Lactation curve model with explicit representation of perturbations as a phenotyping tool for dairy livestock precision farming.

Ben Abdelkrim Ahmed[1, 2], Puillet Laurence[1], Gomes Pierre[1, 3], Martin Olivier[1]

[1] UMR MoSAR, INRA, AgroParisTech, Université Paris-Saclay, 75005, Paris, France

[2] GABI, INRA, AgroParisTech, Université Paris-Saclay, 78350, Jouy-en-Josas, France

[3] NEOVIA, 56250, Saint-Nolff, France

About the Authors

Ahmed Ben Abdelkrim: Conceptualization, Methodology, Visualization, Software implementation, Writing – Original draft preparation

Laurence Puillet: Conceptualization, Data curation, Writing – review & editing

Pierre Gomes: Conceptualization, Methodology, Preliminary tests

Olivier Martin: Conceptualization, Supervision, Writing – review & editing

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Dairy Goats, Milk Yield, Individual Variability, Resilience

Abstract

Background

Understanding the effects of environment on livestock provides valuable information on how farm animals express their production potential, and on their welfare. Ruminants are often confronted with perturbations that affect their performance. Evaluating the effect of these perturbations on animal performance could provide metrics to quantify how animals cope with their environment and therefore better manage them. In dairy systems, milk production records can be used to evaluate this effect because (1) they are easily accessible, (2) the overall dynamics throughout the lactation process have been widely described, and (3) perturbations often occur and cause milk loss. In this study, a lactation curve model with explicit representation of perturbations was developed.

Methods

The perturbed lactation model is composed of two components. The first one describes a theoretical unperturbed lactation curve (unperturbed lactation model), and the second describes deviations from the unperturbed lactation model. The model was fitted on 319 complete lactation data from 181 individual dairy goats allowing the characterization of individual perturbations in terms of their starting date, intensity, and shape.

Results

The fitting procedure detected a total of 2354 perturbations with an average of 7.40 perturbations per lactation. Loss of production due to perturbations varied between 2 % and 19 %. Results show that it is not the number of perturbations is not the major factor explaining the loss in milk yield over the lactation, suggesting that there are different types of animal response to disturbing factors.

Conclusions

By incorporating explicit representation of perturbations, the model allowed the characterization of potential milk production, deviations induced by perturbations, and thereby comparison between animals. These indicators are likely to be useful to move from raw data to decision solutions in dairy production.

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INTRODUCTION

In the context of precision livestock farming, simple interpretive tools are required to convert raw time series datasets, now routinely recorded in animals, into useful information for on-farm decision-making. Such tools are not only expected to provide farmers with good information on performance level of individual animals, but also to detect pathological, nutritional or environmental problems affecting production traits at individual or herd scales. In dairy systems, it is well known that milk yield can be affected by problems such as udder health problems [1], lameness [2], heat stress [3] or nutritional challenges [4]. Such problems induce perturbations in the course of the lactation process and result in a serrated shape pattern in the lactation curve. These perturbations can be seen as deviations of the lactation curve from its typical profile. This typical profile reflects that lactation is a physiological process common to mammal females and as a result, its expression through time follows a general pattern [5]. It can be described in 3 phases. The first phase starts after parturition with the initial milk yield increasing to a maximum or peak yield. The second phase is a plateau-like period in which milk yield is maintained for a more or less long time. The third phase is the decrease from the peak yield. This last phase can be divided into two parts according to the speed of decrease, the first one corresponding to an approximately constant declining rate of milk production after the peak yield and the second corresponding to an acceleration of the decline as pregnancy progresses before the start of the dry period when lactation stops [6–8]. Modelling the lactation curve is a long standing issue [9] and numerous authors have proposed mathematical models allowing the characterization of milk yield dynamics, *i.e.*, the transformation of a series of temporal data into a vector of estimated parameters via a fitting procedure. The most famous and most used model is the one of Wood published in 1967 [10]. The overall objective of lactation models is to reduce the variability or noise in data by extracting a profile and therefore being able to characterize an average animal milk production or to compare the production of different animals. This strategy of using lactation models as phenotyping tools has been very useful in the past years (for instance, test-day models for genetic selection) and in a context of scarce raw data. An important limitation of these modelling approaches is that short-term perturbations are removed during fitting procedure in order to extract an unperturbed phenotype, corresponding to a typical lactation curve. However, characterizing perturbations can be highly relevant for better understanding the resilience of milk production and for making management decisions. Evaluating the effect of perturbations on animal performance could provide metrics to quantify how animals cope with their environment, and therefore better manage them. Taking into account this type of information can provide a proxy to estimate the frequency and severity of disorders such as clinical mastitis [11]. Studying perturbations in lactation curves also makes it possible to compare animals facing the same stress and detect the ones with the greatest adaptive capacities. Finally, the on-farm early detection of perturbations in milk yield can provide farmers with an alert system on udder health. Recently, Huybrechts et al. [12] tested and developed the synergistic control concept for early detection of anomalies in dairy cows based on detection of shifts in milk yield per hour. Of the 49 mastitis cases, 31 cases were detected using this methodology at the same time or earlier than they were detected by the farmer.

The need for incorporating perturbations into lactation curve models is also driven by the development of precision livestock farming. Now, we have more frequent and reliable data and we can move from the logic of reducing variability around average profiles to the logic of extracting variability to provide information as such. High throughput data has led to the development and use of statistical methods to understand perturbations (*e.g.* Codrea et al. [13]). However, such smoothing methods are limited by their lack of an a priori representation of the typical "unperturbed" lactation curve. As such, the quantification of perturbations in such models is underestimated, especially for perturbations of long duration. A final limitation of these purely statistical methods is that the model coefficients in themselves do not have direct biological meaning. There is thus a lack of tools for phenotyping milk production with a systemic representation of perturbations.

We developed a Perturbed Lactation Model (PLM) that incorporates an explicit representation of perturbations and that converts individual raw time-series data into biological meaningful parameters. The fitting procedure of PLM allows the detection and the characterization of perturbations in milk time-series. The objective of the present paper is (1) to introduce the PLM model and the explicit representation of perturbations, (2) to describe the use of PLM to detect and characterize perturbations in milk yield time series with an example in dairy goats, and (3) to illustrate the role of PLM as a phenotyping tool by analyzing the variability in perturbed lactation curves on the basis of the fitting results obtained on the dairy goat dataset.

MATERIALS AND METHODS

The Perturbed Lactation Model (PLM) is composed of a lactation model, denoted Y^*, describing the theoretical unperturbed dynamics of milk yield along the lactation, and a perturbation model, denotedπ, describing deviations from the lactation model.

The dynamics of daily milk yield ($Y(t)$, in kg) during the lactation is thus given by:

$$Y(t) = Y^*(t) \cdot \pi(t)$$

where t is the time after parturition in days.

Unperturbed lactation model

Among the numerous mathematical models developed to study lactation curves, the incomplete Gamma function proposed by Wood [10] has been widely used in different mammals (*e.g.* rabbits [14], sheep [15]). This model gives a general expression for the dynamics of milk yield along the lactation. In this article, we have selected this model as an example to define the unperturbed lactation curve. Because the structure of PLM is generic, any other lactation model can be used.

The Wood model is given by:

$$Y^*(t) = a \cdot t^b \cdot e^{-c \cdot t}$$

where $Y^*(t)$ is the unperturbed daily milk yield in kg, t is the time in days after parturition and$a$, b, c are positive parameters that determine the shape of the lactation curve (a scales the general level of the curve, $b$controls the type and magnitude of the curvature of the function, and c regulates the rate of decrease in milk yield after the lactation peak). Values of these parameters can be used to calculate some essential features of the lactation curve such as the time of peak yield (b/c, in days), the lactation persistency, *i.e.*, the extent to which peak yield is maintained ($-(b+1) \cdot ln(c)$ in kg.d^{-1}), or the peak yield ($a \cdot (b/c)^b \cdot e^{-b}$ in kg)[16].

