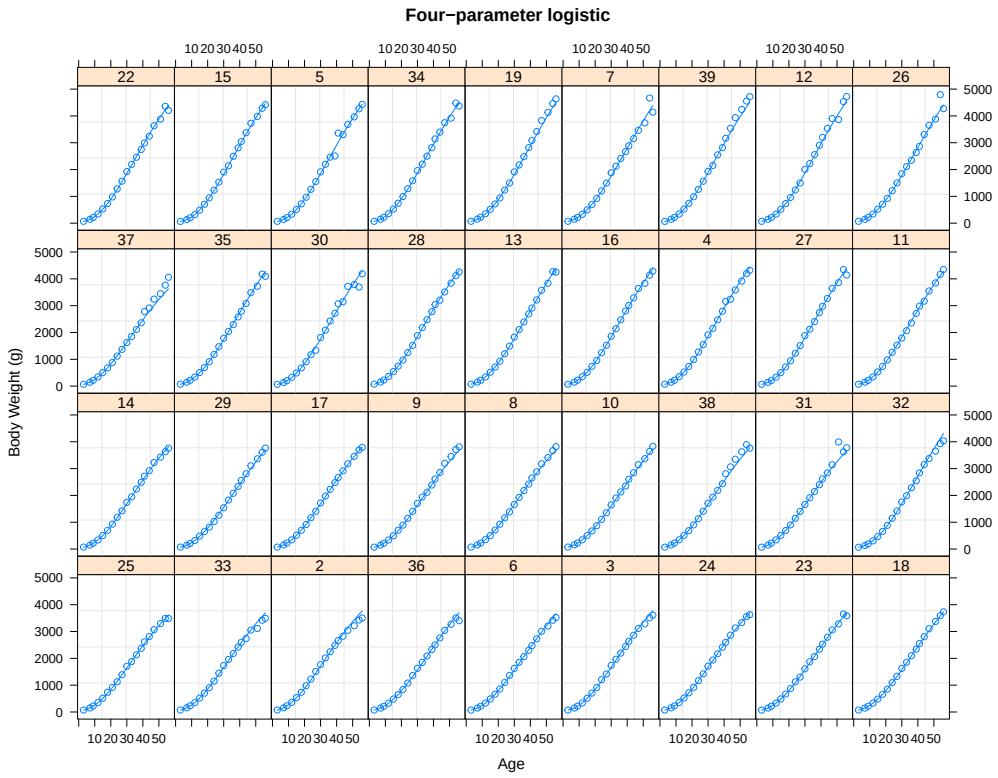


Figure 4.16 – Individual adjusted curves by four-parameter logistic model

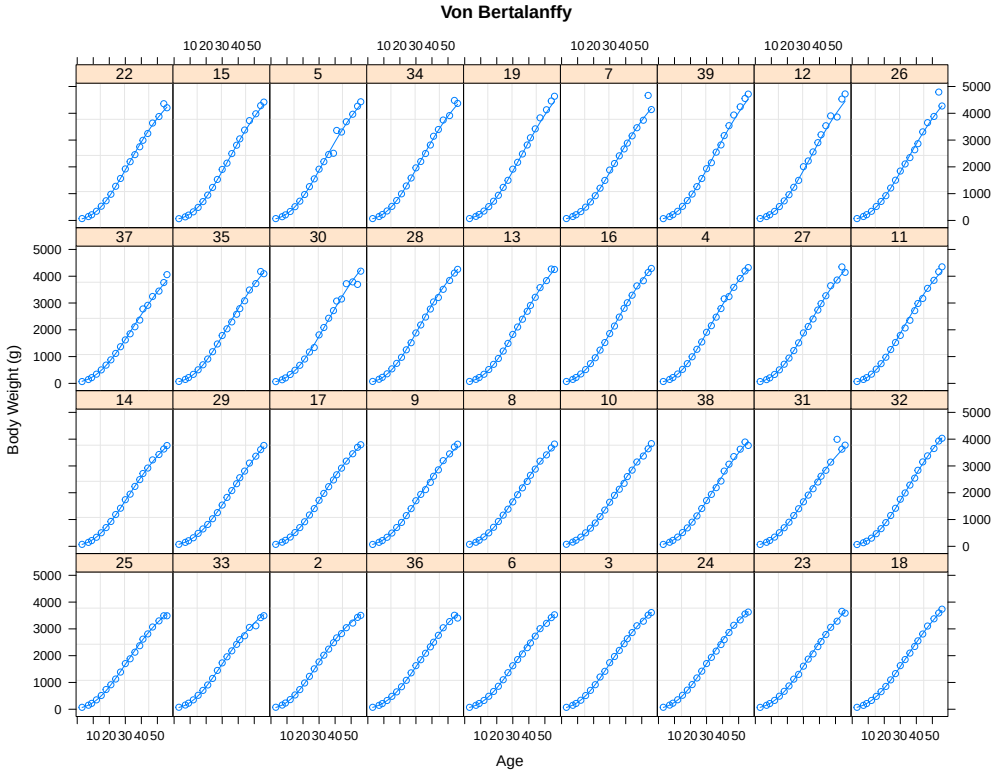


Figure 4.17 – Individual adjusted curves by Von Bertalanffy model

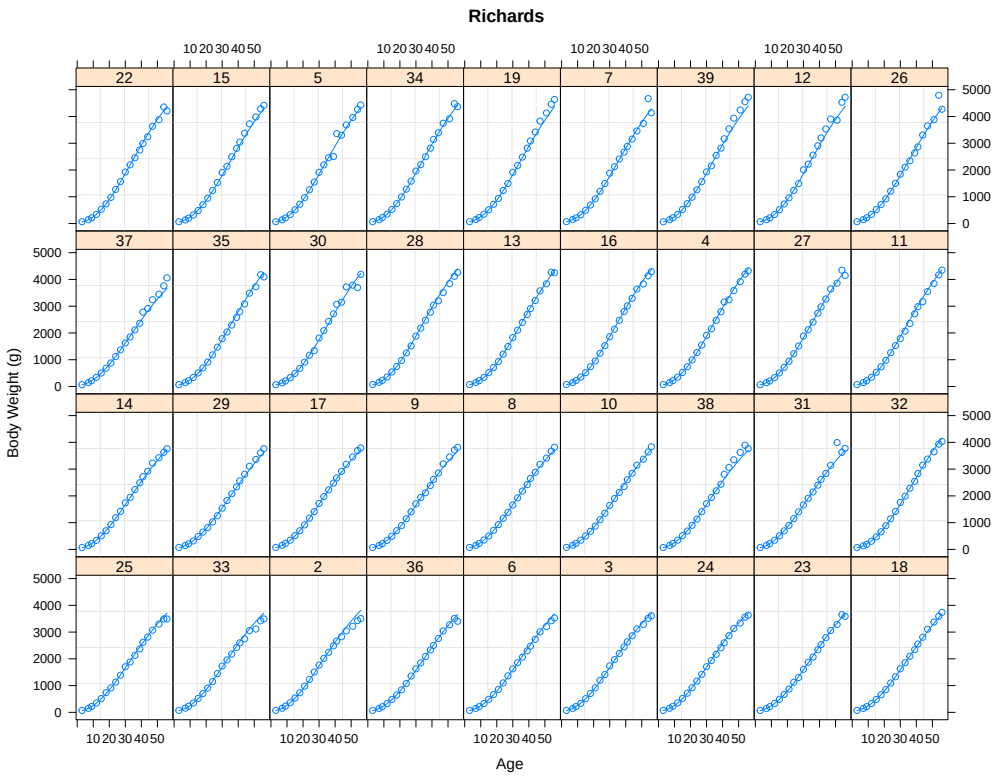


Figure 4.18 – Individual adjusted curves by Richard model

Appendix A8: Three-parameter logistic model

One of the parameterizations used for the three-parameter logistic growth model is given by (OLIVER, 1964):

$$y = \phi_1 / \left[1 + \phi_2 \exp\left(-\phi_3 t\right)\right]$$

where y is the dependent variable or response variable, t is the independent variable, that is, the age of the broiler chickens, ϕ_1 is the asymptote or maximum response of growth, ϕ_2 is a scale parameter related to initial response, and ϕ_3 is the intrinsic growth rate.

