Modelling lactation curve for fat to protein ratio in Holstein cows

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The objective of this study was to examine seven mathematical models to evaluate their efficiency in describing the lactation curve for fat to protein ratio (FPR) in the first three lactations of Iranian Holsteins. Data were 8,103,044 test-day records for FPR from the first three lactations of Iranian Holstein cows which were collected in 2392 dairy herds from 1991 to 2014 by the Animal Breeding Center of Iran. Each model was fitted to test-day records of FPR using the NLIN and MODEL procedures in SAS. The models were tested for goodness of fit using adjusted coefficient of determination, root mean square error, Durbin-Watson statistic (DW), Akaike's information criterion (AIC) and Bayesian information criterion (BIC). The highest values of FPR were observed in early lactation, which was followed by a decline as the lactation progressed and an increase toward the end of the lactation period. For the first three parities, Dijkstra model provided the lowest AIC and BIC values, whereas Nelder model had the greatest values of AIC and BIC. Therefore, Dijkstra equation provided the best fit of FPR for the first three parities of Holstein cows, and Nelder model was fitted worst. According to DW values, it seems that there was only a slight or no problem of residual autocorrelation for FPR in Iranian Holsteins. After selecting an appropriate mathematical model to describe lactation curve of FPR, it is possible to develop an optimal strategy to obtain a desired shape of lactation curve through modifying the parameters of model.

KEYWORDS: dairy cow / fat to protein ratio / Holstein cow / lactation model / model fitting

The lactation may be defined as the secretion of milk produced from simple blood nutrients by the milk-synthesising cells of the mammary glands, together with the removal thereof from the mammary gland [Lombard 2006]. The mathematical description of milk yield over the lactation demonstrates one of the most important

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applications of mathematical models in animal science [Pulina *et al.* 2001, France and Thornley 1984]. Several justifications can be proposed for the need of a mathematical modelling of the lactation pattern. Mathematical models of the lactation curve and, in general, of the mammary gland represent a valuable tool for basic studies aimed at increasing the scientific knowledge of complex physiological mechanisms that underlie the milk secretion process [Dimauro *et al.* 2007]. Lactation curves may be used by physiologists, nutritionists and other researchers to mimic the lactation process and to study the relationships existing between secretory cells, hormones, energy supply and environmental effects affecting the milk production [Strzałkowska *et al.* 2010, Steri *et al.* 2012]. Knowledge of the lactation curve is required for feeding, breeding and economic management of a dairy herd. Lactation curves are especially important when making decisions that are time-dependent [Tozer and Huffaker 1999].

The periparturient period of the dairy cow is one of the most critical periods over the productive and reproductive life. In the late dry period and early lactation, an insufficient dry matter intake in combination with a high energy requirement due to initiation of milk production leads to a negative energy balance. The energy balance is defined as the difference between energy consumed and energy used for maintenance and production [Goff and Horst 1997, Jóźwik *et al*. 2012a]. Typically, fresh cows are not able to consume enough energy to meet their physiological energy requirements and, consequently, they enter into a negative energy balance status [Doepel *et al.* 2002, Bauman and Griinari 2003]. Cows in an extreme state of negative energy balance in early lactation are metabolically stressed and show greater incidence of diseases such as mastitis, lameness, and metabolic disorders including ketosis [Goff and Horst 1997, Collard *et al.* 2000, Ingvartsen *et al.* 2003]. Moreover, fertility is impaired [Veerkamp *et al.* 2000, Wathes *et al.* 2007]. Enhancing nutrient intake seems, therefore, imperative to maximize health and reproduction of periparturient cows [Jóźwik et al. 2012b, Ghavi Hossein-Zadeh 2013]. Milk components can be used as a diagnostic and monitoring tool in nutritional evaluation. Milk fat and protein concentrations follow the inverse of the lactation curve for milk yield, mainly due to the dilution effect [Eicher 2004]. The variation of milk fat and protein concentrations over the lactation should be considered when attempting to use milk components as a nutritional assessment tool [Podpečan *et al.* 2008, Strzałkowska *et al.* 2009]. Several studies have shown a correlation between energy levels and milk composition using different traits such as fat to protein ratio (FPR), protein to fat ratio, fat-lactose-quotient, milk yield and milk protein concentrations [Heuer *et al.* 1999, Reist *et al.* 2002]. Greater values of FPR are associated with decrease in dry matter intake and increase in fat mobilization over negative energy balance phase after calving [Eicher 2004, Čejna and Chladek 2005]. FPR is mostly used as a diagnostic tool to estimate nutritional disbalance, negative energy balance and some metabolic disorders such as subclinical or clinical ketosis and abomasal displacement [Heuer *et al.* 1999, Eicher 2004]. Thus, changes in FPR in milk could be an indication of the ability of a cow to adapt to the demands of milk production and reproduction efficiency in postpartum period [Loeffler *et al.* 1999].

