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PROPOSAL FOR A NEW NON-LINEAR MODEL TO DESCRIBE GROWTH CURVES

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Abstract
This study was developed with longitudinal data measurements of Norfolk rabbits from birth to 119 days of age to estimate the average growth curve, with the primary objective of proposing a non-linear model. It also selected the most appropriate sigmoidal model to describe the growth of Norfolk rabbits. The adjustments provided by the logistic, von Bertalanffy, Gompertz, Brody, Richards, and proposed models were compared. The parameters were estimated using the "nls" function of the "stats" package in R software, the least-squares method, and the Gauss-Newton convergence algorithm. The goodness-of-fit comparison was based on the following criteria: adjusted coefficient of determination ($R^2_{aj.}$), mean square error (MSE), mean absolute deviation (MAD), Akaike information criterion (AIC), and Bayesian information criterion (BIC). Cluster analysis helped select and classify the non-linear growth models, considering the other goodness-of-fit criteria results. The proposed non-linear, von Bertalanffy, Gompertz, and Richards models described the growth curve of Norfolk rabbits satisfactorily, providing parameters with practical interpretations. The goodness-of-fit criteria showed that the proposed and von Bertalanffy models best represented the growth of rabbits.

Keywords: Animal growth. Biological parameters. Cluster analysis. Growth curves. Longitudinal data.

1. Introduction

Rabbit farming is not a significant sector in Brazilian agriculture (Silva et al. 2020). However, this zootechnics branch is prolific because it allows producer profitability throughout the year. However, the lack of Brazilian producers' knowledge in handling species and meat quality and the high cost of rations in the market impairs rabbit farming acceptance (Klinger and Toledo 2018).

Research on growth curves has helped define selection criteria regarding early maturation and weight gain speed. It may also help determine more efficient production systems for each region and breed regarding food programs, animal management, and crossbreeding (Souza et al. 2010; Silva et al. 2011). Thus, understanding animal growth over time is crucial because it directly influences the quality/quantity of the produced meat (Carneiro et al. 2014).

In this sense, non-linear regression models most adequately describe the growth of several animal species because their parameters have biological interpretations (Veloso et al. 2016). Chalh and Gazzah (2014) stated that the logistic (Nelder 1961), von Bertalanffy (Von Bertalanffy 1957), Gompertz (Laird

1965), Brody (Brody 1945), and Richards (Richards 1959) models are traditionally the five most used in animal development studies.

Only a few researchers investigate rabbit growth outside non-linear models (Ferreira et al. 2019; Obioma et al. 2020; de Sousa et al. 2022). The model choice does not rely only on the assessor's findings but also on the knowledge of the studied object (Puiatti et al. 2013). Wang, Tang, and Tan (2011) emphasized the need for new models to provide more relevant results. Santana et al. (2016) and Santos et al. (2018b) also understand that new models are needed, given the dynamics in which regression models have been used in biological research in general and specific situations.

The present study proposed a new non-linear model and compared it to logistic, Gompertz, von Bertalanffy, Brody, and Richards mathematical functions using statistical goodness-of-fit criteria and cluster analysis to classify and indicate the model that best describes the growth of Norfolk rabbits.

2. Material and Methods

Used data

The study used the most proper mass of data to test other models, generating a benchmark, and a Norfolk rabbit bodyweight increase database extracted from Curi et al. (1985). The authors applied the non-linear Gompertz and logistic models to data from Norfolk, New Zealand, White, and California rabbit breeds up to 119 days old (17th week), with weekly mean performance values (Curi et al. 1985).

