Growth curve analysis using nonlinear mixed model in divergently selected Japanese quails

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Introduction

Growth, a trait of prime interest to the animal industry, is a complex physiological process. Mathematical models have the potential to represent the entire growth phase of the chicken and the parameters in the models have biological meaning. Growth curves, which are the graphical illustration of the mathematical functions, are generally used to describe the increase in body weight of an individual or the average growth of population over time, and are also utilized to define the effects of selection on growth or body weight at any stage of life (BLASCO and GOMEZ, 1993). Many studies have been carried out to determine the growth pattern of chicken (TZENG and BECKER, 1981; ANTHONY et al., 1991b; AGGREGY, 2002), turkey (BUFFINGTON et al., 1973; ANTHONY et al., 1991a, 1991b), Japanese quail (MARKS, 1978; ANTHONY et al., 1986; ANTHONY et al., 1991b), swine (SCHINCKEL and CRAIG, 2001) and cattle (CHO et al., 2002) by fitting the most common non-linear growth curve functions such as Gompertz, Logistic, Bertalanffy, Brody and Richards models to the time-body weight information.

The parameters of non-linear growth curve models are estimated by iterative procedures minimizing the error variance or maximizing the likelihood by assuming that the residuals are independently distributed. However, growth curves are built up based on repeated live body weight measurements on the same experimental unit. These serial data usually have underlying relationships or correlations among the serial body weight observations. Therefore, heavier animals at birth or hatch usually have a competitive advantage and remain heavier than the other animals of the group in the later age stages. Also, the variation among the animals for live body weight increases as age increases. This typical result contradicts the assumption that the residual values are independent and have a constant variance at each age (SCHINCKEL and CRAIG, 2001).

Random effects of experimental units or individuals would stem from repeated measurements on the same animal over time. A mixed model is one that incorporates both fixed and random effects simultaneously (PEEK et al., 2002). Therefore, the objective of this study is first to compare non-linear fixed and mixed models and then to determine the effect of short-term divergent selection for 5-week body weights on growth characteristics of Japanese quail by comparing with those of the control line.

Materials and Methods

Material

High (HL) and low (LL) Japanese quail lines were established by applying the individual selection with 10% and 40% selection intensity on males and females, respectively, for increased or decreased 5-week body weights through 5 generations. Quail chicks (351, 272 and 619) in HL, LL, and control line (CL), respectively were hatched, wing-banded and placed in separate brooder batteries. The birds were sexed at 5-week of age according to their plumage color pattern. Random mating between selected parents was taken place within divergently selected lines. All Japanese quail had ad-libitum access to a 24% crude protein and 2400 kcal ME/kg of diet and to water. For all the three lines, hatch weight and thereafter weekly-body weights were collected from progeny of generation 5 until 8-week of age.

Method

The nonlinear model for growth data from the animal i can be expressed as:

\[ BW_{ij} = f(t_{ij}) + e_{ij} \]  

\[ i = 1,\ldots,N \text{ and } j = 1,\ldots,n_i \]  

where \( f \) is the nonlinear function relating the response variable (\( BW_{ij} \)) to time (\( t_{ij} \)), and \( e_{ij} \) is a vector including the parameters of the non-linear function.

Japanese quail growth data were fit to the Richards fixed effect function (RICHARDS, 1959),

\[ BW_{it} = A(1 + B \exp\{-Kt_i\})^{\frac{1}{m}} + e_{it} \]  

\[ A > 0, K > 0 \text{ and } \exp = 2.7818 \]

where \( BW_{it} \) is the body weight of Japanese quail at age (week) \( t_i \); \( A \) is the asymptotic weight or an estimation of...
mature weight as age approaches infinity; K is the rate of maturing and refers to growth rate relative to mature weight; m is the shape parameter determining the position of the inflection point at which the auto acceleration growth phase passes into the auto retardation phase; B is the integration constant defining the degree of maturity at t=0. The θ vector in equation (1) includes fixed parameters A, B and K, e is the residuals with the assumption of N(0, δ²K), where δ²K is the residual variance structure for all subjects, assuming that no covariance structure exists between the residuals of the model. However, a model with some covariance structure could be also proposed to incorporate the heteroskedasticity and correlation of the residuals over all ages.

