The lactation curve in cattle: a mathematical model of the mammary gland

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SUMMARY

A simple model of the mammary gland is described. In this model secretory cells are produced by cell division from undifferentiated cells, and the rate of division is determined by the level of a postulated hormone. The total activity of the milk secreting cells depends on the number of cells, substrate supply (assumed constant), and the amount of milk currently present in the animal. The secretory cells have a finite life, although their death may be expedited by milk remaining in the animal over a longer period of time. The model gives a good description of an experimental lactation curve; it is able to simulate the removal of milk by a suckling calf and machine milking with a variable number of milking periods a day.

INTRODUCTION

A biologically based quantitative description of the lactation curve of a dairy cow is of interest to many, including physiologists, nutritionists, and agricultural extension workers. While it may prove impossible to supply the needs of these different groups simultaneously, at present there is nothing in-between the pure empiricism of a curve-fitting approach and very detailed qualitative descriptions of structure and function. In this paper an attempt is made to bridge this gap by means of a simplified view of the biology of the situation, and its subsequent mathematical representation. The principal objective is to predict the time course of milk production over a single lactation, by means of a simple mechanistic model of the mammary gland of a dairy cow.

Much research has been carried out into the growth and development of the mammary gland, the synthesis of milk by the secretory cells around the alveoli, and the various hormonal and endocrinal mechanisms that ensure that the milk is available when the young animal or machine is ready to remove it (Cowie & Tindal, 1971; Austin & Short, 1972; Mepham, 1976). Curves have been fitted to lactation data by Gaines (1927) and Nelder (1966), and more recently gamma functions have been applied by Wood (1967) principally and by Cobby & Le Du (1978), Dhanoa (1981) and Rowlands, Lucey & Russell (1982). These have been widely used for experimental and practical purposes. Wood (1977) has also examined the path-ways of energy utilization in a cow, in an endeavour to provide a biological interpretation for the coefficients of his fitted curve.

The model of the mammary gland described here is connected to the animal in two points: nutritional inputs and a hormonal input. It is based on the number and activity of secretory cells. Only those biological components are included which appear to dominate the system and determine the main features of the typical lactation curve. While it can always be disputed what can and cannot be reasonably left out of a model that attempts to be mechanistic at a certain level, in this first attempt at this problem, simplicity has been chosen in preference to a rapidly escalating complexity.

THE MODEL

The overall scheme is shown in Fig. 1 and the principal symbols are listed in Table 1. It is assumed that the supply of metabolites by the blood for milk synthesis and cell growth in the mammary gland is non-limiting. The mammary gland itself is represented by undifferentiated cells of number C_u, cells of number C_s, which have differentiated and are adapted to secrete milk, and a storage compartment representing the ducts, alveoli and gland cistern containing M kg milk. It is postulated that a hormone H controls the rate at which the undifferentiated cells C_u divide to give active secretory cells. The amount of milk in the animal, M, which if it is large may indicate incomplete removal of milk from the mammary
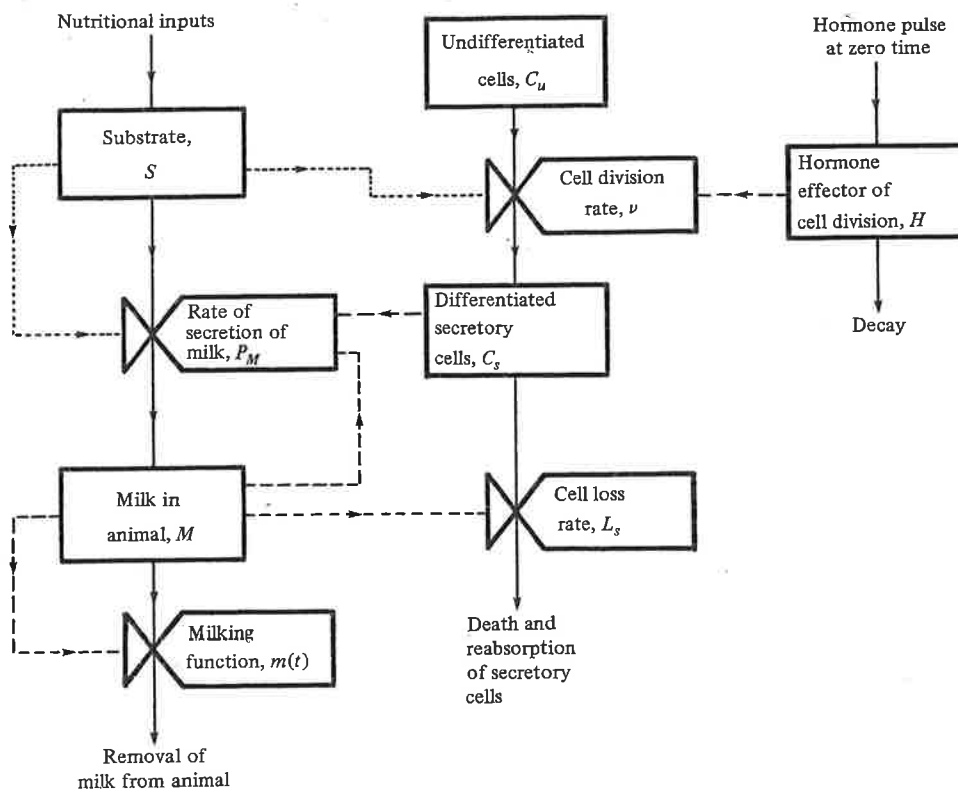
Fig. 1. Model of mammary gland. State variables are shown in the boxes; the valve symbols denote processes of transformation or transport. – – – –, where variables are assumed to affect the rates of processes in the model; · · · ·, potential interactions which are not part of the present model.

gland, may set up immediate direct and long-term indirect responses mediated by hormones, biochemistry and physical pressure. The time variable t is measured in days, and the period of time under consideration is from parturition, throughout a whole lactation, until the cow is dried off.