Proposed model

Two promising methods have been recently proposed to generalize (combine) well-established growth models in the literature, producing (generating) new potentially viable models. These methods were designed separately from a generating function that combines existing non-linear models (Santos et al. 2019) and a general differential equation (Santos et al. 2018b). The authors of the latter reference presented models (Table 1) representing sub-cases of the method that produces growth/decrease models from differential equations. Thus, the model proposed in this study followed such generating method using the equation:

$$\frac{dW(t)}{dt} = aW^{\theta}(t)f(t) - bW^{\lambda}(t)g(t). \tag{1}$$

Where t is time, $W(t)$ is body weight, θ and λ are real numbers, a and b are non-negative real numbers, and $a + b > 0$ and $f(t)$ and $g(t)$ are non-negative functions. Thus, $\theta = 1$, $\lambda = 1$, $f(t) = e^{-k_1 t}$, and $g(t) = e^{-k_2 t}$ generated the following equation:

$$\frac{dW(t)}{dt} = a\,W(t)\,\mathrm{e}^{-k_1 t} - b\,W(t)\,\mathrm{e}^{-k_2 t} \tag{2}$$

Eq. (2) solving and algebraic development produced:

$$W(t) = \exp(\delta)\exp\left(\frac{a}{-k_1}\,\mathrm{e}^{-k_1 t} - \frac{b}{-k_2}\,\mathrm{e}^{-k_2 t}\right), \qquad (\delta \text{ constant}) \tag{3}$$

If $A = \exp(\delta)$, $B = \frac{a}{-k_1}$, and $\frac{b}{-k_2} = 1$, Eq. (3) becomes:

$$W(t) = A\mathrm{e}^{B\mathrm{e}^{-k_1 t} - \mathrm{e}^{-k_2 t}}. \tag{4}$$

Eq. (4) is the solution of Eq. (2), $W(t)$, constituting the proposed model. This model may represent an extension of the Gompertz growth function just by considering $k_1 = k_2$ in Eq. (4). The following section provides further details on the proposed model.

Used models

The logistic, Gompertz, von Bertalanffy, Brody, Richards, and proposed models were adjusted to estimate the weight increase of Norfolk rabbits according to time (days). The non-linear model equations are as follows:

Logistic $$W(t) = A(1 + \mathrm{B}e^{-kt})^{-1} + \varepsilon, \quad (9)$$
Gompertz $$W(t) = A\mathrm{e}^{-\mathrm{B}e^{(-\mathrm{k}t)}} + \varepsilon, \quad (10)$$
von Bertalanffy $$W(t) = A\left(1 - B\mathrm{e}^{-\mathrm{k}t}\right)^{3} + \varepsilon, \quad (11)$$
Brody $$W(t) = A(1 - \mathrm{B}e^{-kt}) + \varepsilon, \quad (12)$$
Richards $$W(t) = A\left(1 - B\mathrm{e}^{-\mathrm{k}t}\right)^{m} + \varepsilon, \quad (13)$$
Proposed $$W(t) = A\mathrm{e}^{B\mathrm{e}^{-k_1 t} - \mathrm{e}^{-k_2 t}} + \varepsilon. \quad (14)$$

In the models of Eq. (9)-(14), $W(t)$ is adult weight, t is time, and k, k_1, and k_2 are the growth rates, and the higher these rates, the shorter the time for animals to reach their maturity weight. A is the model's asymptote, indicating the stabilization value of the dependent variable when t tends to infinity. m is the curve's inflection point, B is a shape parameter without a direct practical interpretation but essentially keeping the sigmoidal shape of the model, e is the exponential function, and ε is the associated random error following a normal distribution with a mean of zero and constant variance.

Parameter estimation for non-linear models

Non-linear model parameters were obtained with the least-squares method using the iterative Gauss-Newton process with the “nls” function of the R software stats package (R Development Core Team 2021).

Residue analysis

Most growth curve adjustment studies usually neglect the residue analysis of models to verify assumption compliances (Santos et al. 2021), possibly using graphic methods or tests known as Durbin-Watson (DW), Shapiro-Wilk (SW), and Breusch-Pagan (BP).

