THE APPLICATION OF CONTROL TO A MATHEMATICAL MODEL FOR THE TRANSMISSION OF MASTITIS IN DAIRY COWS

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ABSTRACT

Using a mathematical model for the transmission of mastitis in dairy cows, a control strategy is derived using parameter estimation. It is optimal in the sense that it minimises the RMS error between the model and a desired target equilibrium state. The strategy takes into account practical constraints on the control measures, and economic and animal welfare issues.

Keywords: Control strategies; Mastitis; Mathematical modelling; Parameter estimation.

1. INTRODUCTION

Mastitis is the most common and costly disease affecting dairy cows [8]. It affects both milk production and milk quality, and is a significant economic and animal welfare issue in the farming industry. The United States National Mastitis Council estimates the annual economic loss due to mastitis in the U.S.A. to be approximately $185 per cow [6].

The mathematical model for the transmission of mastitis used in this paper was developed by White et al. [7], and is shown in Figure 1. The symbols used in the model are defined in Section 2. Data from a study by Lam [2] were used to estimate the model parameters.

The udder of a cow is composed of four secretory glands, which are termed quarters. Mastitis is defined as an infection of the udder caused by bacteria entering the quarter through the teat end. There are two classes of mastitis, namely clinical and sub-clinical. Clinical mastitis can be defined as an infection of the udder that results in visible changes to the quarter and the milk it produces [4], whereas sub-clinical mastitis shows no visible changes to the udder quarter and the milk it produces.

The pathogens that cause mastitis can be split into two categories: major pathogens and minor pathogens. Infection with major pathogens generally results in clinical mastitis, whereas minor pathogen infection is usually sub-clinical. Clinical mastitis has the most adverse effects.

The mathematical model for the transmission of mastitis used in this paper was developed by White et al. [7], and is shown in Figure 1. The symbols used in the model are defined in Section 2. Data from a study by Lam [2] were used to estimate the model parameters.

Figure 1: Mathematical model for the transmission of mastitis
The overall aim of this work was to propose a control strategy for the transmission of mastitis that takes into account not only the practical constraints on the control measures, but also economic and animal welfare issues.

The concept of a comprehensive bespoke dairy herd-level strategy for the control of mastitis is very new in the industry [5]. However, individual control strategies such as dry cow therapy are the subject of current experimental research [1]. The work reported in the present paper provides a preliminary investigation of the concept in preparation for future experimental work.

2. THE MATHEMATICAL MODEL

Details of the derivation of the model in Figure 1 are found in White et al. [7]. The equations for the model are as follows:

\[ \dot{x}_{12} = (1-d_\theta_1 - \theta_2 - d_\theta_{12}) b + (y_1 + \tau) y_1 + v_2 y_2 + \nu y_{12} - \left( a_1 m_1 \lambda_1 + a_2 m_2 \lambda_2 + I_2 + \mu + 3 c_1 \left( \frac{y_1 + y_{12}}{x_{12} + y_2 + q_d} \right) \right) x_{12} \]  

(1)

\[ \dot{y}_1 = d_\theta_1 b + a_1 m_1 \lambda_1 x_{12} + v_2 y_{12} - \left( (1-\lambda_2) (m_2 \lambda_2 + I_2) + v_1 + \tau + \mu + c_1 + q_1 \right) y_1 \]  

(2)

\[ \dot{y}_2 = \theta_2 b + (m_2 \lambda_2 + I_2) y_{12} + v_1 y_{12} - \left( (1-\lambda_1) a_1 m_1 \lambda_1 + v_2 + \mu + 3 c_1 \left( \frac{y_1 + y_{12}}{x_{12} + y_2 + q_d} \right) \right) y_2 \]  

(3)

\[ \dot{y}_{12} = d_\theta_{12} b + (1-\lambda_1) a_1 m_1 \lambda_1 y_2 + (1-\lambda_2) (m_2 \lambda_2 + I_2) y_1 - (y_1 + \tau + v_2 + \mu + c_1 + q_1) y_{12} \]  

(4)

\[ \dot{q}_d = q_1 \left( (y_1 + y_{12}) - \left( \mu + 3 c_1 \left( \frac{y_1 + y_{12}}{x_{12} + y_2 + q_d} \right) \right) \right) q_d \]  

(5)

where

\[ 1 = x_{12} + y_1 + y_2 + y_{12} + q_d \]  