The lactation curves and their features for milk yield and its components (milk fat percentage, milk protein percentage and somatic cell score) for the first three lactations of Iranian Holsteins were evaluated in previous study [Ghavi Hossein-Zadeh 2014]. But studies on the lactation curve for FPR are rare in the literature. Therefore, the aim of this study was to examine seven mathematical models (Brody, Wood, Dhanoa, Sikka, Nelder, Rook and Dijkstra) to evaluate their efficiency in describing the lactation curve for FPR in the first three lactations of Iranian Holsteins.

Material and methods

Data

Initial data set were 8,103,044 test-day records for milk fat to protein ratio (FPR) from the first three lactations of Iranian Holstein cows. Data were recorded in 2392 dairy herds from 1991 to 2014 by the Animal Breeding Center of Iran. Outliers and out of range records were deleted from the analyses. Individual daily fat and protein percentages should be in a range from 1 to 9% [Ghavi Hossein-Zadeh 2014]. Records from DIM <5 and >305 days were eliminated. Records were also eliminated if registration number of a cow was missing. Analyses were applied only to the first three parities and, therefore, data from later parities were discarded. Ages at calving were required to be between 20 and 40, 28 and 49, and 40 and 68 months in lactations one, two, and three, respectively. After editing, 5,729,061 test-day records from 1821 dairy herds were used in the statistical analysis. Number of animals (test-day records) were 372,942 (2,492,385), 290,559 (1,939,442) and 198,484 (1,297,234) in first-, second- and third parities, respectively.

Lactation curve models

The non-linear equations used to describe the lactation curves for FPR are presented in Table 1. A first attempt to describe the changes in milk yield over the lactation with a functional relationship was proposed by Brody *et al.* [1923] which used an exponential function to describe the declining phase of lactation in dairy cattle. In this model, *a* is the parameter representing the approximate initial milk yield at the beginning of lactation and *c* is the declining slope parameter. The incomplete gamma function proposed by Wood [1967] has been used widely to study lactation curves, in which scaling factor *a* represents yield at the beginning of lactation, *b* is the inclining slope parameter up to peak yield, and *c* is the declining slope parameter [Silvestre *et al.* 2006]. Dhanoa [1981] proposed a model which is similar to the Wood model. The correlation coefficient between parameters *b* and *c* was lower in Dhanoa model than in Wood model. The parabolic exponential function introduced by Sikka [1950] to model milk yield resulted in a bell shaped truncated curve that, as a result of the curve symmetry around peak yield, fitted milk yield reasonably only during first lactation [Gahlot *et al.* 1988]. Nelder model (also known as inverse polynomial model) was proposed by Nelder [1966] and is derived from the Sikka model. In the Sikka model,

Table 1. Equations used to describe the lactation curve for fat to protein ratio of Holstein cows

Model	Equation
Brody	$y = a\left(1 - be^{-ct}\right)$
Wood	$y = at^{b}e^{-ct}$
Dhanoa	$y = at^{bc}e^{-ct}$
Parabolic (Sikka)	$y = ae^{\left(bt+ct^2\right)}$
Inverse polynomial (Nelder)	$y = \dfrac{t}{\left(a + bt + ct^2\right)}$
Rook	$y = a\left(\dfrac{1}{1+\dfrac{b}{c+t}}\right)e^{-dt}$
Dijkstra	$y = ae^{\left[\frac{b\left(1-e^{-ct}\right)}{c} - dt\right]}$

y – fat to protein ratio; a, b, c and d – parameters that define the scale and shape of the lactation curve; t – time from parturition.

a is approximate initial FPR after calving, but in the Nelder model, this parameter is related to the declining rate of FPR after calving. In the Sikka and Nelder models, *b* is inclining slope parameter up to peak yield and *c* is declining slope parameter. Rook *et al.* [1993] and Dijkstra *et al.* [1997] were modified forms of mechanistic models, based on a set of differential equations representing cell proliferation and cell death in the mammary gland. In the Dijkstra model, *a* is cell population at parturition or the theoretical initial milk production, *b* is specific rate of cell proliferation, *c* is a decay parameter and *d* is specific rate of cell death. In the Rook model, parameter *a* is milk yield at the beginning of lactation; *b* is a parameter related to the rate to reach peak yield; *c* is a parameter related to maximum milk yield and *d* is a parameter related to changes in curve shape after reaching maximum yield.

Statistical analyses

Each model was fitted to test day FPR records of dairy cows using the NLIN and MODEL procedures in SAS [SAS Institute 2002]. Predicted FPR values were obtained using estimated parameters of different models. The minimum FPR (MY) and time

at which minimum occurred (MT) were found for each model. The Gauss-Newton method was used as the iteration method. The models were tested for goodness of fit using five criteria described below:

Adjusted coefficient of determination (R_{adj}^2) was calculated using the following formula:

where:

$$R_{adj}^2 = 1 - \left[\frac{(n-1)}{(n-p)}\right](1-R^2)$$

R^2 – the coefficient of determination ($R^2 = 1 - \dfrac{RSS}{TSS}$);

TSS – total sum of squares, RSS is residual sum of squares, n is the number of observations (data points) and p is the number of parameters in the model.