From equation (2) the absolute or instantaneous growth rate (AGR₀) and the relative growth rate (RGR₀) in the Richards function were estimated as follows:

\[ AGR_{it} = BW_{it} \left( \frac{KB \exp(-Kt)}{m(1+B \exp(-Kt))} \right) \]  
\[ RGR_{it} = \left( \frac{KB \exp(-Kt)}{m(1+B \exp(-Kt))} \right)^{\frac{1}{m}} \]  

The age (t₀) and weight (W₀) at the inflection point were calculated below:

\[ t_{inf} = \frac{-1\ln(m/B)}{K} \quad \text{and} \quad W_{inf} = A(m+1) \]  

The mixed effects model is:

\[ BW_{it} = (A + a_i)(1 + B \exp(-(K + k_i)t)) \]  
\[ RGR_{it} = \left( \frac{KB \exp(-Kt)}{m(1+B \exp(-Kt))} \right)^{\frac{1}{m}} + e_{it} \]  

where aᵢ and kᵢ are the random effects for the ith Japanese quail. Thus, the θ = [β, uᵢ] includes a fixed component, β = [A, B, K], common to all subjects, and a random component, uᵢ = [aᵢ, kᵢ] specific to each subject. Based on the parametric inference approach, it is assumed that the distribution is uᵢ ~ N(0, G) where uᵢ is independent of eᵢ and G is the variance-covariance matrix of the random effects. Genetic relationship between individuals was also ignored in the analysis.

Thus, the absolute growth rate (AGR₀) and the relative growth rate (RGR₀) from the mixed effects model were:

\[ AGR_{it} = BW_{it} \left( \frac{(K + k_i)B \exp(-(K + k_i)t)}{m(1+B \exp(-(K + k_i)t))} \right) \]  
\[ RGR_{it} = \left( \frac{(K + k_i)B \exp(-(K + k_i)t)}{m(1+B \exp(-(K + k_i)t))} \right)^{\frac{1}{m}} \]  

The age (t₀) and weight (W₀) were found as follows:

\[ t_{inf} = \frac{-1\ln(m/B)}{(K + k_i)} \quad \text{and} \quad W_{inf} = (A + a_i)(m+1) \]  

The advantages of a mixed effect model analysis were combined with the straightforward interpretability of non-linear growth curves in this study. In order to apply non-linear mixed effects model to divergently selected Japanese quail growth curves, we used the procedure of NLmixed available SAS package (SAS, 2000). Initial values for each parameter were obtained from the results of Richards fixed effects model which was run by using PROC NLIN in SAS, and then the PROC NLmixed used an iterative approach based on these initial values to generate a solution that properly account for individual animal effect on repeated body weight measures.

Model Comparison

Model choice is an important issue both in animal and plant science and also in other fields. However, breeders and researchers in animal breeding have not shown a serious interest for statistical model choice criteria until recent years (SORENSEN et al., 1995; KIZILKAYA et al., 2003). The most obvious fact is that the simple models are preferred to more complicated ones. Significant advancements in computing power and statistical software now make possible to use the more complicated models. The two most popular model selection criteria to select the better fit model among candidate ones are the Akaike Information Criteria (AIC),

\[ AIC = -2f(\hat{\theta}) + 2d \]  

and the Bayesian Information Criteria (BIC),

\[ BIC = -2f(\hat{\theta}) + d \ln(n) \]  

where f(\hat{\theta}) denotes the maximum value of the (possibly restricted) log likelihood, \hat{\theta} the vector of parameter estimates, d the dimension of the model, and n the number of effective observations (BOZDOGAN, 1987; WOLFINGER, 1993). They analytically measure how well different models fit the data. Equations (8) and (9) indicate that AIC and BIC reward descriptive accuracy via the maximum likelihood by penalizing lack of parsimony according to the number of free parameters. Therefore, the lowest values of AIC and BIC determine the better fit model among candidate models for the observed data.

Results and Discussion

The observed growth curves for Japanese quail lines (HL, LL and CL) within sex are shown in Figure 1. Live body weights of male and female quails within lines were found to be similar from hatch to 5-week of age, and thereafter females were significantly heavier than the males (P<0.05). Also, divergence of selected lines from control occurred immediately after hatching. The estimates of parameters (A, K and m) for the Richards fixed and mixed effects models, the weight (W₀) and age (t₀) at inflection point, and correlation coefficients (rAK) between mature weight and rate of maturing are given in Table 1. As shown in Table 1, parameter estimates from non-linear fixed and mixed effect models are not identical. Although there were not significant differences between the estimates of A and t₀ for both models, the estimates of K and W₀ between models were determined to be significantly different from each other (P<0.05). In addition, the shape parameter (m) estimates from mixed effects model were found to be lower than those from fixed effects model. Correlation coefficient estimates (rAK) for male quails within HL and for females within LL also indicated that mixed effects model produced non-similar results with fixed effects model.