(6)

\[ b = \mu + 4 c_1 (y_1 + y_2) \]  

(7)

\[ \lambda_1 = \beta_1 (y_1 + y_2) \]  

(8)

\[ \lambda_2 = \beta_2 (y_1 + y_2) \]  

(9)

2.1. Model Variables

In this paper, \( x_{12} \), \( y_1 \), \( y_2 \), and \( y_{12} \) are referred to as the main variables. The variable \( x_{12} \) represents the proportion of the herd population not infected with either class of pathogen; \( y_1 \) the proportion infected with major pathogens; \( y_2 \) the proportion infected with minor pathogens; and \( y_{12} \) the proportion infected with both classes of pathogens. The variable \( q_d \) is included in the model to allow for quarter drying as a control measure. The functions \( \lambda_1 \) and \( \lambda_2 \) (which are functions of the model variables) represent the force of infection for major pathogens at a rate \( \lambda_1 \) day\(^{-1}\) and the force of infection for minor pathogens at a rate \( \lambda_2 \) day\(^{-1}\), respectively.

2.2. Model Parameters

The parameters \( \mu \), \( \theta_1 \), \( \theta_2 \), \( \nu_{12} \), \( v_1 \) and \( v_2 \) were fixed at the same values as in [7]; these were determined from the literature. The parameters represent:

- \( \mu \) (0.0045 day\(^{-1}\)) the average turnover of lactating cows in the herd;
- \( \theta_1 \) (0.045) the proportion of individuals entering the lactating herd already infected with major pathogens;
- \( \theta_2 \) (0.545) the proportion of individuals entering the lactating herd already infected with minor pathogens;
- \( \nu_{12} \) (0.045) the proportion of individuals entering the lactating herd already infected with both classes of pathogens;
- \( v_1 \) (0.01 day\(^{-1}\)) the average recovery rate from major pathogen infection;
- \( v_2 \) (0 day\(^{-1}\)) the average recovery rate from minor pathogen infection.

The remaining model parameters \( \beta_1 \), \( \beta_2 \), \( \pi_1 \) and \( \pi_2 \) were estimated from data collected by Lam [2], using the computer package BERKELEY MADONNA [3]. \( \beta_1 \) and \( \beta_2 \) represent the transmission rate of major pathogens and of minor pathogens, respectively. \( \pi_1 \) represents the level of cross-protection against major pathogen infection provided by minor pathogen infection, while \( \pi_2 \) represents the level of cross-protection against minor pathogen infection provided by major pathogen infection.

2.3. Control Parameters

The model includes traditional control measures such as post milking teat disinfection (PMTD), quarter drying, culling, and antibiotic treatment (lactation and dry cow therapy). PMTD is modelled as a proportional reduction in the susceptibility of quarters to major and minor pathogens by factors of \( m_1 \) and \( m_2 \) respectively. For example, \( m_1 = m_2 = 1 \) implies that the control is not applied or that it has no effect. Quarter drying is modelled as a removal from the lactating herd of those quarters infected with major pathogens at a rate \( q_1 \) day\(^{-1}\), with \( q_1 = 0 \) implying that the control is not applied. Culling is modelled as occurring with a rate constant \( c_1 \) day\(^{-1}\), such that \( c_1 = 0 \) corresponds to no culling. Lactation therapy is modelled as the flow, with rate constant \( \tau \) day\(^{-1}\), from states \( y_1 \) and \( y_{12} \) to \( x_{12} \). When \( \tau = 0 \), treatment is not applied or has no effect. Dry cow therapy is modelled as a reduction in the proportion of quarters entering the herd infected with major pathogens by a factor \( d \), so that \( d = 1 \) implies that the control is not applied or has no effect.

The model also includes two control methods proposed in [7]. The first, inoculation of quarters with iodine resistant minor pathogens, is modelled as a constant additional force of infection for minor pathogens, denoted \( I_2 \), with \( I_2 = 0 \) implying that the control is not applied. The second, use of
topical antibody, is modelled as a proportional reduction in the susceptibility of quarters to major pathogens by a factor $a_1$, with $a_1 = 1$ implying that the control is not applied or that it has no effect.

3. SIMULATION OF THE MODEL TO EQUILIBRIUM

Equations 1 to 9 were numerically solved using the computer package BERKELEY MADONNA [3]. In this part of the work, the control parameters were assigned values corresponding to no applied effect, i.e. an uncontrolled system. From these simulations, it was found that an appropriate length of time for the model to reach equilibrium was approximately 1000 days. In Figure 2, plots of $x_{12}$, $y_1$, $y_2$, and $y_{12}$ against time are shown.