The root mean square error (RMSE) is a kind of generalized standard deviation and was calculated as follows:

$$RMSE = \sqrt{\frac{RSS}{n-p-1}}$$

where:

RSS, n and *p* – described above. RMSE value is one of the most important criteria to compare the goodness of fit of different models and the best model is the one with the lowest RMSE.

The Durbin-Watson statistic (DW) was calculated using the following formula:

$$DW = \frac{\sum_{t=2}^{n}(e_t - e_{t-1})^2}{\sum_{t=1}^{n} e_t^2}$$

where:

e_t – the residual at time t;

e_{t-1} – residual at time t-1.

DW was used to detect the presence of autocorrelation in the residuals from the regression analysis. In fact, the presence of autocorrelated residuals suggests that the function may be inappropriate for the data. The Durbin-Watson statistic ranges from 0 to 4. A value near two indicates non autocorrelation; a value toward 0 indicates positive autocorrelation; a value toward 4 indicates negative autocorrelation.

The Akaike's information criterion (AIC) was calculated using the equation [Burnham and Anderson 2002]:

$$AIC = n \times \ln(RSS) + 2p$$

where RSS, n and p were described above. AIC is a good statistics for comparison of models of different complexity because it adjusts the RSS for number of parameters in

the model. A smaller value of AIC indicates a better fit when comparing models.

The Bayesian information criterion (BIC) was calculated as follows [Schwarz 1978]:

$$BIC = n \ln\left(\frac{RSS}{n}\right) + p \ln(n)$$

where RSS, n and p were described above. A smaller value of BIC indicates a better fit when comparing models.

Results and discussion

Estimated parameters of non-linear models for the first-, second- and third-parity dairy cows are presented in Table 2. Results showed that scaling parameter *a* which represents FPR at the beginning of lactation was greater for Wood and Dhanoa models compared with all equations except for Nelder model. Also, FPR values at the beginning of lactation (parameter *a*) were greater in first parity cows than those in second- and third parities. Parameter *a* in the Nelder model, which associated with declining rate of FPR after calving, was lower in first parity cows compared with subsequent parities. This indicated greater decline rate of FPR after calving in first parity cows.

Goodness of fit statistics for the seven functions fitted to average standard curves of FPR according to parity class are shown in Table 3. R^2_{adj} values for different models fitted to FPR records were similar. Also, no differences were found among different models based on DW values. The goodness of fit statistics for Wood and Dhanoa models were similar or very close in this study. DW values varied from 1.46 to 1.50 across the parities. These values indicated slightly positive autocorrelation between residuals. No differences were found among different models based on RMSE values. Dijkstra model had the lowest AIC and BIC values and Nelder model had the greatest values of these statistics. Therefore, Dijkstra equation provided the best fit of FPR for the first three parities of Holstein cows while Nelder model provided the worst fit.

The FPR values increased a little in the first few days of first-, second- and third lactation and then decreased to the minimum values of 1.03, 1.03 and 1.04 on days 136, 117 and 92, and finally reached to the values of 1.06, 107 and 1.08 on day 305, respectively (Tab. 4, Fig. 1). Nishiura et al. (2015) reported phenotypic values of FPR increased in the first few days of lactation and reached to its peak on days 10 to 20 in Holstein cows of Japan.

Minimum FPR (MY) and time at which daily FPR was minimum (MT) predicted by the seven non-linear functions are shown in Table 4. In the first lactation, the Dijkstra equation estimated the MT more accurately than the other equations, although MT was over-predicted by all models. The Wood, Sikka, Nelder, Rook and Dijkstra models provided closer estimates of MY to the observed values compared with Brody and Dhanoa equations. The Wood model estimated the MT more accurately than the other equations in the second lactation, while other models over-predicted the MT.

Also, Sikka, Nelder and Dijkstra equations provided closer estimates of MY to the observed value of minimum FPR than the other models. For third lactation FPR, the MT was predicted closer to the observed time of minimum FPR by the Dijkstra model, although MT was over-predicted by all models. The Sikka equation provided more accurate prediction of MY than the other models.

