Simple hierarchical and general nonlinear growth modeling in sheep

Mostafa GHADERI-ZEFEH1+, Farjad RAFeIE2, Mohammad Reza BAHEReINI BEHZADI1, Sajad NAZARI1, Mohammad Reza BAHREINI BEHZADI1, Mustafa MUAHGHEGH-DOLATABADY1, Farhad SAMADI1, Thomas M R MAXWELL4, Hamed AMIRPOUR NAJAFABAD1
1Department of Animal Sciences, Faculty of Agriculture, University of Yasouj, Yasouj, Iran
2Department of Agricultural Biotechnology, Faculty of Agricultural Sciences, University of Guilan, Rasht, Iran
3Cold-water Fishes Genetic and Breeding Research Center, Iranian Fisheries Science Research Institute (IFSRI), Yasouj, Iran
4Department of Agricultural Sciences, Faculty of Agriculture and Life Sciences, Lincoln University, Christchurch, New Zealand

Abstract: Differential equations and advanced statistical models have been used to predict growth phenomena. In the present study, general nonlinear growth functions such as von Bertalanffy, Gompertz, logistic, and Brody, along with hierarchical modeling were applied to investigate the phenotypic growth pattern of Iranian Lori-Bakhtiari sheep. Growth data from 1410 Lori-Bakhtiari lambs were used in the present study. The results showed that the Brody function outperformed the other three nonlinear growth functions. In addition, including hierarchical growth modeling results allowed the adoption of many random effect structures, suggesting that hierarchical growth modeling has a useful role in growth data modeling. This method provides an estimation of growth parameters based on individual animals, improving individual growth selection. The results suggest this approach for growth modeling. Combining the strength of individual growth modeling with general growth modeling, e.g., von Bertalanffy, Gompertz, logistic, and Brody would be deeply appealing in the future. In this regard, dealing with sheep growth phenomenon using pure mathematical models, i.e. grey system theory models that could be new powerful prediction tools for breeders and experts, has not been done yet. However, running the analysis on large datasets will require significantly higher computational power than is ordinarily available.

Key words: Growth functions, hierarchical modeling, Lori-Bakhtiari sheep, nonlinear models, prediction of growth phenomena

1. Introduction
Growth is described as an increase in the weight and size of a living organism over a certain period of time. Growth curves have different applications such as constructing livestock feeding programs, determining the optimum slaughtering age, and monitoring the effects of selection (1). Sheep growth data have been fitted into random regression models for growth (2). However, the shape of sheep growth curves is influenced by many factors: breed type, management, environment, selection, and nutrition conditions (3). Well-known general growth functions such as Brody, Gompertz, logistic, and von Bertalanffy have been used to monitor growth curves in sheep (4–10). These models are popular in growth trend modeling because of their generality and simplicity of use.

Fixed and mixed models have been used in analyzing growth data. Mixed models provide robust theoretical statistical frameworks to model dependent variables as a function of random and fixed effects. The Bayesian approach utilizes hierarchical models instead of mixed models to estimate model parameters for mixed effects, containing both fixed and random effects (11). In the present study, a simple hierarchical model was used to estimate individual animal growth parameters. In this case, the hierarchical model shared many features with the growth data random regression model, where fixed effects of regression were fitted to show the overall growth curve. Random effects were used to show deviation of each individual from the overall growth curve (5,12,13). The accuracy of predicting the growth curve of Iranian Lori-Bakhtiari sheep was studied using nonlinear growth functions (von Bertalanffy, Gompertz, logistic, and Brody) to accompany hierarchical modeling. In addition, simple and flexible hierarchical modeling was introduced with general computation requirements that was compatible with different variance–covariance structures when random effects were of interest in repeated data measuring used in animal breeding. Some very advanced pure mathematical models, i.e. the grey system theory models, that could be new powerful growth prediction tools for breeders and experts were pointed out. The mathematical foundation of grey theory was introduced by Deng (14).
After culling the animals with abnormalities, was around 3 months of age. The rate of replacement of ewes and rams, they received maintenance and growth ration until 6 (in pasture form). Male lambs were treated differently and the female lambs were assigned to cultivated alfalfa the lambs were separated into female and male flocks were weaned at about 90 ± 5 days of age. After weaning, and creep feed ad libitum (from 15 days of age). All lambs preweaning time, lambs had access to both mother’s milk lambs remained with their dams until weaning. During the preweaning time, lambs had access to both mother’s milk and creep feed ad libitum (from 15 days of age). All lambs were weaned at about 90 ± 5 days of age. After weaning, the lambs were separated into female and male flocks and the female lambs were assigned to cultivated alfalfa (in pasture form). Male lambs were treated differently and they received maintenance and growth ration until 6 months of age. The rate of replacement of ewes and rams, after culling the animals with abnormalities, was around 30% and less than 10%, respectively. Voluntary culling for the ewes was at 7 years old but the rams were kept until their offspring were available for replacement. Along with different sort of traits and pedigree data, other information such as age of ewes at mating were recorded routinely. The station was located in Shahrekord at 31°9’N, 32°48’E. The average annual rainfall in the region was about 400 to 600 mm with a mean temperature of 16 °C, and an average elevation of 1734 m above sea level.