Perturbation model

The perturbation model is based on the idea that each single perturbation *I* affecting lactation dynamics can be described as a transient proportional decrease in milk yield, through a sequence of collapse and recovery. Each perturbation can thus be modelled by way of a 3-compartment model (Figure 1) representing the dynamics of the proportion of milk withdrawn from the theoretical unperturbed yield.

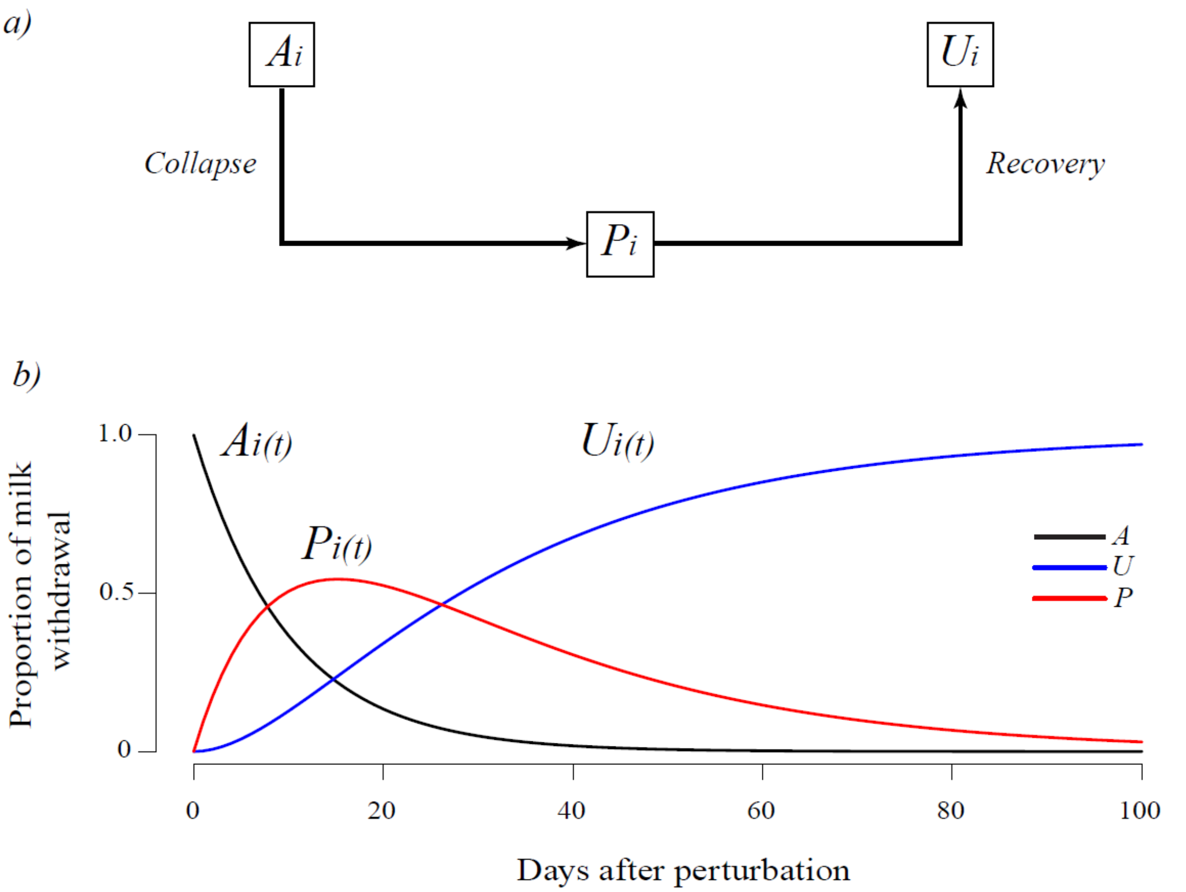

Figure 1. Conceptual model of a single perturbation. A: proportion affected by the perturbation, P: proportion effectively affected by the perturbation, U: proportion unaffected by the perturbation.a) Model diagram andb) Solution dynamics.

The three compartments of the model are: A_i, the maximal proportion potentially affected by the i^{th} perturbation, U_i, the proportion unaffected by the i^{th} perturbation, and P_i, the proportion effectively affected by the i^{th} perturbation. Given the structure of the compartmental model, forming a path from A_i to U_i through P_i, and given that the model is defined such as $A_i + P_i + U_i = 1$, the dynamics of P_i represents the proportional deviation in milk yield.

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The perturbation model for a single perturbation i is defined by the following simple differential system:

$$if\, t \geq t_P: \begin{cases} \dfrac{dA_i}{dt} = -k_{1,i} \cdot A_i \\ \dfrac{dP_i}{dt} = +k_{1,i} \cdot A_i - k_{2,i} \cdot P_i \\ \dfrac{dU_i}{dt} = +k_{2,i} \cdot P_i \end{cases} otherwise: \begin{cases} \dfrac{dA_i}{dt} = 0 \\ \dfrac{dP_i}{dt} = 0 \\ \dfrac{dU_i}{dt} = 0 \end{cases}$$

with the following initial conditions at parturition time ($t = 0$):

$$\begin{cases} A_i(0) = k_{0,i} \\ P_i(0) = 0 \\ U_i(0) = 1 - k_{0,i} \end{cases}$$

and where t_{P_i} is the time of start of the *i*th perturbation, $k_{0,i}$ is the parameter of intensity of the *i*th perturbation ($k_{0,i} \in]0;1]$), $k_{1,i}$ is the parameter of collapse speed of the *i*th perturbation and $k_{2,i}$ is the parameter of recovery speed of the *i*th perturbation.

Assuming that $k_{1,i} \neq k_{2,i}$, the algebraic solution of this differential system is given by:

$$\begin{cases} A_i(t) = k_{0,i} \cdot e^{-k_{1,i} \cdot \Delta_i(t)} \\ P_i(t) = \dfrac{k_{0,i} \cdot k_{1,i}}{k_{1,i} - k_{2,i}} \cdot \left(e^{-k_{2,i} \cdot \Delta_i(t)} - e^{-k_{1,i} \cdot \Delta_i(t)}\right) \\ U_i(t) = 1 - \dfrac{k_{0,i}}{k_{1,i} - k_{2,i}} \cdot \left(k_{1,i} \cdot e^{-k_{2,i} \cdot \Delta_i(t)} - k_{2,i} \cdot e^{-k_{1,i} \cdot \Delta_i(t)}\right) \end{cases}$$

Where $\Delta_i(t)$ is the elapsed time since the beginning of the *i*th perturbation and is given by:

$$\Delta_i(t) = \begin{cases} 0 & if\, t < t_{P_i} \\ t - t_{P_i} & if\, t \geq t_{P_i} \end{cases}$$

Finally, the perturbation model, including n individual perturbations affecting the lactation curve is given by:

$$\pi(t) = \prod_{i=1}^{n} \left(1 - P_i(t)\right)$$

Model Formalism

The detailed algebraic formula of PLM with n individual perturbations is given by:

$$Y(t) = a \cdot t^b \cdot e^{-c \cdot t} \cdot \prod_{i=1}^{n} \left(1 - \frac{k_{0,i} \cdot k_{1,i}}{k_{1,i} - k_{2,i}} \cdot \left(e^{-k_{2,i} \cdot \Delta_i(t)} - e^{-k_{1,i} \cdot \Delta_i(t)} \right) \right)$$

The model includes the three parameters of the Wood model ($a, b,$ and c) to define the unperturbed lactation curve, one parameter to define the number of perturbations affecting the lactation curve (n), and four parameters per individual perturbation i (t_{P_i}, $k_{0,i}$, $k_{1,i}$, and $k_{2,i}$) so that the total number of parameters to define PLM is equal to $4 + 4 \cdot n$.

A simulation of PLM with five perturbations over 300 days of lactation is shown in Figure 2 as an illustration of the model behavior.