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Table 1. Estimates of Richards growth curve parameters by fixed and mixed effects models

<table>
<thead>
<tr>
<th>Parameter</th>
<th>High Line</th>
<th>Low Line</th>
<th>Control Line</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female N=171</td>
<td>Male N=180</td>
<td>Female N=134</td>
</tr>
<tr>
<td>Fixed effects model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$A$</td>
<td>291.78 ± 3.20</td>
<td>228.21 ± 1.63</td>
<td>200.82 ± 2.30</td>
</tr>
<tr>
<td>$B$</td>
<td>1.47 ± 0.71</td>
<td>4.76 ± 1.39</td>
<td>3.78 ± 1.32</td>
</tr>
<tr>
<td>$K$</td>
<td>0.63 ± 0.02</td>
<td>0.88 ± 0.02</td>
<td>0.75 ± 0.04</td>
</tr>
<tr>
<td>$\ell_{0f}$</td>
<td>3.22 ± 0.05</td>
<td>2.87 ± 0.04</td>
<td>3.35 ± 0.05</td>
</tr>
<tr>
<td>$W_{0f}$</td>
<td>122.63 ± 1.32</td>
<td>106.00 ± 0.94</td>
<td>90.17 ± 1.05</td>
</tr>
<tr>
<td>$m$</td>
<td>0.44 ± 0.05</td>
<td>0.81 ± 0.06</td>
<td>0.75 ± 0.09</td>
</tr>
<tr>
<td>$s_{AK}$</td>
<td>-0.573</td>
<td>-0.573</td>
<td>-0.542</td>
</tr>
</tbody>
</table>

Mixed effects model

| $A$ | 291.51 ± 2.422 | 228.71 ± 1.41 | 200.58 ± 1.57 | 160.94 ± 0.97 | 213.31 ± 1.22 | 175.18 ± 0.83 |
| $B$ | 1.53 ± 0.28 | 5.52 ± 0.59 | 3.67 ± 0.66 | 14.23 ± 1.83 | 20.92 ± 3.21 | 30.81 ± 3.64 |
| $K$ | 0.56 ± 0.01 | 0.79 ± 0.01 | 0.63 ± 0.01 | 0.92 ± 0.01 | 0.82 ± 0.01 | 0.98 ± 0.01 |
| $\ell_{0f}$ | 3.17 ± 0.04 | 2.83 ± 0.03 | 3.31 ± 0.04 | 3.03 ± 0.04 | 3.67 ± 0.02 | 3.27 ± 0.02 |
| $W_{0f}$ | 120.30 ± 1.00 | 104.46 ± 0.64 | 88.34 ± 0.69 | 79.22 ± 0.48 | 108.08 ± 0.62 | 91.84 ± 0.44 |
| $m$ | 0.27 ± 0.04 | 0.60 ± 0.03 | 0.47 ± 0.05 | 0.92 ± 0.05 | 1.07 ± 0.06 | 1.27 ± 0.05 |
| $s_{AK}$ | -0.666 | -0.666 | -0.324 | -0.324 | -0.738 | -0.738 | -0.502 | -0.502 | -0.533 | -0.533 | -0.520 | -0.520 |
The parameter of growth rate and the rate of maturing is another variable that describes the growth of Japanese quails. These parameter changes as it moves towards its mature weight. These changes give the quail a growth curve that has a characteristic S shape in Figure 1 (ROSE, 1997). Parameter K of growth rate was significantly higher in males (p<0.05) than females in all the lines (HL, LL and CL) indicating that male quails grew faster than female quails and reached their weight at point of inflection and asymptotic weight at younger age. The effect of sex on the parameter of growth rate and the rate of maturing has also been determined in Japanese quails which were selected for increased or decreased 4-week body weight for 30 generations (AGGREY, 2003; AGGREY et al., 2003); for relative gain between 11 and 28 days of age (HYANKVA et al., 2001); and for higher 4-week body weight for five generations (AKBAŞ and OÜZ, 1998); and in European quail (DU PREEZ and SALES, 1997). In addition, there was a significant decrease in the parameter of growth rate and the rate of maturing of the HL (32% and 19%) and LL (23% and 6%) over the CL for females and males, respectively. It appeared that selection for increased and decreased 5-week body weight resulted in a decline in the parameter of growth rate and the rate of maturing for both sexes. The estimates of correlation between parameters A and K showed that there was a moderately negative relationship between maturation rate and asymptotic weight (Table 1). This antagonistic association indicates that early maturing quails tend to attain smaller mature weight, and high mature weight is strongly related with long growth period or quails with lighter asymptotic weight reached that weight at younger age (AKBAŞ and OÜZ, 1998; KNIZETOVA et al., 1991). Also, the divergent selection resulted in significant correlation coefficient difference between male and female within lines, compared to controls. The maximum maturation rate and weights (Winf) (120.30, 104.46, 88.34 and 79.22 g) indicated by the ages (3.17, 2.83, 3.31 and 3.03 weeks) at the inflection point (tinf) were also given for female and male quails within HL and LL lines (Table 1). Results showed that male quails reached the inflection point significantly earlier than female quails. For LL quails, the age at maximum growth was about 2.5 days later, suggest-