2. Materials and methods

2.1. Data collection and management
The growth data of 1410 sheep of the Iranian Lori-Bakhtiari breed (521 males, 889 females) gathered from 1990 to 2011 were used in the present study. The data included birth weight (BW), weaning weight (WW), 6-month-old weight (W6), 9-month-old weight (W9), and 12-month-old weight (W12). These data were from a research flock at the Lori-Bakhtiari sheep breeding station located in Charmahal and Bakhtiari Province, Iran. This research flock was formed in 1989 with about 206 ewes, which had successfully reared at least one lamb, and 28 rams of typical Lori-Bakhtiari breed. The sheep were managed under semimigratory or village production systems. From December to May at the station, the sheep were fed with alfalfa, barley, and wheat stubbles; however, for the rest of the year, the sheep were grazed on range and cereal pasture including the breeding period. By means of natural mating, ewes were assigned to rams for the first time at an average age of 18 months. In this flock, lambing generally started in late January and they were treated differently than the ewes. Voluntary culling for the ewes was at 7 years old but the rams were kept until their offspring were available for replacement. Along with different sort of traits and pedigree data, other information such as age of ewes at mating were recorded routinely. The station was located in Shahrekord at 31°9’N, 32°48’E. The average annual rainfall in the region was about 400 to 600 mm with a mean temperature of 16 °C, and an average elevation of 1734 m above sea level.

2.2. Nonlinear growth functions
Nonlinear growth curve functions of von Bertalanffy, Gompertz, logistic, and Brody (9,10,16,17) were fitted to the data to estimate the parameters of the models and see if the growth curves fit well (Table 1).

Individual estimation of the growth curve parameters and mean square error (MSE) were obtained using the modified Gauss–Newton iterative procedure available in SAS (version 9.2) and the NLMIXED procedure (18). In general, the NLMIXED procedure can be used to fit different forms of linear models, e.g., simple linear regression, multiple linear regression, and analysis of (co) variance when observations are not normally distributed or contain outliers. Here the error part of the model was assumed to be normally distributed and independent of the random effects of the model. Amounts of Akaike’s information criteria (AIC) and the logarithm of the likelihood function (−2 LogL) values for each of model were obtained at this step.

2.3. Simple hierarchical modeling
In hierarchical growth modeling, as in repeated growth modeling, multiple observations associated with the same animal were considered. The hierarchical models were used as follows:

Model 1: \[ y_i = a_0 + b_1(Time)_i + \varepsilon_i \quad var(\varepsilon_i) \sim \sigma^2_\varepsilon \] (i = j)

Model 2: \[ y_i = a_0 + b_1(Time)_i + \varepsilon_i \quad var(\varepsilon_i) \sim \sigma^2_\varepsilon \] (i = j)

Model 3: \[ y_i = a_0 + b_1(Time)_i + \varepsilon_i \quad var(\varepsilon_i) \sim \sigma^2_\varepsilon \] (i = j)