The concentration of metabolites in the blood is denoted by a single variable, 'substrate', with concentration S (kg/m³).

Hormone, H

In mammals, onset of lactation is caused by a change of hormone concentrations at or around parturition. In cattle, several hormones are involved and their concentrations in the blood decrease as lactation proceeds (Mepham, 1976). In the model, these hormones are represented by a concentration of a single hormone, H, with units of kg/m³. It is assumed that a single pulse of hormone is produced at time $t = 0$ in response to parturition, and this decays exponentially with rate constant k_H (per day), to give the differential equation

$$\frac{dH}{dt} = -k_H H, \quad \text{with } H = H_0 \quad \text{at} \quad t = 0. \quad (1)$$

Integrating equation (1), therefore,

$$H = H_0 e^{-k_H t}. \quad (2)$$

Division of undifferentiated cells, C_u

The progeny of these cell divisions may be undifferentiated, or may differentiate into specialized cells. It is assumed that the rates of division and differentiation are such that the number of undifferentiated cells does not change, to give

$$\frac{dC_u}{dt} = 0 \quad \text{and} \quad C_u = \text{constant}. \quad (3)$$

With binary division, this may be achieved if, for each division producing two cells, one of these cells is committed to differentiation, and the other cell remains undifferentiated. As shown by the dashed line in Fig. 1, the cell division rate ν (divisions/day)

Table 1. *Principal symbols*

Independent variable:

t	time	days

State variables:

C_s	number of secretory cells	*UGN2*
H	hormone effector of cell division	kg/m³ *LHOC*
M	quantity of milk in animal	kg
$\overline{M}$	time average of M	kg

Other variables and quantities:

$m(t)$	milking function, a forced variable (equations 10 and 13)	kg/day
Y	total milk yield over lactation	kg

Parameters:

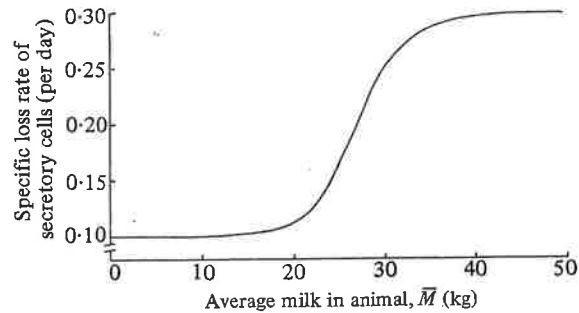|		
C_u	number of undifferentiated cells (equation 3)	
K_H	cell-division rate Michaelis–Menten constant (equation 4)	kg hormone/m³
K_M	milk removal constant (equation 9)	kg
k_H	hormone decay rate (equation 1)	per day
k_M	milk secretion constant (equation 8)	kg/cell/day
K_R	milk secretion rate Michaelis–Menten constant (equation 8)	kg
k_r	milk averaging constant (equation 15)	per day
k_s	basal cell degradation rate (equation 6)	per day
k_{sM}	milk-induced cell degradation rate constant (equation 6)	per day
M_h	parameter of equation (6)	kg
M_m	milk capacity of animal (equation 8)	kg
q	parameter of equation (6)	kg
ν_m	maximum cell division rate parameter (equation 4)	divisions/cell/day
r_c, r_m	parameters of milking function $m(t)$	kg/day
$t_1, \ldots$	parameters of milking function $m(t)$	day

Fig. 2. Specific loss rate of secretory cells, the quantity in curly brackets in equation (6), is plotted against the averaged amount of milk in the animal, $\overline{M}$ (equation 15). Parameters are: $k_s = 0\cdot1$ per day, $k_{sM} = 0\cdot2$ per day, $M_h = 27$ kg, and $q = 10$.

Production and loss of secretory cells, C_s

The number of secretory cells continues to increase in early lactation (Mumford, 1964). Here it is assumed that secretory cells are produced at a rate P_s equal to the cell division rate given by equation (4), so that

$$P_s = \nu = \nu_m \left(\frac{H}{K_H + H} \right) C_u. \qquad (5)$$

Although differentiating cells will often divide slowly, it is assumed here that the differentiated secretory cells are produced fully mature and no further growth or division occurs.

It is assumed that the cells die after a certain length of time with a specific degradation rate k_s (per day). However, this degradation rate will be increased if the milk is not removed from the animal over a period of time, owing to biochemical and physical pressure effects (Mepham, 1976). Thus, a high value of milk in the animal M will lead to a higher rate of degradation. It is assumed that it is an average over a recent time interval that causes this effect, and this average is denoted by $\overline{M}$, which is derived from M by equation (15) below. The basal degradation rate k_s is supplemented by a term dependent on $\overline{M}$, to give a total rate of loss of secretory cells L_s given by

$$L_s = -\left\{ k_s + k_{sM} \left[\frac{(\overline{M}/M_h)^q}{1 + (\overline{M}/M_h)^q} \right] \right\} C_s, \qquad (6)$$

where k_{sM} is a constant (per day) giving the asymptotic value of the second term, M_h (kg) is a parameter giving the half-response point (when $\overline{M} = M_h$, the quantity in square brackets equals $0\cdot5$), and q is a dimensionless parameter which determines the steepness of the response. The specific cell loss rate (equal to the quantity in

is influenced by the hormone concentration H, and it is assumed that

$$\nu = \nu_m \left(\frac{H}{K_H + H} \right) C_u, \qquad (4)$$

where ν_m defines the maximum response (divisions/cell/day), and K_H (kg/m³) is a Michaelis–Menten constant giving half-maximal hormone response.

curly brackets) is shown in Fig. 2 as a function of $\overline{M}$.