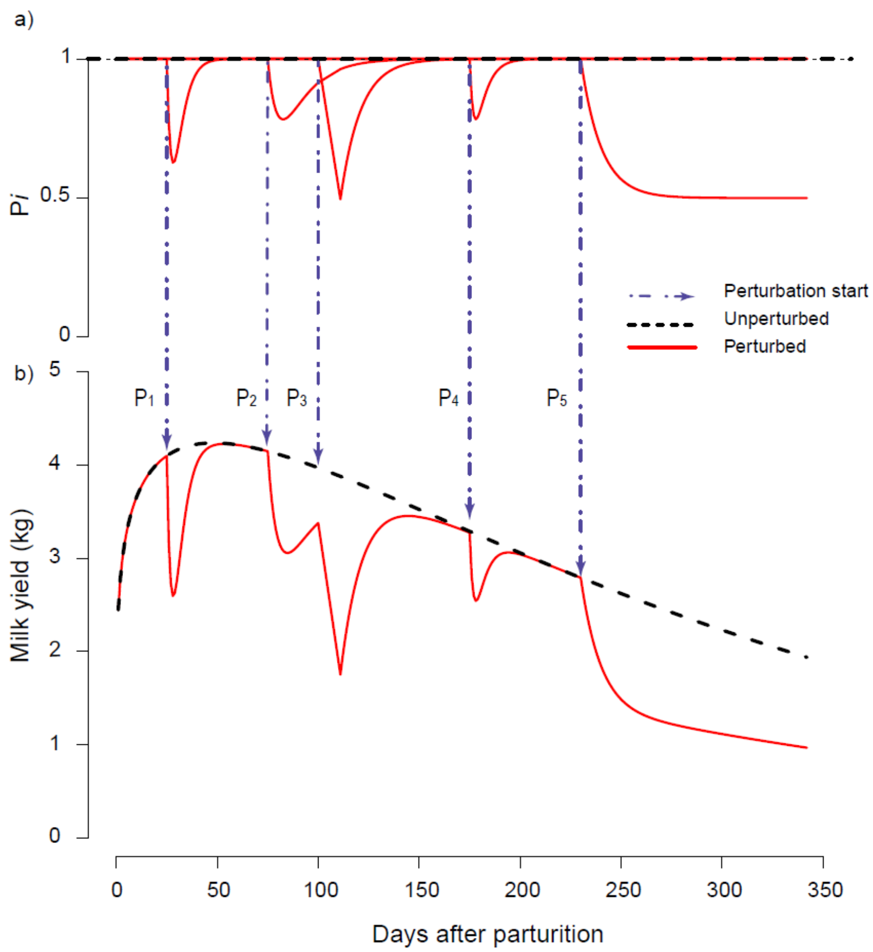

Figure 2. Example of a simulation of the Perturbed Lactation Model (PLM) including five perturbations with a) individual perturbations dynamics expressed as the proportion of unperturbed lactation curve (*Pi*) and b) unperturbed and perturbed milk yield dynamics.

Perturbations are considered individually, so that a perturbation can occur within another one (see P_3 in Figure 2 at $t_{P_3} = 100$). Given that individual perturbations are proportional deviations multiplied between them, when a perturbation is added during another perturbation, the new perturbation is a proportion of the already perturbed curve. Moreover, perturbations can be used to simulate the effect of pregnancy (see P_5 in Figure 2 at $t_{P_5} = 225$) with the recovery parameter $k_{2,i}$ set to zero.

Fitting procedure

PLM is aimed at detecting perturbations in milk yield time-series data and thus provide estimates of (1) a theoretical unperturbed lactation curve and (2) the number, timing and shape of the perturbations leading to the observed perturbed lactation curve. A dedicated algorithm was developed in R (R Core Development Team, 2018) with the aim of fitting PLM on lactation data and deriving parameter estimates $a, b,$ and c to characterize the unperturbed lactation curve, n to define the number of perturbation and parameter estimates $\left(t_{P_i}, k_{0,i}, k_{1,i}, \text{and } k_{2,i}\right)$ for each i^{th} detected perturbation. Preliminary tests have shown that repeated fittings using different starting values can lead to the detection of perturbations differing in total number and detection order. This raised the question of the theoretical identifiability of the model parameters (for further details on identifiability see [17]) and of the use of a stop criterion to estimate n. The structure of the model does not allow a classical identifiability analysis to be performed if n is unknown. However, by using the software DAISY (Differential Algebra for Identifiability of Systems[18]), we could assess that for one perturbation the PLM parameters are locally identifiable. To facilitate the identification of the model parameters, we adopted a fitting strategy in two steps: first, performing numerous repeated fittings to estimate the most frequent number of perturbations. In the second step, we fixed as known the number of perturbations detected in step 1 and proceed to estimate the remaining parameters of the model. This strategy ultimately makes it possible to estimate an optimal number of perturbations and facilitates the estimation of the model parameters.

In the following section, PLM$_n$ stands for PLM with n perturbations, k_{W_n} stands for the triplet of parameters (a, b, c) of Wood's model estimated with$n$perturbations (n ranging from 0 to n_{max}) and $k_{P_{i,n}}$ stands for the quadruplet$\left(t_{P_i}, k_{0,i}, k_{1,i}, k_{2,i}\right)$ of the i^{th} perturbation (n ranging from 1 to n_{max}).

The nls.multstart package [19] performing non-linear least squares regression with the Levenberg-Marquardt algorithm and with multiple starting values was used for each single fit. Two different sampling schemes of starting parameters were used: random sampling of starting parameters from a uniform distribution within the starting parameter bounds or selection of combinations of starting parameters at equally spaced intervals across each of the starting parameter bounds. These two fitting methods are hereafter referred to as 'shotgun search' and 'gridstart search' respectively. Starting parameter bounds are defined as follows: a: $[0; 100]$; b: $[0; 1]$; c: $[0; 1]$; t_{P_i}: $[t_0; t_3]$(where t_0 and t_3 are the times of first and last records of the dataset); $k_{0,i}$: $[0; 1]$; $k_{1,i}$: $[0; 10]$;$k_{2,i}$: $[0; 10]$. For the 'shotgun search', the number of random combinations of starting parameters was set to 100 000. For the 'gridstart search', the number of combinations of starting parameters (*i.e.*, the size of the grid), was set to five for parameters a, b, c, $k_{0,i}$, $k_{1,i}$, $k_{2,i}$ and to 10 for the parameter t_{P_i}.Consequently, for the fit of one perturbation (*i.e.*, estimating 3 + 4 = 7 parameters) the number of tested combinations of starting parameters was 7^6 x 10 = 1176490. For both search methods, the best model was selected on the basis of the lowest Akaike Information Criterion (AIC) score [20].

The whole fitting procedure includes repetitions of a fitting sequence that proceeds by successive addition of perturbations. This fitting sequence is defined in such a way that the estimate of the parameters of each new perturbation is obtained while the parameters of the previously added perturbations are kept fixed. Therefore, the fitting of PLM$_i$ provides parameters estimates for the new added i^{th} perturbation and for a new version of Wood model's parameters k_{W_i} (*i.e.*, each time a new perturbation is added, a new version of the unperturbed lactation is refined). For a given lactation dataset composed of daily milk yield records, the preliminary fitting of PLM_0 (*i.e.*, the original Wood's model without any perturbation) was first performed to estimate k_{W_0}. Then, the fitting sequence starts by the fitting of PLM_1 (*i.e.*, PLM with 1 perturbation) thus providing estimates $k_{W_1}$and $k_{P_{1,1}}$. Then, the fitting of PLM_2 consists in estimating k_{W_2} and $k_{P_{2,2}}$ with $k_{P_{1,2}}$ fixed equal to $k_{P_{1,1}}$. Then, the fitting of PLM_3 consists in estimating k_{W_3} and $k_{P_{3,3}}$ with $k_{P_{1,3}}$ and $k_{P_{2,3}}$ fixed equal to $k_{P_{1,2}}$ and $k_{P_{2,2}}$, respectively. The procedure is applied stepwise until the maximum number of perturbation n_{max} is reached. This maximum number is an *a priori* user defined value to fix a stop criterion. Preliminary tests have shown that setting $n_{max} = 15$ was sufficient. The end of the fitting sequence consists in reordering the n_{max} detected perturbations in decreasing order according to the time of perturbation t_{P_i} (the original obtained order of perturbations is based on the opportunities found by the fitting procedure to improve the goodness of fit for each added perturbation).