The equilibrium values were recorded at 1000 days using the table function in BERKELEY MADONNA and were as follows: $x_{12} = 0.0763$, $y_1 = 0.0595$, $y_2 = 0.685$, and $y_{12} = 0.179$. Thus in a herd where no controls are applied, eventually less than 8% of the quarters are uninfected, while approximately 24% are infected with the more serious major pathogens.

These equilibrium values were then used as the initial conditions in subsequent investigation of the control measures. This procedure set up the model so that control measures could be investigated in the absence of any transient behaviour.

4. INVESTIGATION OF DIFFERENT COMBINATIONS OF CONTROL PARAMETERS

Different combinations of control parameter values were investigated using BERKELEY MADONNA by testing a range of values for the control parameters. During each test, the aim was to obtain a control strategy resulting in a steady state of $x_{12} = 1$, $y_1 = y_2 = y_{12} = 0$ (i.e. an uninfected herd), and such that the model approached this ideal state in as short a time as possible.

In each combination tested, a zero value for $m_2$ gave the best control of the disease (i.e. high $x_{12}$, and low $y_1$, $y_2$ and $y_{12}$).

Using this approach two combinations stood out as being potentially the best control strategy. The first of these, Strategy 1, had $c_1 = 0.2$, while the second, Strategy 2, had $\tau = 1$ (in both cases, in addition to $m_2 = 0$). The results are shown in Figure 3 and Figure 4 respectively. All other control parameters were otherwise at values that meant they had no effect on the main variables.

It is debatable as to which is the better of the two control strategies. For example, Strategy 1 achieves a higher value for $x_{12}$ in a faster time, while Strategy 2 eventually achieves a higher equilibrium value for $x_{12}$. Both strategies result in a higher proportion of uninfected quarters.

5. ESTIMATION OF CONTROL PARAMETERS

An alternative method of finding a good control strategy (i.e. high $x_{12}$, low $y_1$, $y_2$ and $y_{12}$) is to perform estimation of the control parameters. To perform this parameter estimation, ideal data were generated consisting of the desired steady values $x_{12} = 1$, $y_1 = 0$, $y_2 = 0$ and $y_{12} = 0$ after two days of applying the controls. The data were imported into BERKELEY MADONNA and parameter estimation performed.

During the parameter estimation phase, BERKELEY MADONNA employs a simplex method to obtain control parameter values that minimise the root mean square (RMS) deviation of the
model output from the data [3]. The estimates for the control parameters are given in Table 1 and the corresponding output of the model simulations is shown in Figure 5. The control with these parameters is termed Strategy 3.

In the paper so far, no constraints have been placed on the control parameter values. However, in practice there are limitations on the practicality and/or effectiveness of each of the control measures described in Section 2.3. This in turn means that the control parameters can only take values within certain limits for them to be meaningful. These limits (Y.H. Schukken, Personal Communication) are given in Table 2, and were incorporated into the model by defining maximum and minimum values for each control parameter in BERKELEY MADONNA. Hence the parameters were estimated again, but this time with the constraints included. The estimates for the control parameters are given in Table 3 and the corresponding output of the model simulations is shown in Figure 6. The control with these parameters is termed Strategy 4.

Comparing Figures 6 and 5 it is seen that Strategy 4 is not quite as effective as Strategy 3, with a less rapid initial rise in $x_{12}$, but it still produces comparable equilibrium results. Hence applying the constraints did not significantly affect the equilibrium values for the main variables. As expected, the effect of the constraints was to change the control strategy. Strategy 4 has all the control measures being used significantly except for $q_1$ and $I_2$. Strategy 3 only uses $m_2$, $c_1$ and $d$ significantly.

6. INCORPORATION OF ECONOMIC AND ANIMAL WELFARE ISSUES INTO THE CONTROL

The differences in clinical mastitis (major pathogen infection) and sub-clinical mastitis (minor pathogen infection) and the differences between the control measures, in terms of economic and animal welfare issues also needed to be considered.

Using various sources of information, the cost of one cow having clinical mastitis for 1000 days was estimated. This was repeated for a cow having sub-clinical mastitis, and then the cost of applying each of the control measures for 1000 days to one cow was also estimated. It was assumed that only clinical mastitis and culling have a significant effect on animal welfare.