The goodness-of-fit assessors

The precision of adjustments was considered according to the following criteria to determine the adequate model to describe the body weight increase of the studied Norfolk rabbits:

i) Adjusted coefficient of determination ($R^2_{aj.}$):

$$R^2_{aj.} = 1 - \left[\frac{(1 - R^2)(n - 1)}{n - p}\right];$$

ii) Mean square error (MSE):

$$MSE = \frac{\sum_{i=1}^{n}(y_i - \hat{y}_i)^2}{n - p};$$

iii) Mean absolute deviation (MAD):

$$MAD = \frac{\sum_{i=1}^{n}|y_i - \hat{y}_i|}{n};$$

iv) Akaike information criterion:

$$AIC = -2\log L + 2(p + 1);$$

v) Bayesian information criterion:

$$BIC = -2\log L + (p + 1)\log(n)$$

In items i–v, $R^2 = 1 - \frac{RSQ}{TSQ}$ is the coefficient of determination, RSQ is the residual sum of squares, and TSQ is the total sum of squares. y_i is the observed weight, and $\hat{y}_i$ is the estimated weight (prediction) of y_i. L is the maximized log-likelihood, n is the number of observations, and p is the parameter number of the model. The higher the value of the adjusted coefficient of determination, the better the model fits, while lower MSE, AIC, and BIC values indicate improved adjustments.

Cluster analysis and determination of the optimal number of groups

Right after obtaining the goodness-of-fit criteria for each model, the models were applied to the cluster analysis to compare and classify non-linear regression models used to describe the weight of Norfolk rabbits over time, considering the findings of goodness-of-fit assessors as variables. Subsequently, the cophenetic correlation coefficient (CCC) was calculated to indicate and verify the adjustment between the dissimilarity matrix and the dendrograms of each clustering method. Then, the adjusted Rand index (Hubert and Arabie 1985) determined the number of groups. Santos et al. (2018b) found the possibility of identifying the optimal cluster number.

3. Results

Table 1 presents the residue analysis results for the logistic, von Bertalanffy, Gompertz, Brody, Richards, and proposed models adjusted to the weight data of Norfolk rabbits. Normality, independence, and homoscedasticity assumptions for the von Bertalanffy, Richards, and proposed models were determined by tests SW with p-value= 0.618, 0.944, and 0.921; DW with p-value= 0.21840, 0.26170, and 0.26460; and BP with p-value=0.927, 0.746, and 0.706. The residual normality hypothesis of the Gompertz model was rejected in the SW test, with a p-value of 0.023. The logistic and Brody models did not achieve independence assumptions in the DW test, with p-values= 0.00001 and 0.00002, respectively.

Table 1. SW, DW, and BP statistical test results with respective p-values applied to residues of the logistic, Bertalanffy, Gompertz, Brody, Richards, and proposed models adjusted to the weight of Norfolk rabbits.

Models	SW	p-value	DW	p-value	BP	p-value
Logistic	0.914	0.102	0.500	0.00001	0.231	0.630
von Bertalanffy	0.960	0.618	1.771	0.21840	0.008	0.927
Gompertz	0.877	0.023	1.467	0.07123	0.103	0.747
Brody	0.955	0.522	0.576	0.00002	1.519	0.217
Richards	0.979	0.944	1.834	0.26170	0.104	0.746
Proposed	0.977	0.921	1.838	0.26460	0.142	0.706

Table 2 shows parameter estimates and the criteria used in the six evaluated models. Asymptotic weight and growth rate are the two most important parameters. The asymptotic weight represented by the parameter was higher in the von Bertalanffy model (4417), followed by Richards (4221), proposed (4172), Gompertz (3978), and logistic (3496) models.

The growth rate is another critical parameter, indicating the speed of animals approaching their weight in adulthood. Its analysis found the lowest estimates (0.02 and 0.02) in the Richards and von Bertalanffy models. Conversely, the logistic and Gompertz models had the highest values (0.05 and 0.03). The Brody model was an exception that underestimated this parameter (0.002). Regarding the biological interpretation of the growth rate, the proposed model indicated a maturity rate $k_1 = 0.002$ lower than k_2 = 0.06, meaning that animals grow faster in the second sigmoid. The more negligible growth in the first fast-growing sigmoid may be due to weaning in the 4th week (28th day). The second sigmoid had 13 weeks, which is more than the first sigmoid, and the weaned rabbits were separated from their mothers and housed in collective metal cages with commercial pelleted food with a protein level of around 15%, offered in automatic feeders.