In Model 1, it was assumed that the starting point for growth (birth weight) was different across all the sheep in

<table>
<thead>
<tr>
<th>Nonlinear functions</th>
<th>Model*</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>von Bertalanffy</td>
<td>( W_t = A(1 - Be^{kt}) + \varepsilon )</td>
<td>16, 10</td>
</tr>
<tr>
<td>Gompertz</td>
<td>( W_t = Ae^{(-\varepsilon r t)} + \varepsilon )</td>
<td>17, 10</td>
</tr>
<tr>
<td>Logistic</td>
<td>( W_t = A(1 - Be^{kt})^j + \varepsilon )</td>
<td>16, 10</td>
</tr>
<tr>
<td>Brody</td>
<td>( W_t = A(1 - Be^{kt})^j + \varepsilon )</td>
<td>9, 10</td>
</tr>
</tbody>
</table>

* \( W_t \) = the animal weight at a determined age (t), \( A \) = the predicted asymptotic weight at maturity (kg), \( B \) = the integration constant to which initial weight is related or animal maturation rate at birth (kg), \( K \) = the rate of maturity.
with parameters \( (0, \sigma^2) \) was assumed to be independently identically distributed \( a_i \) represents specific intercept for ith sheep, \( b_i \) represents the specific regression coefficient (slope) for the ith sheep, and \( \epsilon_i \) represents the error model and it was assumed to be independently identically distributed with parameters \( (0, \sigma^2) \). Note that the parameters of the model that lack the subscript are assumed to be the same parameters for all sheep (see Models 1 and 2). Model 3 can be expanded as follows:

\[
\begin{align*}
a_i &= \alpha + a_i' \sim N(0, \sigma^2) \\
b_i &= \beta + b_i' \sim N(0, \sigma^2) \\

\end{align*}
\]

Finally, the general model can be written as

\[
y_{it} = \alpha + \beta ((\text{Time})_i - (\overline{\text{Time}})) + a_i + b_i'(\text{Time})_i - (\overline{\text{Time}}) + \epsilon_i,
\]

where \( (\overline{\text{Time}}) \) represents the average time for the ith sheep, \( \alpha \) is the fixed effect for average weight of the sheep at start of recording, \( \beta \) is the fixed effects regression coefficient of time, \( a_i' = a_i - \alpha \) is the random sheep specific effect, and \( b_i' = b_i - \beta \) is the sheep specific random effect. It was assumed that the above random effects were jointly normally distributed with zero mean and variance–covariance \( \psi \) as follows:

\[
\begin{pmatrix} a_i' \\ b_i' \end{pmatrix} \sim iidN \left( \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma^2_a & \sigma_{ab} \\ \sigma_{ab} & \sigma^2_b \end{pmatrix} \right)
\]

As a result, variance–covariance between observations can be shown as follows:

\[
\text{var}(y_{it}) = \begin{pmatrix} 1 & (\text{Time})_i \end{pmatrix} \psi \begin{pmatrix} 1 \\ (\text{Time})_i \end{pmatrix} + \sigma^2_e = \sigma^2_a + \sigma_{ab}(\text{Time})_i + \sigma^2_b = \sigma^2_a + 2\sigma_{ab}(\text{Time})_i + \sigma^2_b
\]

In addition, it was assumed that covariance was

\[
\text{cov}(y_{it}, y_{jk}) = \text{cov}(a_i + b_i'(\text{Time})_i + \epsilon_i, a_j + b_j'(\text{Time})_j + \epsilon_j) = \sigma^2_a + \sigma^2_b(\text{Time})_i + \sigma^2_b(\text{Time})_j + \sigma^2_{ab}(\text{Time})_i(\text{Time})_j
\]

The above hierarchical model parameters were estimated using REML and implemented in SAS MIXED procedure (18). In addition, the procedure is featured with many variance–covariance structures (almost 30) to fit to the data. Figure 1 shows this modeling graphically.