Finally, the whole fitting procedure is carried out following the 3 following steps:

Step1: Repeat 100 times the fitting sequence with the 'shotgun search' and $n_{max} = 15$.

Step2: Compare the fitting results of the 100 repetitions obtained in step1 and identify perturbations systematically detected at t_{P_i}± 3 days. This was performed by counting, for the 15 perturbations over the 100 fitting results, the number of occurrences of the rounded value $t_{P_i}^* = round\left(t_{P_i}/7\right) \cdot 7$. This step provides the optimal number of perturbations denoted N with an estimate of t_{P_i} for each perturbation (calculated as the median of the t_{P_i} with the same rounded value $t_{P_i}^*$).

Step3: Perform the fitting sequence with the 'gridstart search', with $n_{max} = N$ and with starting parameters bounds for each t_{P_i} reset to $\left[t_{P_i} - 10\,; t_{P_i} + 10\right]$. This last fit provides the final estimates k_{W_N} and $\left(k_{P_{1,N}}, \ldots, \text{and } k_{P_{N,N}}\right)$ characterizing respectively the best fit for the unperturbed model and the N detected perturbations. The Root Mean Square Error was calculated to indicate the goodness-of-fit of PLM$_N$. Additionally, the percentage of loss $'L'$ was calculated using the formula $L = 1 - S_0/S_N$ where S_0 and S_N are the total milk yield over $[t_0; t_3]$ calculated with Wood's model without perturbation using parameters a, b and c from PLM$_N$ and PLM$_N$ (i.e., Wood's model with N perturbations).

To provide complementary information on lactation time-series and refine PLM outputs analysis, the model of Grossman et al. [21] was also fit to lactation data as described in Martin and Sauvant [22]. This fitting cuts the lactation period into three stages corresponding to early, middle and late stages (respectively intervals $[t_0; t_1]$: increasing phase, $[t_1; t_2]$: plateau-like phase and $[t_2; t_3]$: decreasing phase). This triphasic model, based on a smoothing logistic transition between intersecting straight lines, specifies the cut points of the three stages (instead of a priori number of days in milk). This fit was performed using the 'gridstart search' with $[t_0; t_3]$ as starting parameters bounds for the interval terminals $t_1$andt_2.

Dairy goat dataset

In this study we used data from 319 lactations(126 primiparous and 193 multiparous; parity ranging from 1 to 7) including 80773 milk records from the dairy goat herd of the INRA-AgroParisTech Systemic Modelling Applied to Ruminants research unit (Paris, France) between 2015 and 2018. Data concerned 181 goats (94 Alpine and 87 Saanen) born between 2009 and 2017. Records are shown in supplementary Figure 1 by breed and parity. All lactations considered had at least one record in the first 5 days of lactation and a last record between 150 and 350 days of lactation (no extended lactation included).

Statistical analysis

All statistical analyses were performed using R (R Core Development Team, 2018).

Fixed effects of breed (Saanen *vs.* Alpine) and parity (1 *vs.*2 and more) were tested on root mean square error (RMSE), on parameters$a, b,$ and$c$, on estimated peak milk yield, peak time and total milk yield over $[t_0; t_3]$ for Wood and PLM models, and on the estimated number of perturbation and percentage loss for PLM model, with a mixed analysis of variance model with goat as a random factor. Fixed effect of lactation stage (early *vs.* middle *vs.* late) was tested on RMSE and on PLM parameters $t_P, k_0, k_1, k_2$with a mixed analysis of variance model with parity as a random factor. Pearson linear correlations were calculated for PLM parameters: intra-class of breed and parity for$a, b, c, N,$ and L and intra-class of stage of lactation for $t_P, k_0, k_1,$ and k_2.

RESULTS

Lactation duration ranged from t_0= 1.21 ± 0.64 to t_3= 270.30 ± 40.77 days in milk. Early, middle and late lactation stages determined with Grossman's model were [1.21, 34.45], [34.45, 171.05] and [171.05, 270.30], respectively.

Fitting

The fitting procedure converged for the 319 lactations and detected a total of 2354 perturbations with an average of 7.40 perturbations per lactation. Figure 3 shows the fitting of PLM on one lactation dataset. The fitting results on individual lactations exhibiting the minimum and maximum values for respectively the RMSE (0.11 kg and 0.41 kg) are provided in supplementary Figure 2. The number of perturbations varied between 4 and 11, the percentage loss between 2 % and 19 %, the total unperturbed milk yield was between 393.56 kg and 1557 kg and the record interval length $t_0 - t_3$ was between ([1, 5] to [165, 358] in days). During the first fitting steps, the Wood's parameters were stabilized on average after the detection of the first 4 perturbations (supplementary Figure 3). This indicates the robustness of the unperturbed curve.

Descriptive statistics of the results obtained from the fitting procedure of PLM_n are given in Table 1 by breed and parity and are compared to the results obtained with PLM_0, corresponding to an adjustment of the Wood model without any perturbation. The value for the parameter *a* greatly increased between the Wood model and PLM_n. The values for parameters *b* and *c* decreased between the Wood model and PLM_n. As a consequence, values for peak milk and peak time increased between the Wood model and PLM_n. Both models did not give a similar level of variance of error according to breed or parity level. Regarding the quality of fitting, the RMSE values showed a fairly significant decline between the Wood model and PLM_n (0.17 ± 0.08 kg). Considering explicit perturbations in the fitting of the

Wood model with PLM compare to fitting directly the Wood function to data led to a decrease in RMSE, reflecting an improvement in the quality of the adjustment procedure.