To include the different economic costs and animal welfare issues into the method for determining the best control strategy, weights were incorporated into the RMS error optimisation routine. The state vector for the model, i.e. $x = (x_{12}, y_1, y_2, y_{12}, q_2)^T$, was augmented with the control parameters, i.e. $u = (c_1, q_1, m_1, m_2, d, I_2, I_1, a_1)^T$, to give a new state vector $z = (x, u)$ to allow minimisation of the control effort to be included. The corresponding idealised data used in the parameter estimation were augmented accordingly, that is, the values corresponding to no control effort were used.

Comparing Figures 6 and 5 it is seen that Strategy 4 is not quite as effective as Strategy 3, with a less rapid initial rise in $x_{12}$, but it still produces comparable equilibrium results. Hence applying the constraints did not significantly affect the equilibrium values for the main variables. As expected, the effect of the constraints was to change the control strategy. Strategy 4 has all the control measures being used significantly except for $q_1$ and $I_2$. Strategy 3 only uses $m_2$, $c_1$ and $d$ significantly.

Based on the estimated costs associated with each state or control, the weights given in Table 4 were chosen in respect to a unit weighting for $x_{12}$. Where an animal welfare issue applied, the initial weight was doubled. Table 4 indicates that the removal of major pathogens is eight times more important than the removal of minor pathogens.

The procedures outlined in Section 5 were repeated with the new weightings used in the RMS minimisation. The resulting estimates for the control parameters are presented in Table 5, while Figure 7 shows the resulting plots of the main variables versus time. The control with these parameter values was called Strategy 5.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>$a_1$</th>
<th>$m_1$</th>
<th>$m_2$</th>
<th>$d$</th>
<th>$I_2$</th>
<th>$c_1$</th>
<th>$q_1$</th>
<th>$\tau$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>0 – 1</td>
<td>0 – 1</td>
<td>0 – 1</td>
<td>0.5</td>
<td>0 – 0.135</td>
<td>0 – 0.02</td>
<td>0 – 0.02</td>
<td>0 – 0.01</td>
</tr>
</tbody>
</table>

Figure 5: Model simulation for Strategy 3.

Figure 6: Model simulation for Strategy 4.
Comparing Figures 6 and 7, it is seen that Strategies 4 and 5 produce similar results for the main variables. The principal difference between Strategy 4 and Strategy 5 is that for the latter, \( m_1 \) is not applied. From the model (Figure 1), it is seen that \( a_1 \) and \( m_1 \) only appear as a product, so that, if either of them is zero, then the other has no effect. Hence the introduction of the weighting has meant that no unnecessary costs have been incurred.

For all of the control strategies investigated, the final value of \( y_2 \) (proportion of quarters infected with minor pathogens only) is significantly different from zero. This is due to the absence of a control measure affecting the influx of minor pathogen infected quarters, combined with the recovery rate constant \( y_2 \) from \( x_{12} \) being zero (see Figure 1). However, the control parameters have been determined such that the RMS error between the main variables and the idealised equilibrium state is minimised. In comparison with the case with no control action (see Figure 2), it is seen that the final value of \( y_2 \) has dropped significantly. More importantly, the final values for the proportions of quarters infected with major pathogens only \( (y_1) \), and both classes of pathogens \( (y_{12}) \) are reduced to almost zero, while the proportion of uninfected quarters \( (x_{12}) \) is increased from below 8% (no control) to over 50% with controls.

### 7. CONCLUSIONS

A theoretical strategy for the control of the transmission of mastitis has been developed using parameter estimation for a disease transmission model. Initially the parameter estimation was unconstrained. The resulting output of the model simulations based on the unconstrained parameter estimation was analysed. An equilibrium value of approximately 0.5 was reached for both \( x_{12} \) and \( y_2 \). An equilibrium value of 0 was reached for \( y_{12} \) and \( y_1 \). Applying constraints to the control parameters did not have a significant impact on the main variables. The incorporation of economic and animal welfare issues into the model meant that no unnecessary costs were incurred. Strategy 5, as described in Section 6, incorporates constraints on the control parameters, and economic and animal welfare issues, and thus is proposed as a particularly good strategy for controlling mastitis in the herd for which model parameter estimation was performed in Section 2.2.

### 8. REFERENCES