The differential equation for the number of secretory cells C_s is therefore

$$\frac{dC_s}{dt} = P_s - L_s = \nu_m \left(\frac{H}{K_H + H}\right) C_u$$
$$- \left\{k_s + k_{sM}\left[\frac{(\overline{M}/M_h)^q}{1 + (\overline{M}/M_h)^q}\right]\right\} C_s. \quad (7)$$

Secretion and removal of milk, M

It is assumed that the rate of secretion of milk, P_M (kg/day), is proportional to the number of secretory cells C_s. According to Knight (1981), secretory cells have a maximum rate of secretion determined by maximum cell size, although here cell size distribution is ignored. The secretory rate is inhibited if the amount of milk in the animal, M, approaches the maximum capacity of the animal, M_m (kg) (Mepham, 1976). Thus, in the model, it is assumed that

$$P_M = k_M C_s (M_m - M)/(M_m - M + K_R), \quad (8)$$

where k_M is a constant (kg/cell/day) and K_R is a Michaelis–Menten constant (kg). $M = M_m - K_R$ gives the half-maximal response. In equation (8), hormones do not play a direct role in regulating the activity of the secreting cells. A large amount of milk in the animal M directly inhibits milk secretion in equation (8), but it should be noted that these large amounts also increase the rate of loss of secretory cells, reducing the number of secretory cells (equation 7) and hence milk secretion. Any further reduction, for instance due to the animal becoming pregnant during lactation, is not included.

The present model allows only a very simple representation of the process of milk ejection and removal. Let R_M (kg/day) be the rate of removal of milk from the animal. A milking function $m(t)$ (kg/day) is defined as the potential rate of removal of milk at time t when quantity of milk is not limiting; the function $m(t)$ is technically known as a driving function; it is set by the environment, that is the demands of the suckling calf or of the machine in the milking parlour. If milk in the animal is not limiting, then $R_M = m(t)$. However, as the amount of milk in the cow decreases, the actual rate of removal R_M must fall increasingly below the demand function $m(t)$. It is assumed that the relation between R_M and $m(t)$ is given by

$$R_M = \left(\frac{M}{K_M + M}\right) m(t), \quad (9)$$

where K_M is a constant (kg).

A calf removes increasing amounts of milk during the first week or two, and thereafter, its appetite and the cow's milk production are generally in balance (Roy, 1980). It feeds usually between six and ten times a day, taking small amounts. In the model, it is assumed that a continuous low rate is a reasonable approximation for removal of milk by a calf, with a milking function m_c given by

$$m_c = r_c, \quad (10)$$

where r_c (kg/day) is a constant.

The milking function for machine milking, $m_m(t)$, is approximated by a pulse of constant height lasting for several minutes, possibly repeated two or three times a day. t^* is defined as the decimal part of the time variable t, by

$$t^* = \text{decimal part } (t). \quad (11)$$

The pulse function Π is defined by

$$\Pi(t^*; t_1, t_2) = 1 \text{ for } t_1 < t^* \leqslant t_2; \quad (12)$$
$$= 0 \quad \text{otherwise.}$$

With two milking periods a day, the machine milking function $m_m(t)$ is given by

$$m_m(t) = r_m[\Pi(t^*; t_1, t_2) + \Pi(t^*; t_3, t_4)], \quad (13)$$

where t_1 and t_2 denote the beginning and end of the first milking period, and t_3 and t_4 those of the second. For example, if the animal is milked at 06.00 and 18.00 h for periods of 0·01 day (about 15 min), $t_1 = 0·25$ day, $t_2 = 0·26$ day, $t_3 = 0·75$ day and $t_4 = 0·76$ day. r_m is a constant (kg/day).

The rate of change of the variable M is given by combining equations (8) and (9), to give

$$\frac{dM}{dt} = P_M - R_M = k_M C_s \frac{M_m - M}{M_m - M + K_R}$$
$$- \left(\frac{M}{K_M + M}\right) m(t). \quad (14)$$

Averaged amount of milk in animal, $\overline{M}$

Although the amount of milk in the animal M appears in equation (8), affecting directly and immediately the rate of secretion of milk, it is the length of time that M has a high value that will have an effect on the rate of loss of secretory cells (Mepham, 1976). Indeed in equation (6) for the loss rate of these cells, the variable $\overline{M}$ is introduced as a quantity derived from M by averaging, which introduces some delay. $\overline{M}(t)$ is defined as an average with an exponential weighting factor, to give

$$\overline{M}(t) = k_r \int_{-\infty}^{t} M(\tau) \, e^{-k_r(t-\tau)} \, d\tau, \quad (15)$$

where k_r is a constant (per day) and τ is a dummy time variable of integration. This equation produces the result that $\overline{M}(t)$ is approximately the

average of the $M(t)$ values over a time interval of $1/k_r$ days.

Computationally, it is more convenient to use a differential equation than an integral equation. It can be shown that equation (15) is equivalent to

$$\frac{d\overline{M}}{dt} = k_r(M - \overline{M}). \qquad (16)$$

Substrate, S

Since the supply of substrate is assumed not to be limiting, this implies that the substrate concentration S is maintained at a constant or high value. The variable S then no longer appears in the model. In Fig. 1, dotted lines are shown connecting S to the cell division rate (equation 4) and the rate of secretion of milk (equation 8). This is to indicate that the substrate concentration S might reasonably be expected to influence these two processes; in a model where the nutritional inputs are limiting or are variable, it may be important to write the substrate concentration S explicitly into equations (4) and (8).