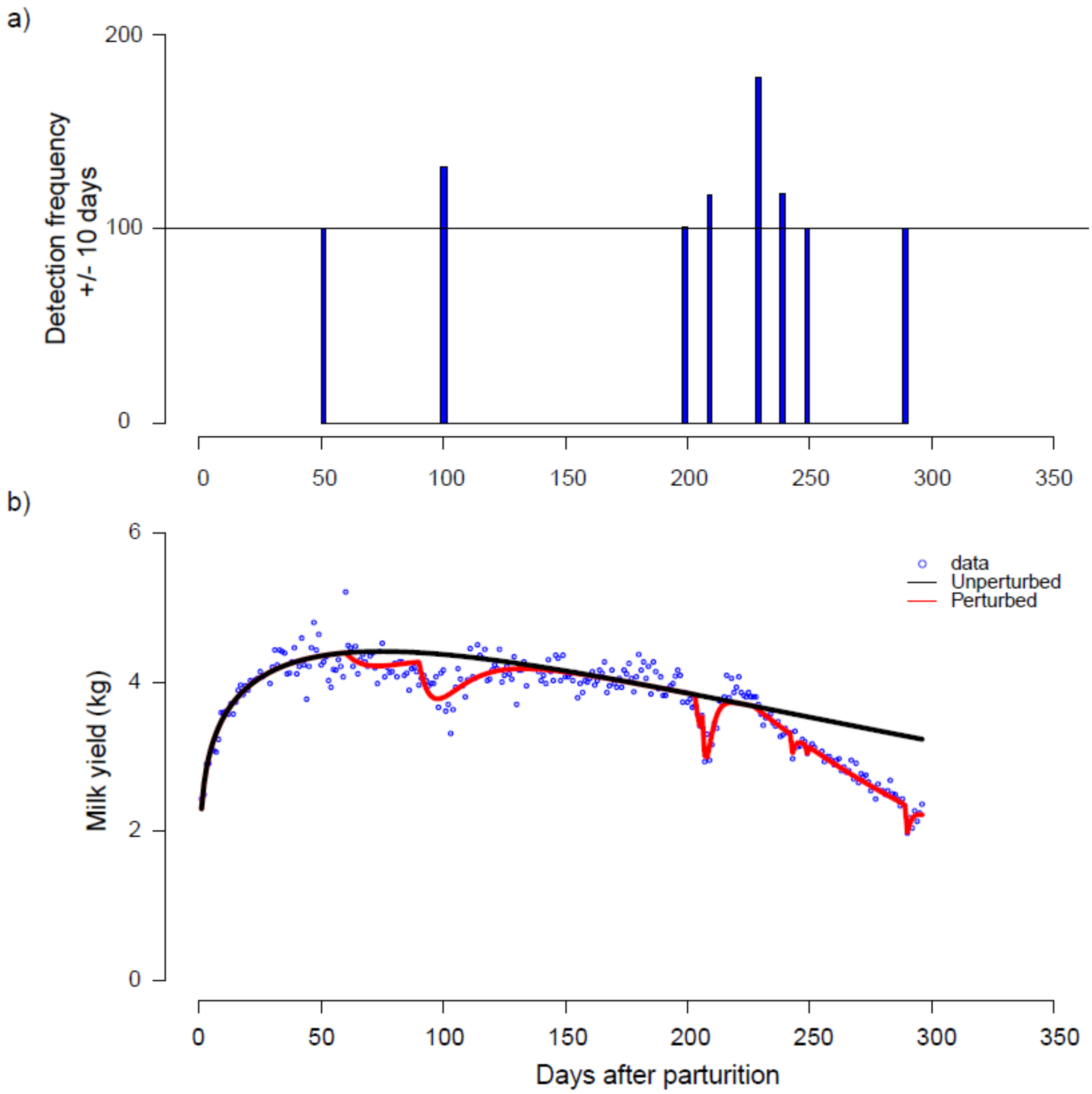

Figure3. Example of the perturbed lactation model fitting procedure result on a lactation dataset. a) frequency of detection of a single perturbation within ± 10 days; b: unperturbed and perturbed lactation models plotted against data.

Table 1. Results of the fitting procedure.

	All				**SAA (143)**				**ALP (176)**					
model	1 (126♦)		2 + (193♦)		1 (59♦)		2 + (84♦)		1 (67♦)		2 + (109♦)		P-value	
Wood[1]	Mean	sd	Mean	sd	Mean	sd	Mean	sd	Mean	sd	Mean	sd	Breed	Parity
a	1.884	0.626	2.385	0.793	1.840	0.551	2.443	0.844	1.922	0.686	2.339	0.761	NS	***
b	0.217	0.111	0.242	0.114	0.215	0.109	0.226	0.107	0.218	0.114	0.254	0.118	NS	NS
c	0.004	0.002	0.004	0.002	0.003	0.002	0.004	0.002	0.003	0.001	0.005	0.002	***	***
RMSE[3] (kg/d)	0.308	0.082	0.441	0.136	0.319	0.871	0.461	0.153	0.297	0.076	0.425	0.120	*	***
peak milk[4] (kg)	3.543	0.550	4.723	0.715	3.558	0.585	4.686	0.704	3.528	0.521	4.751	0.727	NS	***
peak time[5] (d)	63.850	32.180	56.809	22.007	74.280	39.884	60.232	24.758	54.658	19.504	54.170	19.334	*	*
total milk (kg)	719.601	149.136	972.838	204.343	731.910	150.040	986.850	223.174	708.762	148.614	962.039	188.906	NS	***
PLM[2]														
a	2.159	0.599	2.771	0.690	2.137	0.488	2.890	0.712	2.178	0.684	2.679	0.661	NS	***
b	0.167	0.077	0.185	0.078	0.160	0.065	0.162	0.066	0.174	0.086	0.203	0.081	***	NS
c	0.003	0.001	0.003	0.002	0.002	0.001	0.003	0.001	0.003	0.001	0.004	0.001	***	***
RMSE [3] (kg/d)	0.184	0.040	0.245	0.051	0.193	0.050	0.246	0.042	0.176	0.026	0.244	0.057	NS	***
peak milk[4] (kg)	3.573	0.472	4.812	0.709	3.559	0.442	4.751	0.680	3.586	0.500	4.857	0.725	*	***
peak time[5] (d)	63.505	25.649	69.459	37.333	77.73	45.065	67.810	32.259	57.795	24.106	60.564	33.258	***	NS
S_N[6](kg)	712.252	147.601	962.423	201.667	723.989	148.533	976.645	220.736	701.917	147.123	951.362	185.470	NS	***
S_0[7] (kg)	766.280	164.168	1053.915	232.294	780.748	165.600	1069.684	255.555	753.540	163.072	1041.654	212.872	NS	***
N	7.587	1.304	7.380	1.471	7.525	1.278	7.440	1.508	7.642	1.333	7.333	1.447	NS	NS
L (%)	6.016	2.383	7.427	3.502	6.186	2.751	7.512	3.655	5.865	2.014	7.361	3.394	NS	***

Signification codes: 0.001: '***', 0.01: '**', 0.05: '*', NS : not significant.

♦Number of lactation curves

[1] Wood model (1967): *a*, *b*, and *c*: estimated Wood parameters, [2]Perturbated Lactation Model based on Wood,[3]RMSE: root mean square error of model fit, [4]peak milk=$a\,.(\frac{b}{c})^{b}\,.e^{-b}$, [5]peak time = $\frac{a}{b}$, [6]total milk based on the PLM perturbed lactation curve: $S_N = \sum_{t_0}^{t_1} y_{(t)}$, [7]total milk based on the PLM unperturbed lactation curve: $S_0 = \sum_{t_0}^{t_1} y^{*}_{(t)}$, N: number of perturbation detected, L :rate of loss milk yield

Unperturbed lactation curve

Descriptive statistics of the parameters *a*, *b* and *c* for the unperturbed lactation curves are presented in Table 1 for the overall dataset, breed and parity. The parameter *a*, which drives the general scaling of the curve, was not significantly different for the two breeds (2.52 ± 0.71). Consequently, no significant breed effect was found for the peak milk or for the total unperturbed milk production. The same statistical effects were found with the Wood adjustment without perturbation. The parameter *a* was significantly affected by the parity of the lactation, with first lactations having a lower value for parameter *a* than the two and more parities. Consequently, there was a significant parity effect on the peak milk and on the total milk production. The parameter *b*, which drives the curvature of the lactation curve, was significantly affected by breed. Alpine goats exhibited higher values of *b* compared to Saanen goats (Alpine: 0.19 ± 0.08; Saanen: 0.16 ± 0.06). Parity also had a significant effect on the parameter *b*, with first lactations having a lower value for parameter *b* than two and more lactations. Regarding the parameter *c*, which drives the rate of decrease of milk production after the peak, both parity and breed effects were highly significant. Alpine goats exhibited a higher value for the parameter *c* than the Saanen goats (Alpine: 0.003 ± 0.001; Saanen: 0.002 ± 0.001). For this parameter, first lactations had a lower value than two and more lactations (Primiparous: 0.002 ± 0.001; Multiparous: 0.003 ± 0.001). The peak time of the unperturbed curve, resulting from both *b* and *c* parameters, was significantly affected by breed, with Saanen goats exhibiting a peak 14 days later in lactation than the Alpine goats. The statistical effects found for PLM_n parameters were consistent with the effects found for the Wood model (PLM_0), except for the peak time. Regarding peak time, the Wood model peak time was slightly affected by both breed and parity, while for the PLM_n peak time, breed had a very significant effect and parity was not significant.

Individual unperturbed lactation curves obtained with PLM_n for increasing parities are shown in Figure 4. Some of these individual adjusted curves were considered as atypical, in the sense they were not similar to conventional definition of lactation curves. An individual lactation was considered "atypical" if the persistence estimated by PLM, *i.e.* the value of parameter *c*, was an outlier, defined as a value either 3 times above the inter-quartile range (IQR) (above the third quartile of the distribution for the *c* parameter) or 3 times below the IQR (below the first quartile of the distribution for the *c* parameter). A total of 18 curves were classified as atypical. Generally, these atypical curves come from the same goat in different parities or for primiparous that have not started the second parity. The peaks milk of the unperturbed lactation curve were increased by 27.47 % between the first parity and the second parity, by 9.46 % between the second parity and the third parity and by -0.29 % between the third parity and the fourth parity (Figure 4). The total milk production for the unperturbed curve was increased by 32.55 % between the first parity and the second parity, 5.20 % between the second parity and the third parity and by 1.01 % between the third parity and the fourth parity. These results are consistent with Arnal et al. [23].