Fat to protein ratio predicted by different models are depicted in Figure 2. The highest values of FPR were observed in early lactation, which was followed by a decline as the lactation progressed and an increase close to the end of the lactation period. The FPR peak in early lactation could be related to the negative energy balance

Table 2. Parameter estimates for the different lactation equations of the first three parities of dairy cows (standard errors are in parentheses)

Trait	Parameter	Model						
		Brody	Wood	Dhanoa	Sikka	Nelder	Rook	Dijkstra
FPR1	a	1.05 (0.0002)	1.39 (0.002)	1.39 (0.002)	1.16 (0.0006)	-0.82 (0.007)	0.85 (0.006)	1.22 (0.001)
	b	-0.1804 (0.0015)	-0.0697 (0.0005)	163.5 (0.99)	-0.0013 (0.000008)	0.9425 (0.0004)	-29.12 (1.53)	-0.0038 (0.00005)
	c	0.0321 (0.0004)	-0.0004 (0.000005)	-0.0004 (0.000005)	-0.000004 (0.00000003)	0.00007 (0.000002)	94.35 (3.63)	0.0177 (0.0003)
	d	-	-	-	-	-	-0.00053 (0.000015)	-0.00027 (0.000009)
FPR2	a	1.05 (0.0003)	1.24 (0.002)	1.24 (0.002)	1.11 (0.0007)	-0.56 (0.009)	0.93 (0.006)	1.15 (0.002)
	b	-0.1046 (0.0020)	-0.0448 (0.0006)	129.8 (0.97)	-0.0008 (0.00001)	0.9565 (0.0005)	-13.51 (1.15)	-0.0028 (0.00008)
	c	0.0414 (0.0011)	-0.0004 (0.000006)	-0.0004 (0.000006)	-0.000002 (0.00000003)	-0.00002 (0.000003)	69.64 (4.50)	0.0210 (0.0007)
	d	-	-	-	-	-	-0.00036 (0.000014)	-0.00020 (0.000008)
FPR3	a	1.06 (0.0004)	1.28 (0.003)	1.28 (0.003)	1.14 (0.0009)	-0.54 (0.01)	0.93 (0.009)	1.18 (0.002)
	b	-0.1201 (0.0021)	-0.0469 (0.0007)	158.8 (2.00)	-0.0009 (0.00001)	0.9347 (0.0007)	-16.92 (1.78)	-0.0029 (0.00009)
	c	0.0329 (0.0008)	-0.0003 (0.000007)	-0.0003 (0.000007)	-0.000002 (0.00000002)	0.00004 (0.000003)	79.13 (6.10)	0.0204 (0.0008)
	d	-	-	-	-	-	-0.00034 (0.00002)	-0.00016 (0.000011)

a, b, c and d – parameters that define the scale and shape of the lactation curve; FPR1 – first lactation fat to protein ratio; FPR2 – second lactation fat to protein ratio; FPR3 – third lactation fat to protein ratio.

Table 3. Goodness of fit of Brody, Wood, Dhanoa, Sikka, Nelder, Rook and Dijkstra models for fat to protein ratio by parity class

Trait	Parameter	Model						
		Brody	Wood	Dhanoa	Sikka	Nelder	Rook	Dijkstra
FPR1	DW	1.46	1.46	1.46	1.46	1.46	1.46	1.46
	R^2_{adj}	0.9302	0.9302	0.9302	0.9302	0.9300	0.9303	0.9303
	RMSE	0.2912	0.2912	0.2912	0.2913	0.2912	0.2911	0.2911
	AIC	30560379	30560214	30560214	30562124	30568513	30558600	30558530
	BIC	-6149300	-6149465	-6149465	-6147555	-6141166	-6151066	-6151137
FPR2	DW	1.48	1.48	1.48	1.48	1.48	1.48	1.48
	R^2_{adj}	0.9261	0.9262	0.9262	0.9261	0.9261	0.9262	0.9262
	RMSE	0.2990	0.2990	0.2990	0.2990	0.2990	0.2989	0.2989
	AIC	23397125	23395750	23395750	23396656	23398288	23395271	23395203
	BIC	-4682680	-4683281	-4683281	-4682375	-4680743	-4683748	-4683815
FPR3	DW	1.50	1.50	1.50	1.50	1.50	1.50	1.50
	R^2_{adj}	0.9234	0.9234	0.9234	0.9234	0.9233	0.9234	0.9234
	RMSE	0.3088	0.3089	0.3089	0.3089	0.3089	0.3088	0.3088
	AIC	15211155	15211312	15211312	15211868	15213355	15210811	15210727
	BIC	-3048344	-3048186	-3048186	-3047631	-3046144	-3048676	-3048759

R^2_{adj} – adjusted coefficient of determination; RMSE – root mean square error; DW – Durbin–Watson; AIC – akaike information criterion; BIC – bayesian information criterion; FPR1 – first lactation fat to protein ratio; FPR2 – second lactation fat to protein ratio; FPR3 – third lactation fat to protein ratio.