Differential equations

In this section the mathematical definition of the model is summarized. The four significant state variables are H, C_s, M and $\overline{M}$ (S and C_u are constant). From equations (1) and (2)

$$\frac{dH}{dt} = -k_H H \quad \text{and} \quad H = H_0 e^{-k_H t}. \quad (17a)$$

From equation (7)

$$\frac{dC_s}{dt} = v_m \left(\frac{H}{K_H + H}\right) C_u$$
$$- \left\{ k_s + k_{sM} \left[\frac{(\overline{M}/M_h)^q}{1 + (\overline{M}/M_h)^q} \right] \right\} C_s. \quad (17b)$$

From equation (14)

$$\frac{dM}{dt} = k_M C_s \left(\frac{M_m - M}{M_m - M + K_R}\right)$$
$$- \left(\frac{M}{K_M + M}\right) m(t). \quad (17c)$$

From equation (16)

$$\frac{d\overline{M}}{dt} = k_r(M - \overline{M}). \quad (17d)$$

To complete the numerical definition of the model, four initial values (at time $t = 0$) of H, C_s, M and $\overline{M}$ are required. The 13 parameters, k_H, v_m, K_H, C_u, k_s, k_{sM}, M_h, q, k_M, M_m, K_R, K_M and k_r must be specified. In addition the milking function $m(t)$ must be defined, either with equation (10) for a suckling calf

$$m(t) = r_c, \qquad (18a)$$

which involves one extra parameter r_c, or with equation (13) for machine milking with say two milking periods per day

$$m(t) = r_m[\Pi(t^*; t_1, t_2) + \Pi(t^*; t_3, t_4)], \quad (18b)$$

which involves five extra parameters r_m, t_1, t_2, t_3 and t_4. t^* and the pulse function Π are defined in equations (11) and (12):

$$t^* = \text{decimal part } (t), \qquad (18c)$$

and

$$\Pi(t^*; t_1, t_2) = 1 \text{ for } t_1 < t^* \leq t_2; \quad (18d)$$
$$= 0 \quad \text{otherwise.}$$

Integration of equations (17) gives the time course of the lactation, with the rate of removal of milk from the animal being given by equation (9)

$$R_M(t) = \left(\frac{M}{K_M + M}\right) m(t), \qquad (19a)$$

and the total milk yield Y (kg) over the lactation of length t_L (days) is

$$Y = \int_0^{t_L} R_M(t)\, dt. \qquad (19b)$$

NUMERICAL ASSUMPTIONS

Three criteria are applied in assigning values to the quantities in the model. First, the predictions of the model about the time course of lactation must approximate to reality; although the model in Fig. 1 has a mechanistic structure, some of the parameter values are used empirically. Secondly, biological realism should not be violated; although Fig. 1 does not pretend to represent reality at the biochemical and physiological levels, it contains an overview of certain assumed principal processes, which should agree reasonably with expectation. Thirdly, convenient numerical magnitudes can make computation easier and reduce the probability of error; for instance, to assume the hormone concentration is about unity and the number of cells is in the range 1–1000 simplifies matters, although biologically reasonable values would be about 10^{-9} and 10^{12} respectively.

Initial values

These are assigned the values

$$H(t = 0) = 1 \text{ kg/m}^3 \text{ (arbitrary scale)}, \quad (20a)$$
$$C_s(t = 0) = 0 \text{ cells (arbitrary scale)}, \quad (20b)$$
$$M(t = 0) = 0 \text{ kg}, \quad (20c)$$
and
$$\overline{M}(t = 0) = 0 \text{ kg}. \quad (20d)$$

This choice of initial values sets the milk output at the beginning of lactation to zero, which is not strictly accurate for a dairy cow, but is a convenient starting point for a simulation of lactation.

Hormone decay rate, k_H

This is set to

$$k_H = 0.01 \text{ per day}, \qquad (21)$$

which corresponds to a half-life of about 70 days.

Number of cells and division rate, C_u, ν_m and K_H

The number of undifferentiated cells is set to a convenient but arbitrary number with

$$C_u = 1000 \text{ cells}. \qquad (22a)$$

The maximum cell division rate parameter ν_m of equation (4) is also of arbitrary magnitude and is given the value

$$\nu_m = 1 \text{ division/cell/day}. \qquad (22b)$$

The parameter K_H of equation (5) determines for how long, as the hormone concentration H falls, the production of secretory cells is maintained at its maximum rate. Using the same scale as in equation (20a), it is assumed that

$$K_H = 0.2 \text{ kg/m}^9. \qquad (22c)$$

Cell degradation, k_s, k_{sM}, M_h, q and k_r

The first four parameters appear directly in equation (6). k_s determines how quickly the number of cells decreases and a value of

$$k_s = 0.1 \text{ per day}, \qquad (23a)$$

is used. Parameters k_{sM}, M_h, q and k_r determine how rapidly milk production capacity declines in an animal that is not milked, or is dried off; this is an irreversible process as formulated in the model. These parameters are assigned the values

$$k_{sM} = 0.2 \text{ per day}, \qquad (23b)$$
$$M_h = 27 \text{ kg}, \qquad (23c)$$
$$q = 10, \qquad (23d)$$

and

$$k_r = 0.048 \text{ per day}. \qquad (23e)$$

Note that k_r affects cell degradation in equation (6) via equation (16) and $\overline{M}$; a value of 0.048 per day approximately averages milk amount M over a 21-day period to give $\overline{M}$.