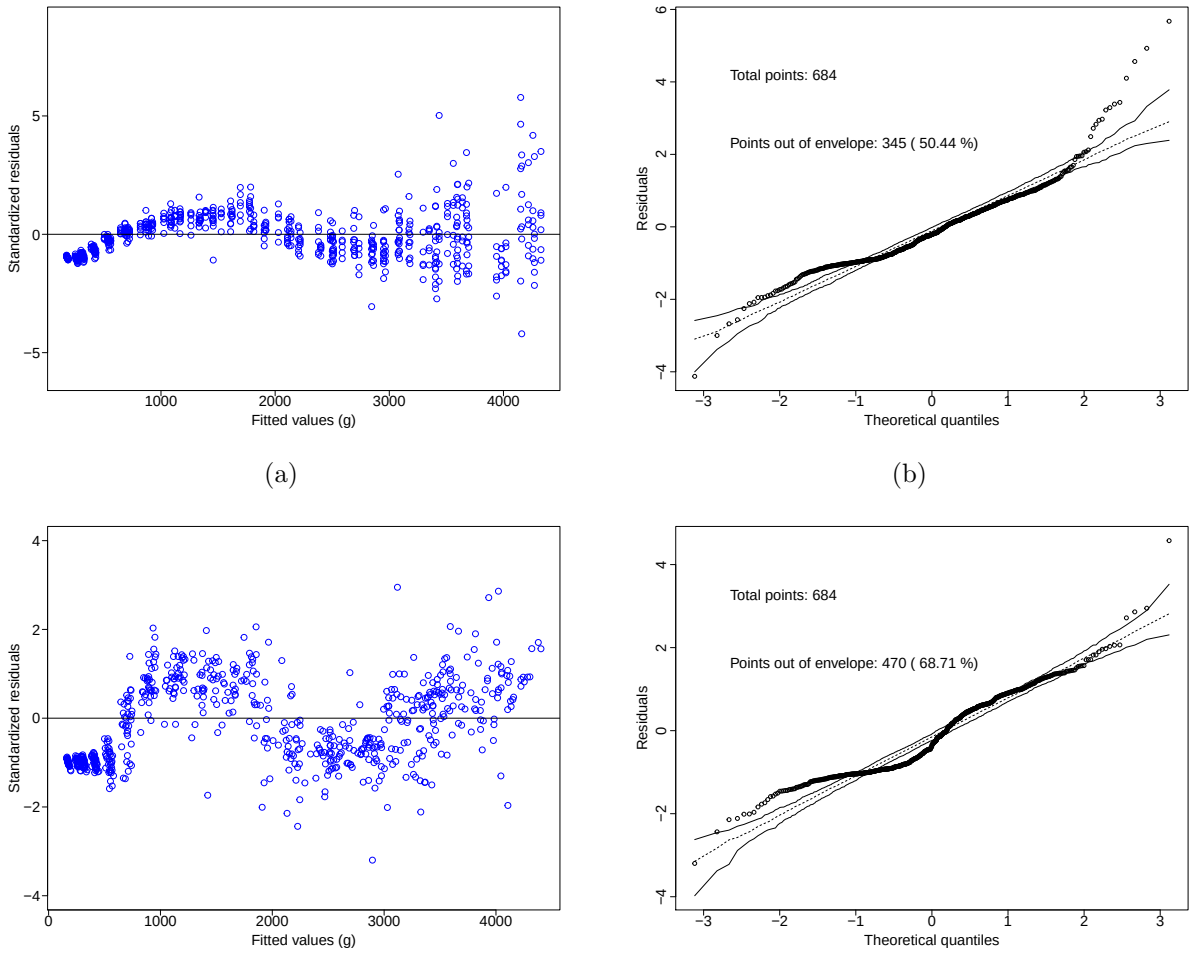
Table 4.13 presents the results of the selection for the three-parameter logistic model. Considering the information criteria (AICc and BIC) and the likelihood ratio test, the selected model was the L11.

Table 4.13 – Selection of Logistic models with mixed effects

Mod.	RE	$\boldsymbol{G}$	$\boldsymbol{R}$	npar	$-2logL$	AICc	BIC	Comp.	p-value
LF	-	-	VC	19	8389.62	8428.76	8513.65	-	-
L1	ϕ_1	-	VC	20	8253.82	8295.09	8384.38	LF *vs* L1	$< .0001$
L2	ϕ_1, ϕ_2	UN	VC	22	8217.04	8262.58	8360.66	L1 *vs* L2	$< .0001$
L3	ϕ_2	-	VC	20	8359.36	8400.64	8489.93	L2 *vs* L3	$< .0001$
L4	ϕ_1, ϕ_2, ϕ_3	UN	VC	25	8217.06	8269.04	8380.26	L2 *vs* L4	0.9995
L5	ϕ_1, ϕ_3	UN	VC	22	8227.66	8273.19	8371.27	L2 *vs* L5	-
L6	ϕ_2, ϕ_3	UN	VC	22	8278.94	8324.47	8422.55	L2 *vs* L6	-
L7	ϕ_3	-	VC	20	8318.98	8360.25	8449.55	L2 *vs* L7	$< .0001$
L8	ϕ_1,ϕ_2	VC	VC	20	8359.30	8400.57	8489.86	L2 *vs* L8	$< .0001$
L9	ϕ_1,ϕ_2	VCH	VC	21	8253.82	8297.22	8390.91	L2 *vs* L9	$< .0001$
L10	ϕ_1,ϕ_2	UN	VCH(Sex)	23	8192.28	8239.96	8342.43	L2 *vs* L10	$< .0001$
L11	ϕ_1,ϕ_2	UN	VCH(Age)	40	7856.58	7941.67	8117.69	L10 *vs* L11	$< .0001$