Table 4. Average time (MT) and value (MY) of minimum fat to protein ratio predicted by Brody, Wood, Dhanoa, Sikka, Nelder, Rook and Dijkstra models by parity class

Trait	Statistics	Observed	Model						
			Brody	Wood	Dhanoa	Sikka	Nelder	Rook	Dijkstra
FPR1	MT	136	305	174	164	162	305	155	149
	MY	1.03	1.05	1.04	1.06	1.04	1.04	1.04	1.04
FPR2	MT	117	305	112	130	200	305	131	126
	MY	1.03	1.05	1.05	1.01	1.02	1.04	1.05	1.04
FPR3	MT	92	305	156	212	225	305	153	142
	MY	1.04	1.06	1.06	0.97	1.03	1.06	1.06	1.06

FPR1 – first lactation fat to protein ratio; FPR2 – second lactation fat to protein ratio; FPR3 – third lactation fat to protein ratio.

and the consequent tissue mobilization associated with stresses of calving and peak milk production [Buttchereit *et al.* 2010, Toni *et al.* 2011, Jamrozik and Schaeffer 2012]. In this period, an energy deficit leads to an increased fat synthesis in the udder, and inadequate intake of carbohydrates can cause an insufficient protein synthesis by ruminal bacteria resulting in a decrease in milk protein content [Buttchereit *et al.* 2009, Gürtler and Schweiger 2005]. Therefore, FPR may be an easy tool to differentiate between cows that can or cannot cope with the challenges of an early lactation [Jamrozik and Schaeffer 2012].
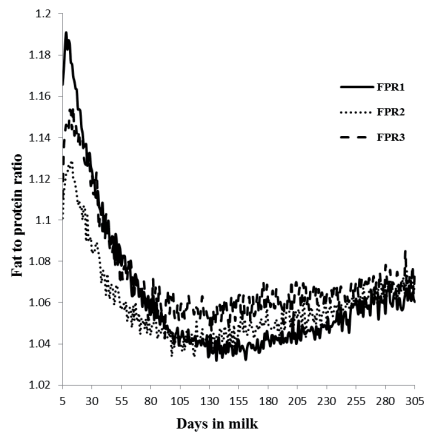
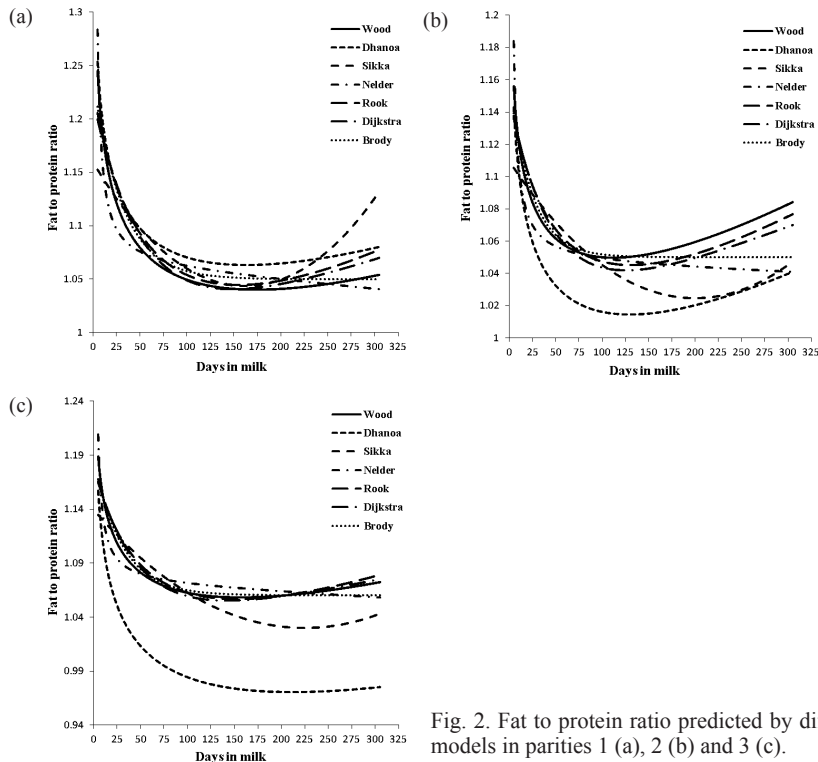Fig. 1. Milk fat to protein ratio in first three parities of Iranian Holsteins.

Fig. 2. Fat to protein ratio predicted by different models in parities 1 (a), 2 (b) and 3 (c).

Increasing trend of FPR nearing to the end of lactation after reaching the minimum could be due to increased energy requirements by heavily pregnant cows to support milk production and advanced fetal growth [Negussie *et al.* 2013]. Buttchereit *et al.* [2010] observed a slight increase in FPR toward the end of the lactation in German Holsteins.

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Cows with very high lipo-mobilization, as shown through a high FPR in early lactation, may be flagged for additional attention to prevent disease occurrence and milk loss [Duffield *et al.* 2003] or to diagnose postpartum problems earlier. An increase of FPR in a large number of early-lactation cows indicates a transition problem at the herd level. This situation should be carefully controlled by herd persons to prevent any problem in the early dry period and transition period [Grummer *et al.* 2004, Mulligan *et al.* 2006, Tony *et al.* 2011]. Similar trend for FPR variation over the lactation was reported in previous studies [Čejna and Chládek 2005, Buttchereit *et al.* 2010, Jamrozik and Schaeffer 2012].