Milk secretion and removal, k_M, M_m and K_M

The three parameters of equation (14) are crucial to the milk yields predicted. k_M and C_s appear as a product, and the numerical size of C_s is fixed by the choices for C_u and ν_m in equations (22a) and (22b). C_s will be of order 10^3 cells, and therefore the values

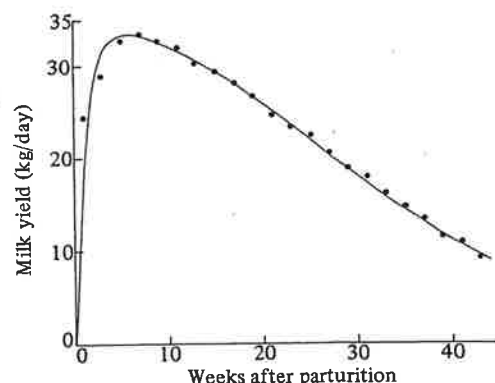$$k_M = 0.005 \quad \text{and} \quad 0.001 \text{ kg/cell/day} \quad (24a)$$

Fig. 3. Predicted lactation curve fitted to experimental data. ●, Observed values; ——, prediction. Only half the data points are depicted.

are chosen. Capacity M_m is physically determined, and is taken to be

$$M_m = 30 \text{ kg}. \qquad (24b)$$

Also K_M can be estimated from milking characteristics; the values

$$K_M = 5.0 \quad \text{and} \quad 15.0 \text{ kg} \qquad (24c)$$

are assumed.

Milking function, $m(t)$

It is of interest to calculate milk secretion under conditions where milk retention in the animal is not a factor depressing yield; for this purpose one takes a high constant value for the milking function, namely

$$r_c = 40 \text{ kg/day}, \qquad (25a)$$

for use in equation (18a). A more realistic value for suckling by a calf is (Baker, Barker & Le Du, 1982)

$$r_c = 12 \text{ kg/day}. \qquad (25b)$$

For machine milking it is assumed that

$$r_m = 4000 \text{ kg/day}, \qquad (25c)$$

which means that in 7.2 min (0.005 day) the machine is capable of removing 20 kg.

For an animal milked twice a day

$$\left. \begin{array}{ll} t_1 = 0.250, & t_2 = 0.255 \ (06.00 \text{ h}); \\ t_3 = 0.750, & t_4 = 0.755 \ (18.00 \text{ h}). \end{array} \right\} \quad (25d)$$

For an animal milked three times a day

$$\left. \begin{array}{ll} t_1 = 0.25, & t_2 = 0.255 \ (06.00 \text{ h}); \\ t_3 = 0.583, & t_4 = 0.588 \ (14.00 \text{ h}); \\ t_5 = 0.916, & t_6 = 0.921 \ (22.00 \text{ h}). \end{array} \right\} \quad (25e)$$

Table 2. *Initial and parameter values for fitted curve*

Initial values

C_s	520·0	Secretory cells
H	1·0	kg hormone/m³
M	0·0	kg milk
$\bar{M}$	0·0	kg milk
Y	0·0	kg milk

Parameters

C_u	1,000	Undifferentiated cells
K_H	0·2	kg hormone/m³
K_M	4·43	kg milk
k_H	0·0102	per day
k_M	0·00506	kg milk/cell/day
K_R	3·0	kg milk
k_r	0·048	per day
k_s	0·1	per day
k_{sM}	0·2	per day
M_h	27·0	kg milk
M_m	30·0	kg milk
q	10	
ν_m	1·0	Divisions/cell/day
r_c	45·0	kg milk/day

Integration method

Using the values assigned above, equations (17) were integrated using Euler's method with a time step $\Delta t = 0.1$ day and 0·001 day for continuous and pulsed demand functions respectively. The problem was programmed in the simulation language CSMP.