2.4. Linear model

To analyze the effect of environmental factors on the observed live weights of sheep and the growth curve parameters A, B, and K, the following linear model was used:

\[
y_{dil} = \mu + S_i + A_j + T_k + B_l + \epsilon_{ij}
\]

where \( y_{dil} = \) weight, \( \mu = \) the overall mean, \( S_i = \) the effect of ith sex, \( A_j = \) the effect of age of ith dam, \( T_k = \) the effect of ith type of birth, \( B_l = \) the effect of ith year of birth, and \( \epsilon_{ij} = \) random error of the model. The GLM procedure (SAS 9.2) was used to estimate the parameters of the model.

3. Results and discussion

3.1. Nonlinear growth functions

The estimation of parameters A (predicted live weight at maturity), B (difference between mature live weight and birth weight), and K (growth rate to maturity) and associated R², MSE, AIC, and the −2log likelihood (−2 LogL) for the 4 models are shown in Table 2. Predicted live weight at maturity (A) was largest in the Brody model (59.12 kg) and lowest in the logistic model (54.4 kg). Difference between mature and birth live weight (B) was largest in the logistic model (6.05 kg) and smallest in the von Bertalanffy model (0.85 kg). Predicted growth rate to maturity (K) was largest in the logistic model (0.59 kg) and smallest in the Brody model (0.25 kg), which may indicate an earlier maturity rate in the logistic model compared to those in the other models.

Abegaz et al. (9) reported 37.6, 0.88, and 0.27 kg for predicted live weight at maturity, difference between live weight at maturity and birth, and growth rate to maturity, respectively when applying the Brody growth function to Horro sheep. Similarly, Bathaei and Leroy (4), Topal et al. (6), Gbangboche et al. (7), and Malhado et al. (19) reported different A, B, and K values when they fitted different growth functions to the same growth data, indicating that the applied model sharply affects the estimated model parameters. In the current study, the Brody model based on the lowest MSE and AIC and the highest R² was the best fitted model to describe growth in Iranian Lori-Bakhtiari sheep. The results showed high agreement with those obtained by Bahreini et al. (10) in Iranian Balouchi sheep. The results also support Bathaei and Leroy (4), who analyzed and evaluated different growth functions in Iranian Mehraban fat-tailed sheep. They used the Brody function because of its simplicity of interpretation and ease of estimation. Lewis et al. (5) showed that the Gompertz function had desirable properties to describe growth in Suffolk sheep. Topal et al. (6) reported that the Gompertz and the von Bertalanffy models showed the best estimation.
of growth in Morkaraman and Awassi sheep breeds, respectively. Certain properties such as goodness of fit to data, lower computational cost, biological interpretability of parameters, and managing missing data support the Brody model as the best model to monitor sheep growth patterns. However, in the current study, there were no missing data values.

The effects of the linear model factors on sheep live weights measured at different ages are shown in Table 3 and they were mostly significant (P < 0.01). The male lambs
and the single-born lambs had higher live weights, which may have been due to the hormonal and physiological differences between sexes, maternal conditions and milk production capacity, and the size of the uterus to grow single lambs relative to twin lambs (20). The effect of dam age on 9-month-old weight was significant. Figures 2A and 2B show that the male and the single lambs had higher growth rates than those of the female and the twin lambs. The results were in agreement with those reported in previous papers (5,8). Figure 2C indicates that dams that were 3, 4, and 5 years old delivered lambs with higher growth rates than those delivered by the younger and the older dams. Usually with increasing maternal age, lamb weight also increases. Physical maturity of the dam and reduced need to grow further increases fetal and birth weight as well as allowing better milk production (10).

There were significant effects of model factors on all the Brody model parameters (Table 3). Previous studies reported significant effects of type of birth, sex, and birth year on parameter $A$ of the Brody growth model (4,9). In the present study, a significant effect was observed for birth type on parameter $B$ estimated by the Brody growth model. Several studies have reported significant effects of sex on it (4,9,21). The observed significant effect of birth year on the growth model parameter is in agreement with the results reported by Batheai and Leroy (4) and Abegaz et al. (9). However, the effects of birth type, sex, and herd on any Brody and Gompertz growth model parameters were not reported as significant (22). Figures 2D–2H show how data were fitted to the respective models. As the Brody model (Figure 2H) had the best fit, much more attention was given to different aspects of this model, which can be seen in different subsets of Figure 2. Table 4 shows the significant effects of birth type and sex on Brody and Gompertz growth model parameters. The effect of birth year on maturity weight could be due to management and model factors in the birth year of the sheep because it could affect maternal ability to provide the right motherhood environment for her offspring.