It is worth noting that Dijkstra equation, as the best model for describing the lactation curve for FPR in this study, has two benefits over the Wood model, namely, the precise biological meaning of the parameters and the value of the intercept that is not null [Ghavi Hossein-Zadeh 2014]. The similarity of Wood and Dhanoa equations for modelling lactation curve of FPR could be expected because Dhanoa model is the reparameterized form of the Wood equation [Ghavi Hossein-Zadeh 2014]. Buttchereit *et al.* [2010] evaluated five lactation curve models (Ali and Schaeffer, Guo and Swalve, Wilmink, Legendre polynomials of third and fourth degree) fitted for FPR of milk and selected Ali and Schaeffer as the best fitting model for FPR in German Holsteins.

It seems there was no problem of residual autocorrelation for FPR because DW values were close to two. Positive autocorrelation is serial correlation in which a positive error for one observation increases the chance of a positive error for another observation [Ghavi Hossein-Zadeh 2014].

Goodness of fit statistics obtained from non-linear models was different between primiparous and multiparous cows. Differences between the lactation curve characteristics in primiparous and multiparous animals might be the reason for this result. The variation in the fit of non-linear equations may have arisen from the differences in mathematical form of the models, test day yields, number of test day records and number of days between tests [Ghavi Hossein-Zadeh 2014]. Differences in lactation curves are a combination of genetic and environmental elements [Pérochon *et al.* 1996]. To interpret the output data obtained from fitting mathematical models it is necessary to consider the biological and physiological properties of these equations.

The FPR is a trait with an intermediate optimum and its inclusion into breeding programs should be made carefully. Selection on a low FPR may be beneficial for cow robustness, but, on the other hand, a very low fat to protein ratio is known to be an indicator for acidosis [Seggewiß 2004].

The choice of an appropriate mathematical model to describe lactation curve of FPR could provide the possibility of direct selection on the level of the lactation curve for individual animal. Therefore, it is possible to develop an optimal strategy to obtain a desired shape of lactation curve through modifying the parameters of model. The change in FPR over the lactation might be an appropriate selection criterion in order to improve the energy status and minimize the metabolic disorders in dairy cows. This change can consequently reduce the cost of the production system. Of the seven

mathematical functions investigated in this study, Nelder model was fitted worst and Dijkstra model provided the best fit of the lactation curve for FPR in the first three lactations of Holstein cows because of the lower values of AIC and BIC compared with other models. According to DW values it seems that there was no problem of residual autocorrelation for FPR. Dijkstra equation was able to estimate the time at which FPR was minimum closer to the observed values compared with other equations, although minimum time was over-predicted by all models in each of the first three lactations.

REFERENCES

1. BAUMAN D.E., GRIINARI J.M., 2003 – Nutritional regulation of milk fat synthesis. ***Annual Review of Nutrition*** 23, 203-227.

2. BRODY S., RAGSDALE AC., TURNER C.W., 1923 – The rate of decline of milk secretion with the advance of the period of lactation. ***Journal of General Physiology*** 5, 441-444.

3. BURNHAM K.P., ANDERSON D.R., 2002 – Model Selection and Multimodel Inference: a Practical–theoretic Approach, 2nd edn. Berlin, Germany: Springer-Verlag.

4. BUTTCHEREIT N., STAMER E., JUNGE W., THALLER G., 2009 – Evaluation of five lactation curve models fitted for fat:protein ratio of milk and daily energy balance. ***Journal of Dairy Science*** 93, 1702-1712.

5. BUTTCHEREIT N., STAMER E., JUNGE W., THALLER G., 2010 – Evaluation of five lactation curve models fitted for fat-protein ratio of milk and daily energy balance. ***Journal of Dairy Science*** 93, 1702-1712.

6. ČEJNA V., CHLÁDEK G., 2005 – The importance of monitoring changes in milk fat to protein ratio in Holstein cows during lactation. ***Journal of Central European Agriculture*** 6, 539-545.

7. COLLARD B.L., BOETTCHER P.J., DEKKERS J.C.M., PETITCLERC D., SCHAEFFER L.R., 2000 – Relationships between energy balance and health traits of dairy cattle in early lactation. ***Journal of Dairy Science*** 83, 2683-2690.

8. DHANOA M.S., 1981 – A note on an alternative form of the lactation model of wood. ***Animal Production*** 32, 349-351.

9. DIJKSTRA J., FRANCE J., DHANOA M.S., MAAS J.A., HANIGAN M.D., ROOK A.J., BEEVER D.E., 1997 – A model to describe growth patterns of the mammary gland during pregnancy and lactation. ***Journal of Dairy Science*** 80, 2340-2354.

10. DIMAURO C., CAPPIO-Borlino A., MACCIOTTA N.P.P., PULINA G., 2007 – Use of a computer-aided design to develop a stress simulation model for lactating dairy sheep. ***Livestock Production Science*** 106 (2-3), 200-209.