RE: Random effect; $\boldsymbol{G}$: Variance-covariance matrix for the random effects; $\boldsymbol{R}$: Variance-covariance matrix intra-individual; npar: number of model parameters; $-2logL$: -2(logarithm of the likelihood); UN: Unstructured; VC: Variance Components; VCH(Age): Heterogeneous variance components for age; VCH(Sex): Heterogeneous variance components for sex; VCH(Age∗Sex): Heterogeneous variance components for interaction age and sex.

Figure (4.19) shows the residual graphs for the fixed model LF (items a and b) and the selected model L11 (items c and d). Note that the models did not fit properly to broiler chickens weight data.



(a) (b)

(c) (d)

Figure 4.19 – Graph of standardized residuals versus adjusted values and half-normal simulated envelope graphs for the models three-parameter logistic with fixed effects (LF), items (a) and (b), and three-parameter logistic with random effects (L11) items (c) and (d)

Appendix B: Additional information about Chapter 4

Appendix B1: Code related to Chapter 4

```
#-------------------------------------------------------
# Dataset read
rm(list=ls())
data <- read.csv2("Dados_Desempenho.csv",head=T)
str(data)
Box <- data$Box
Sex <- data$Sex
Nutrition <- data$Nutrition
Treatment  <- data$Treatment
Age <- data$Age
FC <- data$FC
BW <- data$BW
#-------------------------------------------------------
#Organizing the bivariate data
BW.d <- data.frame(Box = data$Box,
Sex = data$Sex,
Nutrition = data$Nutrition,
Treatment = data$Treatment,
resp = data$BW,
Age = data$Age,
d_BW = 1,
d_FC = 0,
var = 'BW')

FC.d <- data.frame(Box = data$Box,
Sex = data$Sex,
Nutrition = data$Nutrition,
Treatment = data$Treatment,
resp = data$FC,
Age = data$Age,
d_BW = 0,
d_FC = 1,
var = 'FC')

multivariate <- rbind(BW.d,FC.d)
#-------------------------------------------------------
```

```
#Bivariate Gompertz model fit
options(contrasts = c("contr.treatment","contr.poly"))
require(nlme)
lmeCtlList <- lmeControl(maxIter = 500, msMaxIter = 200,
tolerance = 1e-4, niter = 100,
msTol = 1e-5, nlmStepMax = 500,
msVerbose = FALSE,
returnObject = TRUE)
#-----------------------------------------------------------
data.multi <- groupedData(resp ~ Age| Box, data=multivariate,
labels=list(x="Age", y="BW-FC"),units=list(y="(g)"))
#-----------------------------------------------------------
# Modelo Gompertz
Gompertz <- function(Age,A,E,I){
A*exp(-E*exp(-I*Age))}
#-----------------------------------------------------------
#Model to estimate initial values
fit0 <- nlsList(resp ~ Gompertz(Age,A,E,I)|d_BW,
start =list(A=5.748048e+03,E=4.913225,I=4.694446e-02),level=2, data=multivariate)
ini <- fixef(fit0)
#-----------------------------------------------------------
#fit1:G1
fit1 <- nlme(resp ~ d_BW*(B11*exp(-B21*exp(-B31*Age)))+
d_FC*(B12*exp(-B22*exp(-B32*Age))),
data  =  multivariate,
fixed = B11+B21+B31+B12+B22+B32~Treatment,
random = B11+B31+B12+B22+B32~1,
group = ~ Box,
start = c(5500,0,0,0,0,0,
5,0,0,0,0,0,
0.04,0,0,0,0,0,
13500,0,0,0,0,0,
6,0,0,0,0,0,
0.04,0,0,0,0,0),
weights = varComb(varIdent(form =
~1|var),varIdent(form =
~1|Sex)),
control = lmeCtlList
)
```

```
fit2: G2
fit2 <- nlme(resp ~ d_BW*(B11*exp(-B21*exp(-B31*Age)))+
d_FC*(B12*exp(-B22*exp(-B32*Age))),
data  =  multivariate,
fixed = B11+B21+B31+B12+B22+B32~Treatment,
random = B11+B31+B12+B22+B32~1,
group = ~ Box,
start = c(5500,0,0,0,0,0,
5,0,0,0,0,0,
0.04,0,0,0,0,0,
13500,0,0,0,0,0,
6,0,0,0,0,0,
0.04,0,0,0,0,0),
weights = varComb(varIdent(form =
~1|var),varIdent(form =
~1|Age)),
control = lmeCtlList
)
fit3: G3
fit3 <- nlme(resp ~ d_BW*(B11*exp(-B21*exp(-B31*Age)))+
d_FC*(B12*exp(-B22*exp(-B32*Age))),
data  =  multivariate,
fixed = B11+B21+B31+B12+B22+B32~Treatment,
random = pdDiag(B11+B31+B12+B22+B32~1),
group = ~ Box,
start = c(5500,0,0,0,0,0,
5,0,0,0,0,0,
0.04,0,0,0,0,0,
13500,0,0,0,0,0,
6,0,0,0,0,0,
0.04,0,0,0,0,0),
weights = varComb(varIdent(form =
~1|var),varIdent(form =
~1|Sex*Age)),
control = lmeCtlList
)
```