RESULTS

Fitting the predicted lactation curve to experimental data

This was carried out to see how satisfactory a fit could be obtained between model and experiment, and to compare parameter values adjusted to give best fit with those assigned in the last section. The data were taken from experiments in which Friesian cows with expected peak yields of 30 kg were fed a maintenance allowance according to live weight plus two types of milk production allowance (Johnson, 1983). The animals lost little or no weight in early lactation, and it was deduced that they
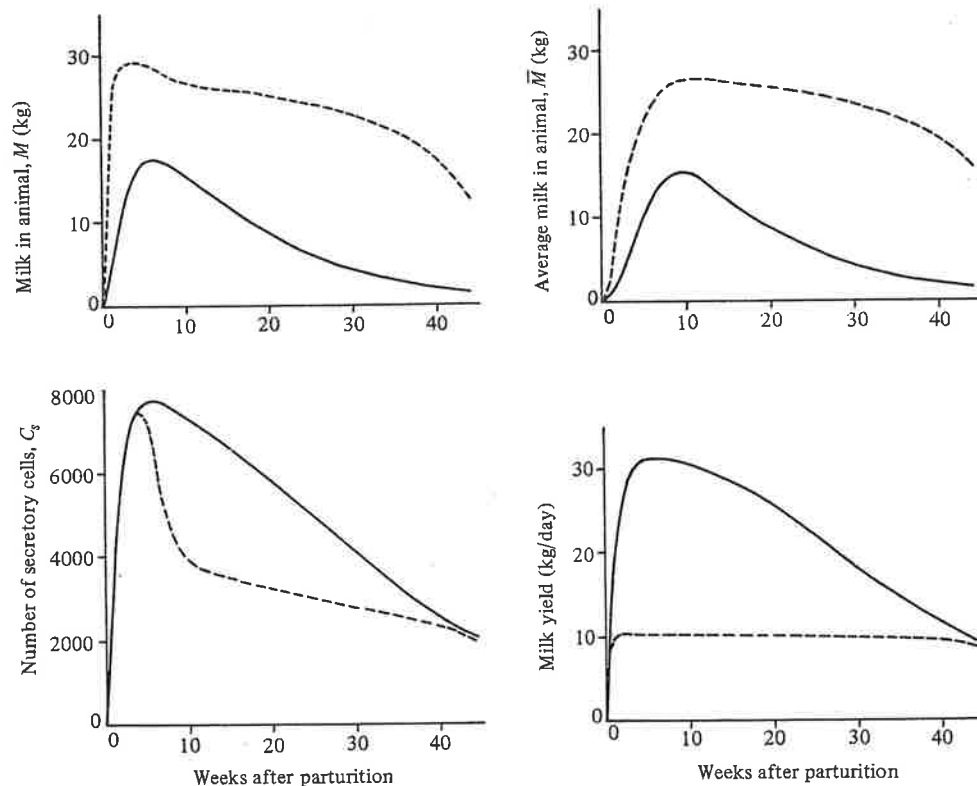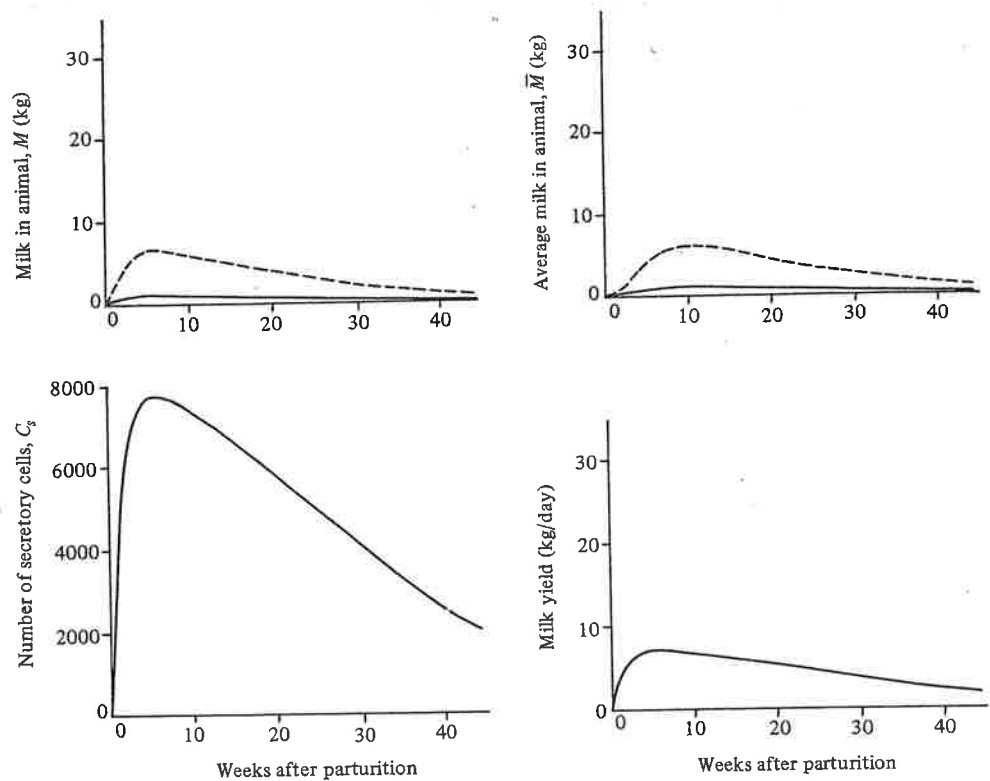

Fig. 4. Time courses of the milk in the animal, M, the average milk in the animal, $\bar{M}$, the number of secretory cells, C_s and the milk yield per day, when the demand rate is continuous and set at 40 kg/day, shown by solid line (———) and 12 kg/day, shown by broken line (– – – –). The milk secretion rate of secretory cells, $k_M = 0.005$ kg/day.

Fig. 5. Time courses of the milk in the animal, M, the average milk in the animal, $\overline{M}$, the number of secretory cells, C_s and the milk yield per day, when the demand rate is continuous and set at 40 kg/day, shown by solid line (———) and 12 kg/day, shown by broken line (————). The milk secretion rate of secretory cells, $k_M = 0.001$ kg/day.

were close to their potential milk production. There was no significant difference between the means of the lactations of the two treatments, and the averages of the means for each of the 44 weeks of lactation were used as experimental data to which the model was fitted (Fig. 3). The parameter values were varied so that the sum of the squared log residuals from each observation time (RSS) were minimized using the modification to CSMP of R. A. Lainson, D. G. Sweeney and J. H. M. Thornley (unpublished) described in the paper by Lainson & Thornley (1982). When the milk removal function r_c was set at 40 kg/day, the best fit to the 44 points obtained had a residual sum of squares (RSS) of 0.048 but the peaks of the observed values and the prediction were distinct. The prediction shown in Fig. 3 was obtained when r_c was set at 45 kg/day. This gave coincident peaks but RSS = 0.092. However, 70% of this was accounted for by the residual at the first observation point. The parameter values of the fitted curve are listed in

Table 2. It will be noticed that only the parameter K_M, and the initial value of C_s, are very different from the previously assigned values.