11. DOEPEL L., LAPIERRE H., KENNELLY J.J., 2002 – Peripartum performance and metabolism of dairy cows in response to prepartum energy and protein intake. ***Journal of Dairy Science*** 85, 2315-2334.

12. DUFFIELD T.F., LEBLANC S., BAGG R., LESLIE K., TEN HAG J., DICK P., 2003 – Effect of a monensin controlled release capsule on metabolic parameters in transition dairy cows. ***Journal of Dairy Science*** 86, 1171-1176.

13. EICHER R., 2004 – Evaluation of the metabolic and nutritional situation in dairy herds: diagnostic use of milk components. *Medecin Veterinaire du Quebec* 34, 36-38.

14. FRANCE J., THORNLEY J.H.M., 1984 – Mathematical Models in Agriculture. Butterwoths, London.

15. GAHLOT G.C., GAHLOT R.S., JAIRATH L.K., 1988 – Pattern of lactation curve in Rathi cattle. *Indian Journal of Animal Science* 58 (9), 1112-1114.

16. GHAVI HOSSEIN-ZADEH N., 2013 – Effects of main reproductive and health problems on the performance of dairy cows: a review. *Spanish Journal of Agricultural Research* 11(3), 718-735.

17. GHAVI HOSSEIN-ZADEH N., 2014 – Comparison of non-linear models to describe the lactation curves of milk yield and composition in Iranian Holsteins. *The Journal of Agricultural Science* 152, 309-324.

18. GOFF J.P., HORST R.L., 1997 – Physiological changes at parturition and their relationship to metabolic disorders. *Journal of Dairy Science* 80, 1260-1268.

19. GRUMMER R.R., MASHEK D.G., HAYIRLI A., 2004 – Dry matter intake and energy balance in the transition period. *Veterinary Clinics of North America: Food Animal Practice* 20, 447-470.

20. GÜRTLER H., SCHWEIGER F.J., 2005 – Physiologie der Laktation. In: W. von Engelhard, C. Breves (ed.), Physiologie der Haustiere. Vol. 2. Enke Verlag, Stuttgart, Germany, pp. 552-573.

21. HEUER C., SCHUKKEN Y.H., DOBBELAAR P., 1999 – Postpartum BCS and results from the first test day milk as predictors of disease, fertility, yield, and culling in commercial dairy herds. *Journal of Dairy Science* 82, 295-304.

22. INGVARTSEN K.L., ANDERSEN J.B., 2000 – Integration of metabolism and intake regulation: A review focusing on periparturient animals. *Journal of Dairy Science* 83, 1573-1597.

23. JAMROZIK J., SCHAEFFER L.R., 2012. Test-day somatic cell score, fat-to-protein ratio and milk yield as indicator traits for sub-clinical mastitis in dairy cattle. *Journal of Animal Breeding and Genetics* 129, 11-19.

24. JÓŹWIK, A., KRZYZEWSKI, J., STRZAŁKOWSKA, N., POŁAWSKA, E., BAGNICKA, E., WIERZBICKA, A., NIEMCZUK, K., LIPIŃSKA, P., HORBAŃCZUK, J.O., 2012a – Relations between the oxidative status, mastitis, milk quality and disorders of reproductive functions in dairy cows - a review. *Animal Science Papers and Reports* 30 (4), 297-307.

25. JÓŹWIK, A., STRZAŁKOWSKA, N., BAGNICKA, E., GRZYBEK, W., KRZYZEWSKI, J., POŁAWSKA, E., KOŁATAJ, A., HORBAŃCZUK, J.O., 2012b – Relationship between milk yield, stage of lactation, and some blood serum metabolic parameters of dairy cows *Czech Journal of Animal Science* 57 (8), 353-360.

26. LOEFFLER S.H., DE VRIES M.J., SCHUKKEN Y.H., 1999 – The effects of time of disease occurrence, milk yield and body condition on fertility of dairy cows. *Journal of Dairy Science* 82, 2589-2600.

27. LOMBARD C.S., 2006 – Hierarchical Bayesian modelling for the analysis of the lactation of dairy animals. Ph.D Dissertation. University of the Free State Bloemfontein. Pretoria, South Africa. Available at: http://etd.uovs.ac.za/ETD-db/theses/available/etd-11032006-105824/unrestricted/LombaardCS.pdf. Accessed: 26 March 2015.

28. MULLIGAN F.J., O'GRADY L., RICE D.A., DOHERTY M.L., 2006 – A herd health approach to dairy cow nutrition and production disease of the transition cow. *Animal Reproduction Science* 96, 331-353.

29. NEGUSSIE E., STRANDÉN I., MÄNTYSAARI EA., 2013 – Genetic associations of test-day fat: protein ratio with milk yield, fertility, and udder health traits in Nordic Red cattle. *Journal of Dairy Science* 96, 1237-1250.