The models reached R^2_{aj} values higher than 99%. The R^2_{aj} analysis showed that the proposed, Richards, von Bertalanffy, and Gompertz models presented optimal values for this selection criterion. The assessment criteria for the goodness-of-fit, MSE, and MAD indicated the proposed model as the most appropriate for describing the bodyweight growth curve of Norfolk rabbits, followed by the Richards, von Bertalanffy, Gompertz, logistic, and Brody models. Regarding AIC and BIC, the von Bertalanffy model presented the lowest values, followed by the proposed, Richards, Gompertz, logistic, and Brody models.

Table 2. Estimates of model parameters and selection criteria.

	Parameters					Criteria				
Models	A	B	k_1	k_2	m	$R^2_{aj.}$	MSE	MAD	AIC	BIC
Logistic	3496	16.63	0.050			99.52	7669.07	69.06	216.80	220.37
Bertalanffy	4417	0.790	0.020			99.91	1391.18	27.78	186.10	189.64
Gompertz	3978	3.790	0.030			99.90	1587.30	29.02	188.46	192.02
Brody	19080	1.010	0.002			99.29	11409.16	76.78	223.95	227.52
Richards	4221	0.590	0.020		4.70	99.92	1356.81	26.55	186.39	190.84
Proposed	4172	-3.20	0.020	0.06		99.92	1342.07	26.14	186.19	190.64

The CCC oscillated between 0.7116736 and 0.9943304 (Table 3), indicating Average Linkage as a more consistent method based on the Canberra distance. Adjusted Rand statistics showed the optimal number of three clusters (Figure 1). The first cluster was formed by Gompertz, von Bertalanffy, Richards, and proposed models, the second by the logistic model, and the third by the Brody model. Figure 1 shows that the first cluster is the best because it presented overall good values for all the criteria considered simultaneously.

Table 3. CCC between the Euclidean, Manhattan, Minkowski, Canberra, Maximum, and Mahalanobis distance matrices and the cophenetic matrix of the Average Linkage, Single Linkage, Complete Linkage, Ward, and Centroid hierarchical clustering methods, based on five criteria.

	Hierarchical clustering methods				
Distances	Average linkage	Single linkage	Complete linkage	Ward	Centroid
Euclidian	0.9417	0.9386	0.9407	0.9331	0.9412
Manhattan	0.9425	0.9395	0.9415	0.9341	0.9420
Minkowski	0.9417	0.9386	0.9407	0.9331	0.9412
Canberra	0.9943	0.9941	0.9942	0.9927	0.9942
Maximum	0.9417	0.9386	0.9407	0.9331	0.9411
Mahalanobis	0.7961	0.7613	0.7116	0.7553	0.7917