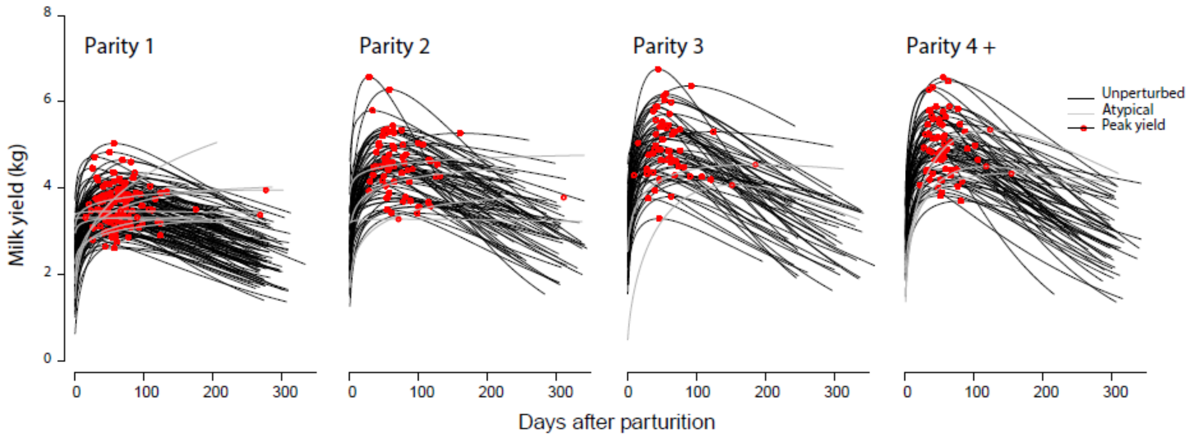

Figure 4: Individual unperturbed PLM-based lactation curves for increasing parity number (fit on 319 lactation data; atypical curves correspond to outlying estimates of the parameter c governing milk persistency).

The Pearson linear correlation matrix by breed and parity between the PLM-based unperturbed parameters is shown in Figure 5 (panels a and b). A strong negative correlation was found between *a* and *b* (-0.65), indicating that high values of *a* (scaling of the lactation curve), were associated with low values of *b* (shaping the curve). A positive correlation was found between the parameters *c* and *b* (0.64) indicating a positive association between the shape of the curve and the rate of decrease of lactation. Finally, a low negative correlation between *c* and *a* (-0.11) was found. These results are consistent with the well-known features of lactation curves: higher milk at peak yield being associated with higher speed of decline after peak [24].

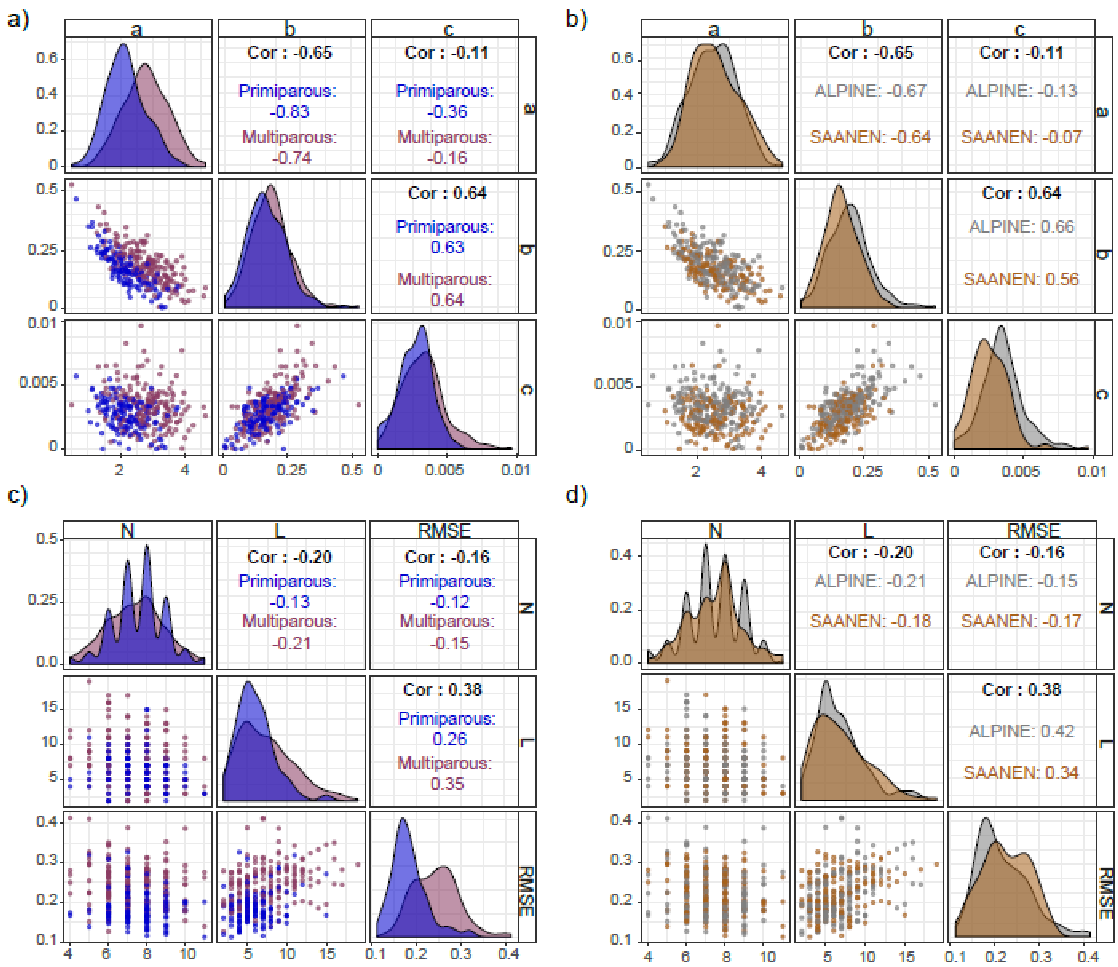

Figure 5. Pearson linear correlation matrix on the PLM-based parameters estimates: panels (a) and (b): the *a*, *b*, *c* parameters defining the unperturbed curve (a: by parity and b: by breed). (c) and (d) : the number of perturbations N, milk loss and RMSE (c: by parity and d: by breed).

Number of perturbations and milk loss

The effects of parity and breed on the total number of perturbations were not significant (7.59 for the primiparous 7.38 for the multiparous and 7.45 for the Alpine and 7.47 for the Saanen). By contrast, the rate of milk yield loss was significantly affected by the parity. A Pearson linear correlation matrix by breed and parity between PLM-based estimates of the number of perturbations (N), percentage loss of milk yield (L) and goodness of fit RMSE was also carried out (Figure 5, panels c and d). A positive correlation was noted between RMSE and milk loss (0.38). However, weak negative correlations between the number of detected perturbations and RMSE (-0.16), and the number of perturbations and the milk loss (-0.20) were also noted. Distributions of$N$, L and RMSE showed an even larger difference according to the parity than to the breeds. These results show that it is not the number of perturbations that contribute the most to the loss in milk yield over the lactation.

Perturbation timing and shape

Table 2 gives descriptive statistics on the parameters of PLM characterizing the 2354 perturbations detected during the fitting procedure: timet_P, intensityk_0, collapse speedk_1 and recovery speed$k_2$according to the lactation stage determined with Grossman's model. Most of the perturbations were detected during the late stage of lactation (n = 1063). The number of perturbations tended to decrease in middle stage (n = 1054) and for early stage (n = 237). The parameter k_0 increased from early, middle and late lactation stage. These results suggest that throughout the lactation process, perturbations become more intense. The parameter k_1 decreased from early to late stages of lactation. This suggests that perturbations tended to be sharper at the beginning of lactation, with a high speed of collapse and recovery, while they tended to be more smooth as lactation progressed. Several factors (*e.g.,* breed, parity, seasonality and season of kidding) can affect characteristics of the lactation curve. The differences found in this study between primiparous and multiparous goats are consistent with previous studies [23,24] with primiparous goats being less productive, with a lower peak yield and a greater persistency. Despite the lack of a significant effect of parity, our results are consistent with previous studies [24] where primiparous goats had a peak later than multiparous (see Table 1). The strong breed effect we observed on peak time is consistent with previous studies [24] with Saanen goats having a peak yield later than Alpine goats.