Continuous demand functions

With a demand function of 40 kg/day, the predicted lactation curve is very similar to that found in much experimental work (Fig. 4). With a demand function of 12 kg/day, the lactation curve is almost flat throughout the lactation. Although the two lactation curves are quite different, in each case the cells multiply and then decrease in number. For the low demand function, milk in the animal M is higher, cell death rate is greater, and the rate of milk production per cell is much reduced. Once the secretory cells have multiplied to the point where the milk secretion rate, $k_M C_s$, is equal to the demand rate, $m(t)$, then the regulatory terms in equation (17c) come into play, and the lactation curve follows the demand function. When the demand function is equal to or greater than the
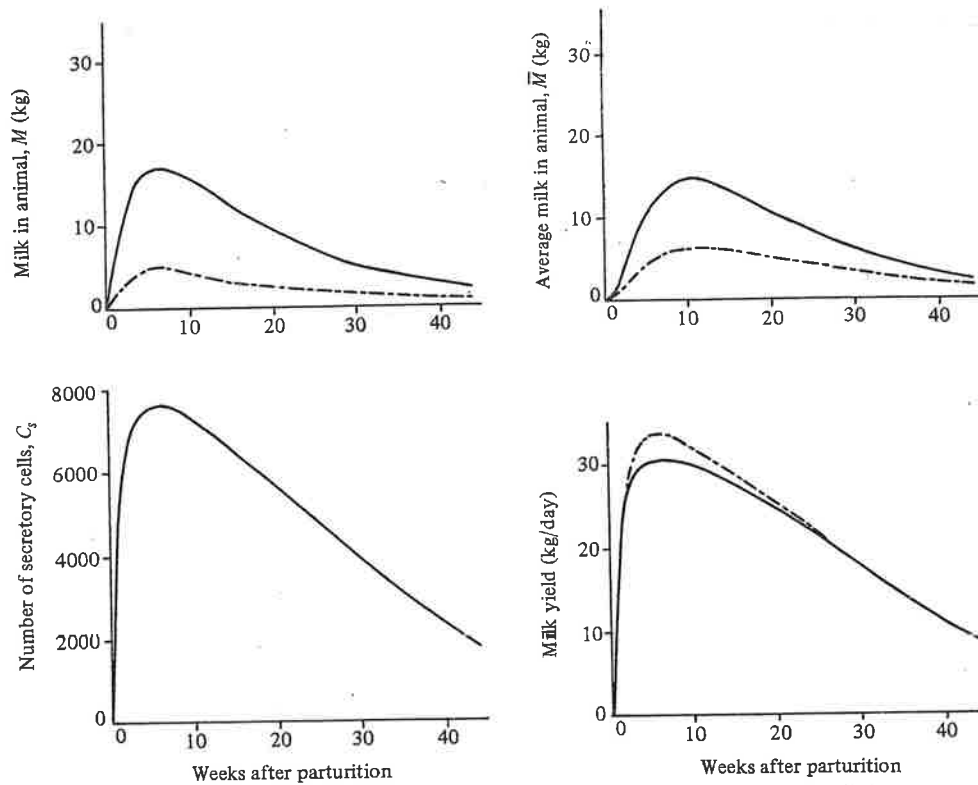
Fig. 6. Time courses of the milk in the animal, M, the average milk in the animal, $\overline{M}$, the number of secretory cells, C_s and the milk yield per day, when the demand rate is pulsed twice a day shown as solid line (——) and three times a day shown as broken line (— · — · —). The Michaelis–Menten parameter of milk removal, $K_M = 5 \cdot 0$.

Table 3. *Comparison of predictions of milking two and three times a day with experimental data*

	Poole (1981)		Model predictions			
			$K_M = 5 \cdot 0$		$K_M = 15 \cdot 0$	
Number of milking periods/day	2	3	2	3	2	3
Total lactation yields (305 days, kg)	5259	5885	6650	6920	5770	6650
% Increase of 3 times a day milking	12		4		15	
Average daily milk yield in first 20 weeks (kg)	21·4	24·9	28·1	29·8	22·8	28·2

maximum secretion rate of the cow, then the growth and decline in the number of secretory cells dictate the shape of the lactation curve. The contrasting lactation curves in Fig. 4 may be regarded as illustrating the differences between machine milking, which gives a supply limited lactation with a well-defined maximum, and a suckling calf, which gives a demand-limited lactation that is relatively flat.