30. NELDER J.A., 1966. Inverse polynomials, a useful group of multi-factor response functions. *Biometrics* 22, 128-141.

31. NISHIURA A., SASAKI O., AIHARA M., TAKEDA H., SATOH M., 2015 – Genetic analysis of fat-to-protein ratio, milk yield and somatic cell score of Holstein cows in Japan in the first three lactations by using a random regression model. *Animal Science Journal* 86, 961-969.

32. PÉROCHON L., COULON J.B., LESCOURRET F., 1996 – Modelling lactation curves of dairy cows with emphasis on individual variability. *Animal Production* 63, 189-200.

33. PODPEČAN O., MRKUM J., ZRIMŠEK P., 2008 – Diagnostic evaluation of fat to protein ratio in prolonged calving to conception interval using receiver operating characteristic analyses. *Reproduction in Domestic Animals* 43, 249-254.

34. PULINA G., NUDDA A., 2001 – La produzione del latte. In L'alimentazione degli ovini da latte (ed. G. Pulina), pp. 9-31. Avenue Media, Bologna, Italy.

35. REIST M., ERDIN D., VON EUW D., TSCHUEMPERLIN K., LEUENBERGER H., CHILLIARD Y., HAMMON HM., MOREL C., PHILIPONA C., ZBINDEN Y., KUENZI N., BLUM J.W., 2002 – Estimation of energy balance at the individual and herd level using blood and milk traits in high-yielding dairy cows. *Journal of Dairy Science* 85, 3314-3327.

36. ROOK A.J., FRANCE J., DHANOA M.S., 1993 – On the mathematical description of lactation curves. *The Journal of Agricultural Science* 121, 97-102.

37. SAS, 2002 – SAS User's guide v. 9.0: Statistics. SAS Institute, Inc, Cary, NC.

38. SCHWARZ G.E., 1978 – Estimating the dimension of a model. *Annals of Statistics* 6 (2), 461-464.

39. SEGGEWIß S., 2004 – Überprüfung der Bedeutung von Milchinhaltsstoffen für die Beurteilung der Energie-, Protein- und Strukturversorgung von HF-Kühen. Diss. Hannover. Available at: http://elib.tiho-hannover.de/dissertations/seggewisss_ws04.pdf. Accessed 26 March 2015.

40. SIKKA L.C., 1950 – A study of lactation as affected by heredity and environment. *Journal of Dairy Research* 17, 231-252.

41. SILVESTRE A.M., PETIM-BATISTA F., COLASO J., 2006 – The accuracy of seven mathematical functions in modelling dairy cattle lactation curves based on test-day records from varying sample schemes. *Journal of Dairy Science* 89, 1823-1821.

42. STERI R., DIMAURO C., CANAVESI F., NICOLAZZI E.L., MACCIOTTA N.P.P., 2012 – Analysis of lactation shapes in extended lactations. *Animal* 6, 1572-1582.

43. STRZALKOWSKA, N., JÓŹWIK, A., BAGNICKA, E., KRZYZEWSKI, J., HORBAŃCZUK, K., PYZEL, B., HORBAŃCZUK, J.O., 2009 – Chemical composition, physical traits and fatty acid profile of goat milk as related to the stage of lactation. *Animal Science Papers and Reports* 27 (4), 311-320.

44. STRZAŁKOWSKA, N. JÓŹWIK, A., BAGNICKA, E., KRZYZEWSKI, J., HORBAŃCZUK, K., PYZEL, B., SŁONIEWSKA, D., HORBAŃCZUK, J.O., 2010 – The concentration of free fatty acids in goat milk as related to the stage of lactation, age and somatic cell count. *Animal Science Papers and Reports* 28 (4), 389-395.

45. TONI F., VINCENTI L., GRIGOLETTO L., RICCI A., SCHUKKEN Y.H., 2011 – Early lactation ratio of fat and protein percentage in milk is associated with health, milk production, and survival. *Journal of Dairy Science* 94, 1772-1783.

46. TOZER P.R., HUFFAKER R.G., 1999 – Mathematical equations to describe lactation curves for Holstein-Friesian cows in New South Wales. *Australian Journal of Agricultural Research* 50, 431-440.

47. VEERKAMP R.F., OLDENBROEK J.K., VAN DER GAAST H.J., VAN DER WERF J.H.S., 2000 – Genetic correlation between days until start of luteal activity and milk yield, energy balance, and live weights. *Journal of Dairy Science* 83, 577-583.

48. WATHES D.C., FENWICK M., CHENG Z., BOURNE N., LLEWELLYN S., MORRIS DG., KENNY D., MURPHY J., FITZPATRICK R., 2007 – Influence of negative energy balance on cyclicity and fertility in the high producing dairy cow. *Theriogenology* 68(Suppl. 1), S232-S241.

49. WOOD PDP., 1967 – Algebraic models of the lactation curves in cattle. *Nature* 216, 164-165.