Appendix B2: ANOVA

We can evaluate the significance of the treatments for each of the coefficients of the studied models using the `anova()` function. Note that in the bivariate Gompertz mixed model, the treatment factor was significant for all coefficients, that is, we have different estimates of the specific coefficient for each of the treatment factor levels. In the bivariate four-parameter logistic mixed model, the treatment factor was not significant for the coefficient β_{4,Y_2}. Thus, the treatment factor of the β_{4,Y_2} coefficient in the bivariate four-parameter logistic mixed model was removed. Then, the `anova` function was again used to evaluate the significance of the other coefficients.

Bivariate Gompertz mixed model (G3)

```
ANOVA
numDF denDF    F-value  p-value
B11.(Intercept)     1   1297     9376.7   <.0001
B11.Treatment       5   1297     2398.6   <.0001
B21.(Intercept)     1   1297  1820317.2   <.0001
B21.Treatment       5   1297       34.4   <.0001
B31.(Intercept)     1   1297   114613.3   <.0001
B31.Treatment       5   1297       19.6   <.0001
B12.(Intercept)     1   1297     9426.8   <.0001
B12.Treatment       5   1297     2312.5   <.0001
B22.(Intercept)     1   1297   538667.4   <.0001
B22.Treatment       5   1297      352.1   <.0001
B32.(Intercept)     1   1297    47417.6   <.0001
B32.Treatment       5   1297        8.1   <.0001
```

Mixed four-parameter logistic growth model (L3.6)

ANOVA: Model with the treatment factor in the coefficient β_{4,Y_2}.

```
ANOVA
numDF denDF F-value p-value
B11.(Intercept)     1  1285  949269  <.0001
B11.Treatment       5  1285  258780  <.0001
B21.(Intercept)     1  1285 3757925  <.0001
B21.Treatment       5  1285    2509  <.0001
B31.(Intercept)     1  1285   91668  <.0001
B31.Treatment       5  1285     104  <.0001
B41.(Intercept)     1  1285   35242  <.0001
B41.Treatment       5  1285      10  <.0001
B12.(Intercept)     1  1285 3425043  <.0001
B12.Treatment       5  1285   27261  <.0001
B22.(Intercept)     1  1285 1865836  <.0001
B22.Treatment       5  1285    5820  <.0001
B32.(Intercept)     1  1285   53987  <.0001
B32.Treatment       5  1285      37  <.0001
B42.(Intercept)     1  1285    8893  <.0001
B42.Treatment       5  1285       1  0.3647
```

ANOVA: Model without the treatment factor in the coefficient β_{4,Y_2}.

```
B11.(Intercept)     1  1290 2306840  <.0001
B11.Treatment       5  1290  120270  <.0001
B21.(Intercept)     1  1290 3696068  <.0001
B21.Treatment       5  1290    1343  <.0001
B31.(Intercept)     1  1290   76772  <.0001
B31.Treatment       5  1290      93  <.0001
B41.(Intercept)     1  1290   29820  <.0001
B41.Treatment       5  1290       4   0.002
B12.(Intercept)     1  1290 2564712  <.0001
B12.Treatment       5  1290    3742  <.0001
B22.(Intercept)     1  1290  743236  <.0001
B22.Treatment       5  1290     318  <.0001
B32.(Intercept)     1  1290   34504  <.0001
B32.Treatment       5  1290       7  <.0001
B42                 1  1290   11940  <.0001
```