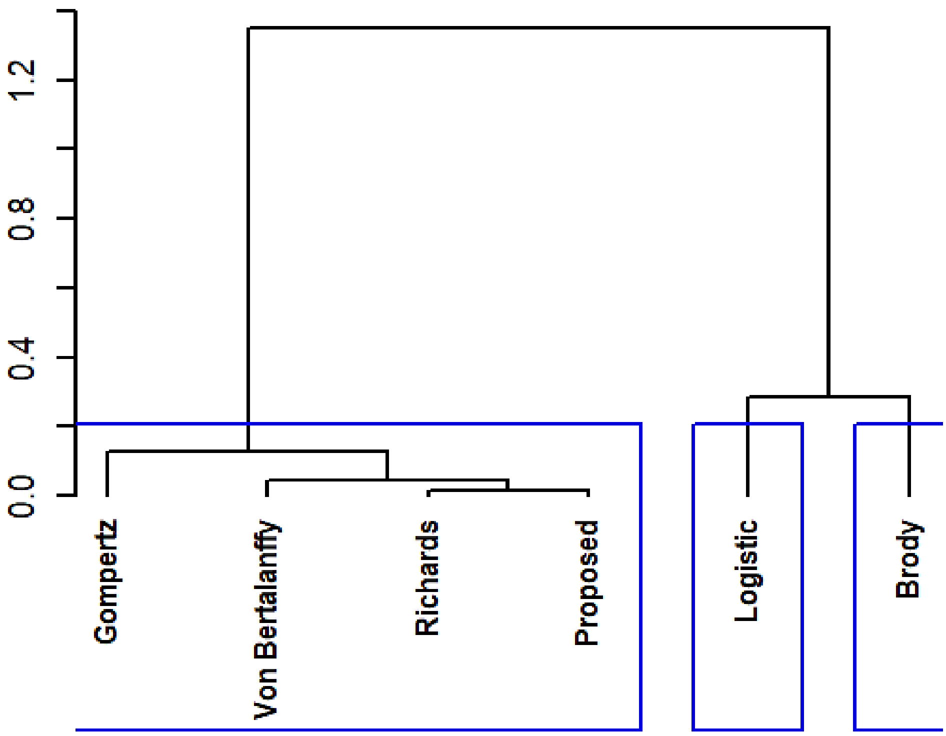

Figure 1. Dendrogram obtained by the clustering method based on quality assessors (R^2_{aj}, MSE, MAD, AIC, and BIC) for the logistic, von Bertalanffy, Gompertz, Brody, Richards, and proposed models.

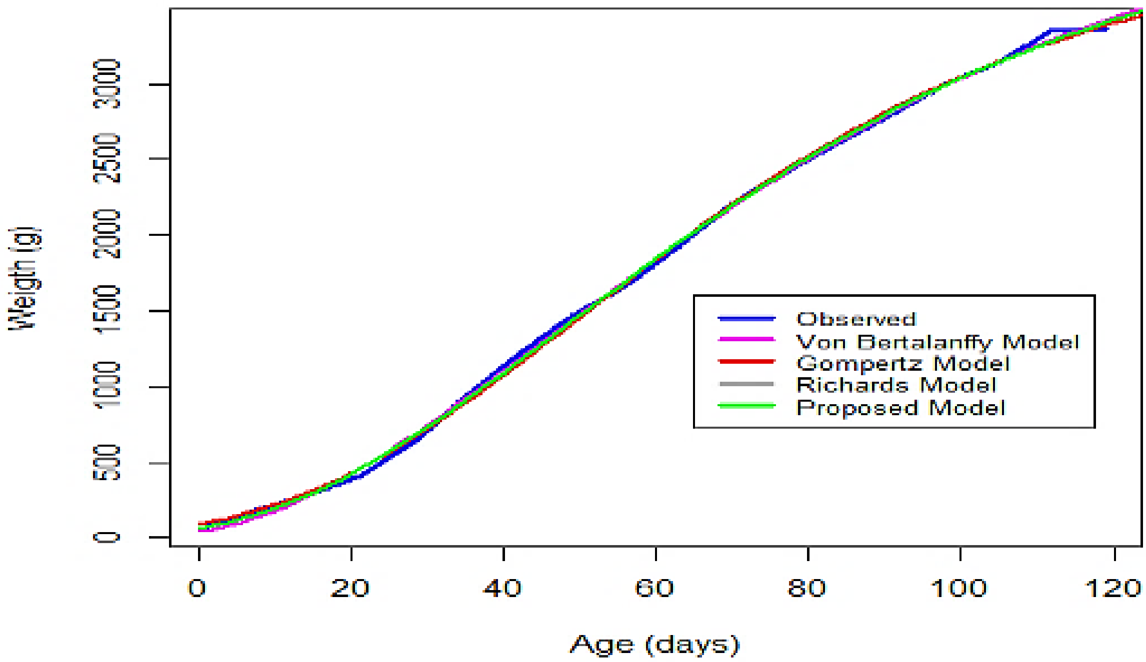

Figure 2. Estimated and observed growth curves by the proposed, von Bertalanffy, Gompertz, and Richards models.