Table 2. AIC and BIC values for non-linear fixed and mixed effects models

<table>
<thead>
<tr>
<th>Model</th>
<th>High Line</th>
<th>Low Line</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Fixed</td>
<td>AIC</td>
<td>BIC</td>
<td>AIC</td>
</tr>
<tr>
<td></td>
<td>13697</td>
<td>13723</td>
<td>13683</td>
</tr>
<tr>
<td>Mixed</td>
<td>11697</td>
<td>11722</td>
<td>11401</td>
</tr>
</tbody>
</table>

Figure 2. Estimated absolute growth rate of Japanese quail lines divergently selected for 8-week body weight and their control (a males, b females)

Geschätzte absolute Wachstumsrate von Japanischen Wachteln, die auf das 8-Wochengewicht selektiert wurden, und der Kontrolllinie (a Hähne, b Hennen)

Figure 3. Estimated relative growth rate of Japanese quail lines divergently selected for 8-week body weight and their control (a males, b females)

Geschätzte relative Wachstumsrate von Japanischen Wachteln, die auf das 8-Wochengewicht selektiert wurden, und der Kontrolllinie (a Hähne, b Hennen)
ing a prolonged growing period. Also, significant sex and line effects were found on the weight at inflection point. Divergence selection for 5-week body weight in this study altered the $W_{inf}$ of HL and LL quails compared to controls because of the positive correlation between asymptotic weight and weight at inflection point (Knizetova et al., 1991).

The shape of growth curve, which has a variable point of inflection for the Richards mixed effects model, is defined by the shape or growth trajectory parameter $m$ (Aggrey et al., 2003). However, popular growth models, such as the Gompertz and Logistic models have fixed growth shapes with inflection point at 37% and 50% of the asymptote, respectively. When the values of $m$ are close to 0 or 1, the Richards model corresponds to the Gompertz or Logistic growth curve models (Brisbin et al., 1987). Although both females and males of CL had growth curve shapes of Logistic model, the selection for increased and decreased 5-week body weight resulted in the decline in the values of $m$, which were 0.27, 0.60 in HL and 0.47, 0.92 in LL for both sexes. Therefore, the shape of the growth curve of females in HL resembles more the Gompertz growth curve; however, others still were equivalent to the logistic model.

The estimated absolute and relative growth rates by line and sex were presented in Figure 2 and Figure 3. As seen in Figure 2, all lines for absolute growth rate increased until about week 3 which is the age of maximum accumulation; and thereafter a rapid decline occurred. Females produced significantly larger absolute growth rates than males ($p<0.05$) within all ages. For both sexes, the absolute growth rates were found significantly higher in HL than LL and CL through growth period; however, the differences between lines got smaller after the age of maximum growth rate. In addition to the asymmetric response for absolute growth rate to divergent selection, Figure 3 indicated that selection resulted in significantly higher relative growth rate for HL and LL in the first two weeks compared to the CL within sexes. The lower birth weight at hatch in line LL could result in larger relative growth rate in LL than line CL. Initial advantage of quails from HL diminished with age. So, LL and CL quails maintained a slightly higher relative growth rate over the HL until week 5. Marks (1979, 1980) indicated that selection for high 8-week body weight in chicken resulted in an increase in relative growth rate in the first two weeks. Aggrey (2003) studied Japanese quail lines divergently selected for 4-week body weight, suggested that the initial spurt in the relative growth rates in the first few weeks may determine the asymptotic body weight and this being the case, relative growth may decline by a factor proportional to the amount of the remaining growth.

### Acknowledgements

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### Summary

This study was undertaken to apply non-linear mixed effects model to examine the effect of short-term selection for 8-week body weight on growth parameters in divergently selected lines of Japanese quail and their controls. The parameters of Richards models were utilized to describe growth pattern of Japanese quails from the generation 5 including growth curves; and absolute and relative growth rates.

### Key words

Japanese quail, non-linear mixed model, divergence selection, growth curve, Richard's model

### Zusammenfassung

Analyse der Wachstumskurven von in entgegengesetzter Richtung selektionierten japanischen Wachteln mittels eines nicht linearen gemischten Modells


### Growth parameter estimates were significantly different in mixed model from in fixed effects model for all lines by sexes, except asymptotic weight and age of inflection point. There was a significant increase and decrease in maturing weights of divergently selected lines over the control for both females and males. However, growth rates and ages of maximum growth rate for lines decreased significantly compared to control. Although Richards model is equivalent to the Logistic model for both females and males of control line, the selection for increased and decreased 8-week body weight resulted in the decline in the values of the growth curve for both sexes. Therefore, the trajectory of the growth curve of females in high line resembles more of the Gompertz growth curve; however, the selection did not alter the shape of growth curves in males of high line and in females and males of low line. Absolute and relative growth rates were also affected by the divergence selection. The high line quails showed significant absolute growth rate through growth period and relative growth rates were found significantly higher for lines compared to control in the first two weeks.

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References