Table 2. Descriptive statistics of perturbation parameters for the 2354 perturbations detected by the perturbed lactation model in the dairy goat lactation dataset.

	Stage of lactation (2354)					
	Early (237)		Middle(1054)		Late (1063)	
Perturbations	Mean	sd	Mean	sd	Mean	sd
tp : time	33.767	34.000	107.183	62.996	202.182	59.584
k0 : intensity	0.450	0.331	0.506	0.349	0.672	0.359
k1 : collapse	4.013	4.170	3.407	3.870	2.760	3.694
k2 : recovery	1.128	1.961	1.181	1.794	0.954	1.714

The PLM parameter k_0, which drives the intensity of the perturbation, varied considerably between 0.001 and 1 (set as a boundary). The parameterk_1, which drives the collapse speed of the perturbation varied between 0 and10. The parameter k_2, which drives the speed of recovery, varied between 0 and 10. A gradient according to the stage lactation was noted for these parameters with a gradual increase in k_0 and a gradual decrease in k_1 and k_2 according to early, middle and late lactation stages. In the late stage, 30.20 % of the perturbations were detected with a parameter k_2 equal to 0, which implied a perturbation without any recovery period. Among these perturbations, 85.39 % had a k_0 value equal to 1. On the other hand, in the early and middle stages, the perturbations detected with an k_2 equal to 0 were 1.70 % and 7.07 %, respectively.

Discussion

1) Combining two types of models

In this study, we described the PLM model, a tool for extracting simultaneously perturbed and unperturbed lactation curves from daily milk time-series. The key original feature of PLM is to combine an explicit representation of perturbations with a mathematical representation of the lactation curve.

Regarding the mathematical representation of the lactation curve, the structure of PLM is generic and any equation can be used to describe the general pattern of milk production throughout lactation (see appendix including Figure 4 showing illustrating results with other lactation models). The Wood model was chosen in this study as it is one of the most well-known and commonly used mathematical model of lactation curve. Behind the choice of considering a general pattern of lactation that is distorted by perturbations, the biological assumption is that the dairy female has a theoretical production potential (the unperturbed curve) corresponding to the expression of its genetics. This genetic potential may be not fully expressed in the farm environment because of perturbations (the perturbed curve).

Regarding the representation of perturbations, we chose an explicit formalism with a compartmental structure. Developing models that are able to capture perturbations in lactation curve is a longstanding issue in animal sciences. Historically, perturbations in milk production data were considered as impairing the quality of fitting of the mathematical equation of the lactation curve. Therefore, authors have developed approaches to take into account external factors that alter the lactation curve. Wood [25] himself was the first to modify his model in order to consider external factors affecting the shape of the lactation curve with a depressed production during the winter months (18-8 % in January) and an increased production in spring (14-7 % in May) regardless of the stage of lactation. With the same idea of altering the general model of the lactation curve to increase the goodness of fit, models were developed to be more representative of the variability in the lactation curve. For example, Dhanoa [26] showed that by considering the time required to achieve maximum milk yield in the Wood model, the correlations between non-linear parameters were reduced. After this, Dhanoa and Le Du [27] introduced the autocorrelation notion between milk yield in a given stage of lactation and yield in the preceding stage. Another example is provided by Goodall and Sprevak [28] that, based on the Wood model, developed a stochastic model for milk yield to improve the fit of the lactation curve. The relationship between the maximum milk yield and Wood's parameter *a* is linear, but all three parameters affect maximum milk yield. Thus, any model attempting to explicitly represent alterations in milk yield and under-achievement relative to a theoretical potential should not be conceptually applied to parameter *a* but to the whole function.

With the development of on-farm data acquisition, allowing more frequent milk production measurements, and the development of more sophisticated statistical methods, modelling approaches have moved toward an explicit consideration of perturbations, instead of just eliminating them to improve the overall fitting of the lactation curve. Codrea et al. [13] studied the effect of nutritional challenge on the lactation curve using differential smoothing procedures for quantifying biological perturbations in animal performance. Results of this experience highlighted the decline in milk yield during the challenge period for each cow, and showed the presence of other deviations with unknown causes or unrelated to the "off-feed" experiment. Friggens et al. [4] used a clustering procedure linked to a piecewise mixed model to characterize different responses between lactation stages and types of response for the nutritional challenges. Other studies have highlighted the large differences in milk production in goats that are subject to the same dietary and environmental conditions [29]. There are few other approaches to describe the shape of the lactation curves from animals faced to health problems. Lescourret and Coulon [30] had shown the huge variability of milk production response to mastitis in both form and intensity. Adriaens et al. [1] developed a novel methodology to predict quarter milk yield during clinical mastitis. The main shortcoming of these approaches is the lack of an explicit representation of perturbations which are only captured through statistical objects. To overcome this limit, models have been developed with a more explicit representation of perturbations. In the work of Revilla et al. [31] on growing piglets, a classical Gompertz equation, used to capture the unperturbed growth curve, is combined to an equation of the perturbation, used to capture the perturbation in body weight change induced by the weaning event. Sadoul et al. [32] used a model based on a spring and a damper to capture perturbations in physiological responses to challenges. This formalism allows to characterize perturbations with stiffness and resistance to the change of the system. The same concept has been applied to dry matter intake data [33]. These recent developments exhibit limits for capturing perturbations in the lactation curve. They were not extended to make it possible to capture multiple perturbations that may be imbricated. PLM overcomes these limitations as it allows the capture of multiple perturbations with contrasted features: from a sharp and short drop (for instance due to a diarrhoea episode) to a long and slow decrease (for instance due the gestation status). PLM also allows to determine the time at which the perturbations occur. This last point is of great interest to add value to on-farm data where challenge imposed to animals are not controlled and arise from the farm environment.

Like all lactation models, the good functioning of PLM depends on several factors. The most important factor is the quality of datasets. If there is an inconsistency in the data, PLM loses its relevance.

By combining a general model of lactation curve with an explicit model of perturbations, PLM provides two key outputs: first, the unperturbed curve of the female which reflects its production potential in a non-perturbed environment and second the perturbed curve which reflects the production permitted by the farm environment. The PLM parameters ($k_{0,i}$,

$k_{1,i}$ and $k_{2,i}$) provides the most useful information on characteristics of the perturbed lactation curve including scale and shape for each perturbation. Indeed, by providing a perturbed curve, we give an estimate of the number of perturbations and for each perturbation an estimate of intensity ($k_{0,i}$, the collapse $k_{1,i}$ and recovery $k_{2,i}$ speed with a good capture of the time of the perturbation. This not only allows PLM to be flexible in capturing different types of perturbations (*e.g.* gestation, drying), but also to produce metrics to compare the effect of these perturbations on milk yield. In such cases, and by introducing the information concerning these perturbations as an explicit component in the Wood model, we force the model to take into account these perturbations to build the unperturbed curve.

With the development of on-farm technology measurements, an interesting perspective for PLM is to be used on other biological time-series data (*e.g.* body weight, dry matter intake, hormones).

2) Fitting algorithm

Beyond the original concepts behind PLM, a key methodological development has been the fitting algorithm. The number of parameters to be determined is substantial, between on the one hand the Wood parameters of the unperturbed curve, and on the other the PLM parameters (time of perturbation and 3 parameters for each perturbation). To overcome the difficulty of estimating a high number of parameters, a 2-step algorithm was implemented. The first step of the procedure is to determine Wood parameters and the time when the perturbation starts. The second step of the procedure is to determine PLM parameters. Another difficulty in PLM development has been the choice of a maximum number of perturbations. After several attempts, this 2-step algorithm was selected for three main reasons. The first one was related to the visual quality of the fitting results itself. Indeed, the obtained fitted curve is always very close to what the human hand would have drawn after simply looking at the raw data and wondering what could be the curve without perturbations.