4. Discussion

The Brody model overestimated the weight of rabbits. Santos et al. (2018a) studied the growth curve of New Zealand rabbits, reporting the overestimation of their weight up to adulthood in the Brody model.

Blas (1989) stated that rabbits have a high growth rate in the first week after weaning when animals gain significantly more weight. McNitt and Lukefahr (1993) reported that New Zealand White rabbits are little affected in extreme environmental conditions, with more significant post-weaning weight gain than commercial hybrid breeds. However, the same authors observed, during the summer, lower weight gain among New Zealand rabbits. The estimates of A in the von Bertalanffy and logistic models were similar to the growth curve analysis of Norfolk rabbits (Costa et al. 2020). Nevertheless, these estimates presented lower values in other studies for the Gompertz and logistic models (Curi et al. 1985).

Santos et al. (2020) affirmed that, considering that R^2_{aj} does not assess the biological coherence of the data, not applying it as the sole assessment criterion is essential. Oliveira et al. (2000) suggest using other assessors because of the usually low differences between the R^2_{aj} in different used models.

Teleken et al. (2017) compared logistic, von Bertalanffy, Gompertz, Brody, and Richards models in different animals. They indicated the Gompertz (von Bertalanffy) as the most appropriate model for the Californian rabbit data (Norfolk and New Zealand), respectively. This study made comparisons according to the coefficient of determination, root-mean-square error, Akaike information criterion, and Bayesian information criterion.

However, Curi et al. (1985) compared the goodness-of-fit of two non-linear growth models in Norfolk, New Zealand, and Californian rabbits. They concluded that the Gompertz model adjustments were more efficient than the logistic model. Costa et al. (2020) assessed the growth pattern of Norfolk rabbits using the logistic, Santos, and von Bertalanffy models, concluding that the Santos model was the most suitable to represent a growth curve. The R^2, MAD, and AIC criteria values and the logistic and von Bertalanffy model estimates were identical to our results.

Freitas (2005) compared the Brody, Richards, and von Bertalanffy models and two Gompertz and logistic alternatives adjusted to data from male New Zealand White rabbits obtained by weekly weighing them from birth to 70 days old, at Jaboticabal, SP, Brazil (UNESP). Only the logistic $y = \frac{A}{(1+e^{-kt})^m}$ and von

Bertalanffy models were adequate to estimate growth, with coefficients of determination= 0.9412 and 0.9999, respectively.

De Sousa et al. (2022) compared non-linear models adjusted to the growth of New Zealand rabbits, recommending the logistic model and von Bertalanffy for the weight and carcass growth trajectory analyses. Santos et al. (2018a) assessed the growth curves of New Zealand rabbits from birth to 150 days old, reporting that the Gompertz model presented a better adjustment to the data among the various tested models. Obioma et al. (2020) adjusted non-linear logistic models to growth data of California and New Zealand White rabbits, finding that the logistic and Gompertz models were adequate and parsimonious to describe the growth pattern from birth to 56 days of age.

When considering several adjustment criteria, choosing the best model may become complicated because a specific model may perform better in one criterion and perform worse in another. Using multivariate classification methods, such as cluster analysis, to group similar models simultaneously, considering all analyzed criteria, might solve this problem. Santos et al. (2018) used this recommendation.

5. Conclusions

The cluster analysis showed that the first cluster formed in the Gompertz, von Bertalanffy, Richards, and proposed models best described the weight of Norfolk rabbits. The proposed and von Bertalanffy models stood out among the others according to the goodness-of-fit criteria. Therefore, the proposed model may represent an alternative for describing the growth curve. However, further studies are needed to investigate the performance of the proposed new model.

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