### 3.2. Simple hierarchical modeling

Table 5 displays partial results of the hierarchical modeling, which is a part of the full hierarchical model in the current study (i.e. model 3 on sheep growth data). In terms of model fitting criterions, for full hierarchical modeling, $–2 \log L$ (53114) was competitive with the Brody model. However, statistical comparisons between the results of these models failed. Comparison of the models should be based on some valid and motivated assumptions and assumptions of these models, in terms of type and number of parameters, were different. The data had no missing values and it took a long time for the model to get converged. This may have been due to the structures of random effects. Two predictions of animal-specific intercept and slope were given for each animal. For example, both predicted parameters for sheep 100154 in Table 5 are negative. It might indicate that the growth trend for this sheep is lower than the population mean; therefore, this animal is less desirable for breeding purposes. However, for a predicted specific slope of animal, the null hypothesis cannot be rejected so easily ($P > 0.05$), however, for sheep 100225 this argument is justified. In this type of modeling, parameters for each sheep were randomly selected from a bigger population. Thus, implementing hierarchical modeling utilizes random parameter selection (here the Gaussian distribution was used as it was desirable that weights followed up this distribution asymptotically).
Figure 2. The results of different models for different factors: A) The Brody model for twin and single birth types, B) Trend of growth for the male and female sheep, C) The Brody model at different dam ages, D) Logistic model for average weights at different ages, E) The von Bertalanffy model for average weights at different ages, F) The Gompertz model for average weights at different ages, G) The Brody model for average weights at different ages, H) The Brody model for sex of sheep.
Pertaining to the hierarchical modeling, it should be noted that such a model has its advantages and disadvantages. In this type of modeling, it is possible to obtain the parameters for each animal independently. This model has great ability to fit and explore a wide range of different statistical distributions for random intercept and slope effects. Variance–covariance structure used in this type of modeling could impose a wide range of communications between random coefficients in the model. As the number of the records increases, it takes too much time to get convergence. Depending on the model structure and the conditions under which the records are collected, fitting the model could be quite complex. Having a good pedigree, a genetic analysis of two traits (here the first trait is intercept and the second trait is slope) can be carried out and therefore, the amount of heritability and genetic correlation can be grasped. If the covariance is considered to be zero, it can be postulated that early-measured weight will not have any impact on other weight behaviors over time. As mentioned above, most of the models used in the growth pattern modeling have a nonlinear nature (16,23). However, further studies using hierarchical modeling can

### Table 4. Effects of model factors on parameter estimations ± standard error of the Brody and Gompertz models in Lori-Bakhtiari sheep.

<table>
<thead>
<tr>
<th>Factors*</th>
<th>Brody</th>
<th>Gompertz</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Sex:</td>
<td>**</td>
<td>*</td>
</tr>
<tr>
<td>Male (521)</td>
<td>72.12 ± 0.73</td>
<td>5.44 ± 0.06</td>
</tr>
<tr>
<td>Female (889)</td>
<td>57.54 ± 0.62</td>
<td>5.85 ± 0.07</td>
</tr>
<tr>
<td>Birth type:</td>
<td>*</td>
<td>**</td>
</tr>
<tr>
<td>Single (1065)</td>
<td>62.24 ± 0.25</td>
<td>6.14 ± 0.05</td>
</tr>
<tr>
<td>Twin (345)</td>
<td>66.42 ± 0.77</td>
<td>5.52 ± 0.05</td>
</tr>
<tr>
<td>Age of dam (years)</td>
<td>**</td>
<td>*</td>
</tr>
<tr>
<td>Birth year</td>
<td>**</td>
<td>**</td>
</tr>
</tbody>
</table>

*The numbers within parentheses show the number of observations, **ns = not significant (P > 0.05), * = significant (P < 0.05), ** = significant (P < 0.01), A = the predicted asymptotic weight at maturity (kg), B = the integration constant to which initial weight is related or animal maturation rate at birth (kg), K = the rate of maturity.