This proximity to what the human eye could have inferred was considered decisive, although subjective. The second reason was related to the issue of finding the number of perturbations. The procedure allows an automated determination of an optimal number of perturbations, without *a priori* or use of an arbitrarily chosen stopping criterion. Preliminary results have shown that allowing a maximal number of 15 perturbations to be detected in the first step of the algorithm was enough for the considered dataset. The third reason pertained to the model identifiability issue [17]. Since the fitting is based on a huge number of repeated fittings from which the systematically detected times of perturbations are retained, the 2-step fitting algorithm facilitates the practical identifiability of the model parameters. Indeed, the overall fitting algorithm was applied several times to the same dataset. That the parameter estimates were the same between the different runs strengthen the convergence properties of the algorithm.

Fitting results (see Figure 6) have shown that, in some cases, parameter estimates characterizing an individual perturbation reached their initial upper boundaries (1 for parameter $k_{0,i}$ and 10 for parameters $k_{1,i}$ and $k_{2,i}$). This situation concerns perturbations with a narrow and deep peak-shape. By construction, as a percentage, the value of the parameter k_0 is not supposed to exceed 1. For the parameters k_1 and k_2, a value of 10 already represents a very abrupt collapse or recovery, respectively. These results are therefore considered relevant. However, a next step may be to test the model on a larger dataset to assess the need to broaden these boundaries. Furthermore, another working step will consist in developing an application where the settings of the PLM algorithm can be user-defined (for instance, the maximal number of detectable perturbations or the size of the search grid in step one, boundaries of parameters, etc)

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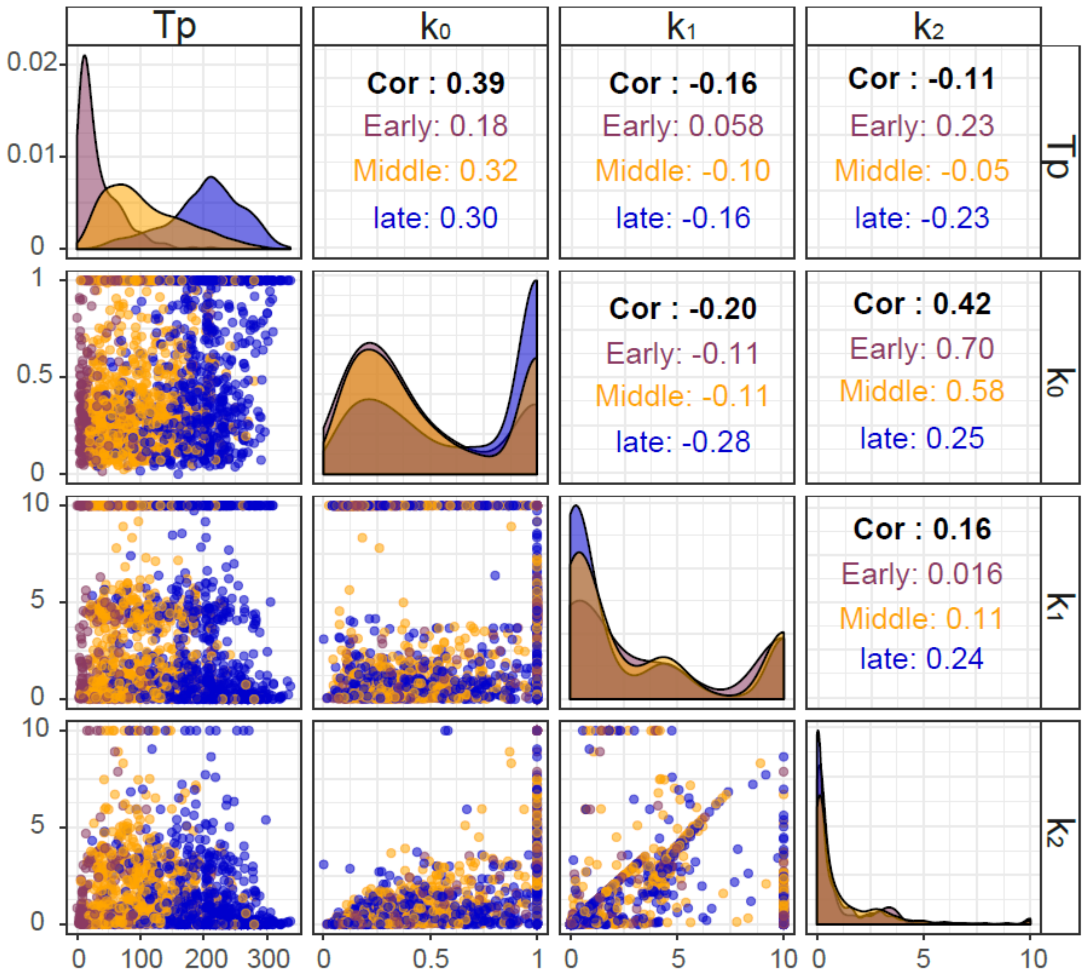

Figure 6: Pearson liear correlation matrix on the PLM parameters by stage of lactation: (tp : perturbations times detected; k_0 : intenstity, k_1: collapse and k_2 : recovery of perturbation.)

3) Phenotyping tool

PLM has been developed to improve our ability to phenotype animals by extracting biological meaningful information from raw data. The unperturbed curve fitted by PLM makes it possible to compare animals based on their potential of production. With this information, animals can be ranked based on the production level they would have achieved in a non-perturbed environment, instead of being ranked based on the measured production level. This ranking may be of interest for the famer's breeding strategy, avoiding to cull animals that have faced a challenge and decreased their production while still having high genetic merit.

The perturbed curve and the characteristics of each perturbation (time, intensity, collapse and recovery) open the perspective of working on perturbations as such and using this information for breeding and management. As a phenotyping tool, PLM can be useful for genetic selection. Studying characteristics of perturbations throughout many lactations of a large number of individuals and linking them to genetic or genomic information opens perspectives to evaluate their heritability and their potential genetic basis. PLM can also be a valuable tool for on-farm management. Linking perturbations with other information on the animals (such as lactation stage, parity, gestation stage…) can help to detect sensitive periods where perturbations are more likely to occur. By cross-checking information on perturbations from all animals with information on the farm environment (for instance temperature, diet quality), it would be possible to detect synchronous occurrences of perturbations and link them to farm environment. With this better understanding of environmental effects on animal production, preventive measures at farm scale could be undertaken.

Understanding the effects of the environment on farm animals and how they cope with perturbations is crucial to gain insights on resilience and robustness. These complex dynamic properties are highly desirable to face the changes occurring in the livestock sector [34]. While the conceptual framework to work on resilience and robustness is now well defined in animal sciences, we still need operational metrics [35]. Such metrics have been proposed for a single perturbation (*e.g.*, Revilla et al., [31]; Sadoul et al. [32]).To our knowledge, existing metrics for the lactation curve, as proposed by Elgersma et al. [36], are based on a variance approach applied to the whole curve. Fluctuations in milk yield are summarized with a single statistical measure. Complementary to this type of approach, PLM can decompose the whole curve and characterize each perturbation, with metrics that are consistent with the concept of resilience (intensity, collapse, recovery). It offers a way of quantifying the consequences of external factors and exploring hypotheses about the biological types of response. By giving a biological meaning to these parameters, we reconcile a phenotyping tool with the opportunity of an explanatory approach.

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Conclusion

By combining a general description of the lactation curve with an explicit representation of perturbations, the PLM model allows the characterization of the potential milk production, reflecting animal genetics, and the deviations induced by the environment, reflecting how animals cope with real farm conditions. The translation of raw time series data into quantitative indicators makes it possible to compare animals and bring insights on their resilience to external factors. In that sense, PLM is a valuable phenotyping tool and it contributes to provide decision solutions for dairy production that are grounded in a biologically meaningful framework. Further modelling studies should strive for integrating high throughput data analysis with such biological framework.

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