When the lower value of k_M is used (equations 8 and 24a), the lactation curve reflects the growth and decline of secretory cells even with the demand function of 12 kg/day (Fig. 5). The numbers of secretory cells and lactation curves for both demand
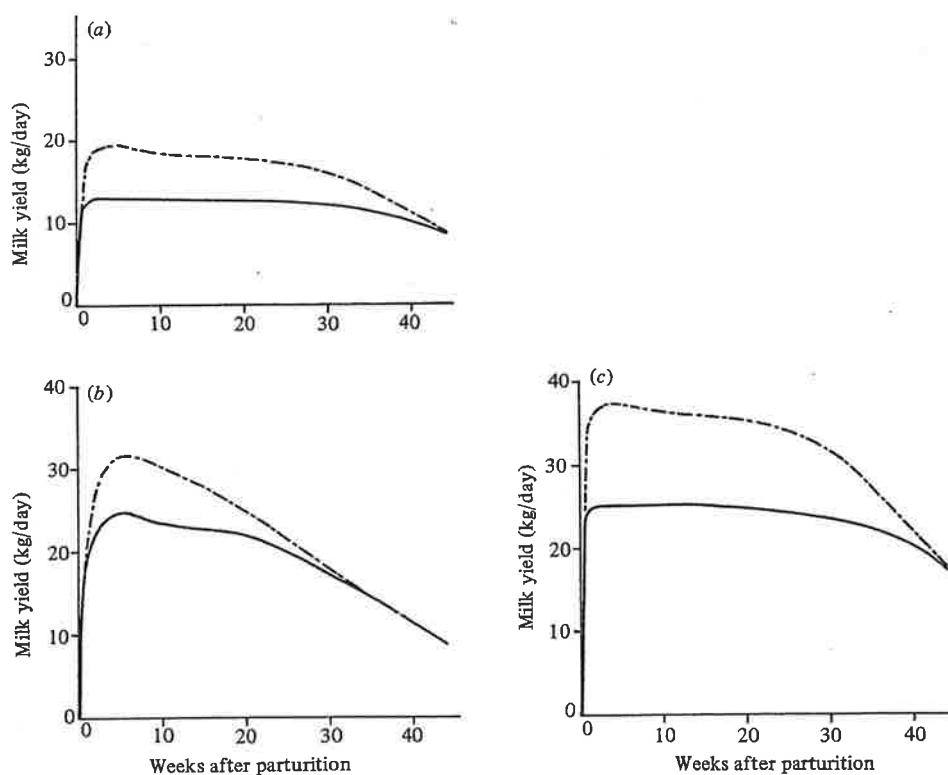
Fig. 7. Time courses of milk yield per day when demand rate is pulsed twice a day shown as solid line (——) and three times a day shown as broken line (– · – · –) and the ratio between values of the parameters of cell milk secretion, k_M, and milk removal r_m is varied. (a) $r_m = 2000$ kg/day, $k_M = 0.005$ kg/cell/day; (b) $r_m = 4000$ kg/day, $k_M = 0.005$ kg/cell/day; and (c) $r_m = 4000$ kg/day, $k_M = 0.01$ kg/cell/day. The Michaelis–Menten parameter of milk removal, $K_M = 15.0$.

levels have very similar time courses, the difference being too small to show on the graph. This demonstrates that when the demand function is increased to values well above the maximum secretion rate of the cow, the secretion rate of the cells tends towards its maximum asymptotically, thereby producing a maximum lactation curve for these parameter values.

Pulsed demand functions

If a demand of 4000 kg/day is applied twice a day for 0.005 day (7.2 min), this is equivalent to a total daily demand of 40 kg/day. With a given daily demand of say 40 kg/day, similar amounts of milk can be removed whether the demand is applied continuously or in pulses, although in the latter case, milk resides in the animal for longer. However, whether this larger amount of residual milk will depress milk secretion (equation 8), or increase secretory cell death rate (equation 6),

depends upon the parameter values used. With the present parameter values, the pulsed and continuous demand functions give very similar results (Figs 4 and 6).

When the cow is milked three times a day, the maximum number of cells and peak milk yield occur at the same time in lactation as with twice-a-day milking (Fig. 6). Although, in the latter case, there is more milk residing in the animal for longer, the amount is insufficient to affect cell death rate and therefore the curve of the number of cells appreciably. However, there is a 10 % difference in peak yields and a difference of 4 % in total milk yield, 6920 and 6650 kg for milking three and two times a day respectively.

When the milk removal parameter K_M of equation (9) is increased from 5 to 15 kg (equation 24c), equation (9) becomes more linear in M (the milk in the animal); this reduces milk secretion and increases the difference between two- and three-

times-a-day milking. These predictions may be compared with experimental data (Poole, 1981) concerning cows that were milked either two or three times a day for the first 20 weeks and twice a day for the rest of the lactation (Table 3). In this experiment, the animals were fed at a roughly constant level with a complete diet. In Table 3, it can be seen that the model is able to simulate the observed differences.

It is interesting to compare two- and three-times-a-day milking for different values of the ratio k_M/r_m; k_M and r_m are the milk secretion and removal constants. Figure 7 (a) and (c) shows that if the demand rates of milking two and three times a day are easily met by the milk secretion rate (high k_M/r_m), then there is an appreciable difference in the daily yields. If the k_M/r_m ratio is lowered (Fig. 7b), the differences become smaller, and decrease away from the lactation peak.

DISCUSSION

The model presented here incorporates some of what is known about the physiology of the milk secretion processes in the mammary gland into a single quantitative scheme, which predicts, amongst other things, the time course of milk production. The problem has been parameterized in a way that allows a variety of lactation curves to be produced, with a single maximum which may be quite pronounced or hardly evident. Some of the parameters (for instance k_H, k_s and k_M) appear likely to be genetic characters of the animal which might be manipulated by breeding, whereas others relate to the demand function and are determined by management. The model permits the interaction of these parameter sets to be examined, which may lead to a greater understanding and control of milk production.

The model can predict a range of experimental data. Some situations have not been examined, but fall within the scope of the present formulation. For instance, a suckling calf would present a varying demand function to the mother animal, which rises in the first 2 weeks and then falls as the calf begins to eat solid food. However, some problems could not be encompassed by the model without extension or alteration. For example, it has been suggested that the greater decreasing slope in the lactation curve of a machine-milked cow compared with a suckled cow, may be caused by a greater death rate of the secretory cells through overwork (Mepham, 1976). This is an alternative hypothesis to that considered in this model. To relax the assumption that the nutritional status of the mammary gland is constant (in Fig. 1, substrate compartment S is constant), and possibly examine lactation in relation to partitioning of energy and nitrogen in the rest of the animal, would require a major and difficult development of the model. The milking demand function represents the removal of milk from a gland of large capacity offering no resistance; this may not be a realistic representation of a milking machine or a suckling calf.

In conclusion, the model provides a simple semi-mechanistic representation of lactation, which might give a useful approach to more complex and more difficult problems.

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