### Table 5. A small part of full hierarchical modeling results

<table>
<thead>
<tr>
<th>Effect</th>
<th>Sheep ID</th>
<th>Estimate</th>
<th>Pred</th>
<th>DF</th>
<th>Pr&gt;</th>
<th>t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercepts</td>
<td>100154</td>
<td>−0.1318</td>
<td>0.0</td>
<td>9300</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>time</td>
<td>100154</td>
<td>−0.1344</td>
<td>0.3205</td>
<td>9300</td>
<td>0.6751</td>
<td></td>
</tr>
<tr>
<td>Intercepts</td>
<td>100225</td>
<td>−1.6356</td>
<td>0.0</td>
<td>9300</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>time</td>
<td>100225</td>
<td>−1.1037</td>
<td>0.3205</td>
<td>9300</td>
<td>0.0006</td>
<td></td>
</tr>
<tr>
<td>Intercepts</td>
<td>100229</td>
<td>−1.3137</td>
<td>0.0</td>
<td>9300</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>time</td>
<td>100229</td>
<td>−0.9041</td>
<td>0.3205</td>
<td>9300</td>
<td>0.5048</td>
<td></td>
</tr>
<tr>
<td>Intercepts</td>
<td>100237</td>
<td>−1.2722</td>
<td>0.0</td>
<td>9300</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>time</td>
<td>100237</td>
<td>−0.9618</td>
<td>0.3205</td>
<td>9300</td>
<td>0.0027</td>
<td></td>
</tr>
<tr>
<td>Intercepts</td>
<td>100241</td>
<td>−1.3452</td>
<td>0.0</td>
<td>9300</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>time</td>
<td>100241</td>
<td>−0.9392</td>
<td>0.3205</td>
<td>9300</td>
<td>0.0034</td>
<td></td>
</tr>
<tr>
<td>Intercepts</td>
<td>100243</td>
<td>−0.6392</td>
<td>0.0</td>
<td>9300</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>time</td>
<td>100243</td>
<td>−0.5284</td>
<td>0.3205</td>
<td>9300</td>
<td>0.0993</td>
<td></td>
</tr>
</tbody>
</table>
find a link between A, B, and K parameters in nonlinear functions, which may help in selecting the right animals for growth purposes.

Hierarchical models are powerful tools that can capture the undefined part of covariance among growth data. However, future growth research on animals or all living organisms should thoroughly be canalized to avoid mistaken inferences. In this regard, apart from the nature of character, adopting new intelligent machine learning algorithms and pure mathematical methods are of great importance. For example, a new algorithm has recently been introduced based on the combination of least square support vector machine and genetic algorithm (24). The algorithm outperformed all general functions of growth phenomenon modeling. However, there has not been any sign of grey system theory models in the context of animal growth modeling. Grey system theory as an interdisciplinary scientific area was introduced by Deng (14,25). This model is inherently suited for modeling positive variables explicitly. Growth phenomena lie in this area as well. Nowadays, growth is recorded over a limited number of times (as in the present study). Superiority of the grey models to the conventional statistical models is that with limited amount of information, a valid estimation of the behavior of an unknown growth system can be well achieved (26). As a suggestion for groundbreaking further research, the grey systems paradigm can be integrated with BLUP based concept. This integration would pave the way for new mainstream studies.

One of the main advantages regarding the proposed method in comparison with the general growth modeling schemes is that it allows us to derive growth function solely based on data but not on presumptions about growth function (no fixed number of parameters). The proposed method can be integrated with pedigree data and, therefore, a BLUP estimation of growth over any single time can be grasped soundly. Moreover, a large amount information of different (co)variance functions across random affects can be well fitted, which cannot be done with general growth modeling paradigms (like the four models used in the present study).

Acknowledgments
Authors extend their gratitude to Dr Vatankhah (University of Sharekord), and Dr Asadi (University of Sharekord) for providing the data and assisting in the analysis of data.

References