A model for exploring lactic acidosis: 1. Model description

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ABSTRACT. Incorporating our experimental data with information in the literature, a computer model was developed using the program STELLA II to study acid production and absorption, to predict the concentrations of volatile fatty acids (VFAs) and lactic acid as well as pH, and to control acid-base balance during rumen fermentation in sheep. The features of this model are based on authors’ experimental data and these data have been supplemented by and checked against a wide range of additional information described in the scientific literature. The rate of buffering capacity and the relative rates of absorption of VFAs and lactic acid from the rumen were used to control lactic acid build up that are novel of this model. This model is a first step in the building of a rumen model suitable for exploring lactic acidosis.

KEY WORDS : model, volatile fatty acids, lactic acid, acidosis, rumen, sheep.
and Ding & Xu (2003). These data have been supplemented by and checked against a wide range of additional information described in the scientific literature as indicated in the following sections.

Fig. 1. – Diagrammatic representation of the model for the rumen fermentation of sheep. The model includes three major sections: (i) nutritional input; (ii) acid conversion, absorption and outflow; and (iii) regulation. The rectangular boxes indicate pools or state variables. The circles indicate metabolites, absorption and outflow of acids, and regulating factors. Spirals indicate beginnings or ends. Arrows indicate fluxes. Locks and triangles indicate the states and directions of three major sections, respectively.
TABLE 1
General notation used in the model

<table>
<thead>
<tr>
<th>Notation</th>
<th>Description</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>G</td>
<td>Grain ‘intake’</td>
<td>g/min</td>
</tr>
<tr>
<td>PFG</td>
<td>Potential fermentability of grain</td>
<td>mmol acids produced/g</td>
</tr>
<tr>
<td>FSG</td>
<td>Fermentable substrate produced from grain</td>
<td>mmol acids/min</td>
</tr>
<tr>
<td>PFSG</td>
<td>Pool of fermentable substrate produced from grain</td>
<td>mmol acids</td>
</tr>
<tr>
<td>H</td>
<td>Hay ‘intake’</td>
<td>g/min</td>
</tr>
<tr>
<td>PFH1</td>
<td>Potential fermentability of hay</td>
<td>mmol acids produced/g</td>
</tr>
<tr>
<td>HFPH</td>
<td>Effect of pH on hay ferment ability</td>
<td>% of PFH1</td>
</tr>
<tr>
<td>PFH2</td>
<td>Actual fermentability of hay</td>
<td>mmol acids produced/g</td>
</tr>
<tr>
<td>FSH</td>
<td>Fermentable substrate produced from hay</td>
<td>mmol acids/min</td>
</tr>
<tr>
<td>PFSH</td>
<td>Pool of fermentable substrate produced from hay</td>
<td>mmol acids</td>
</tr>
<tr>
<td>LAR</td>
<td>Propportion of PFSG converted to lactic acid</td>
<td>% of PFSG</td>
</tr>
<tr>
<td>LAG</td>
<td>Lactic acid (LA) produced from grain</td>
<td>mmol/min</td>
</tr>
<tr>
<td>LAH</td>
<td>Lactic acid produced from hay</td>
<td>mmol/min</td>
</tr>
<tr>
<td>VFAG</td>
<td>VFAs produced from grain</td>
<td>mmol/min</td>
</tr>
<tr>
<td>VFAH</td>
<td>VFAs produced from hay</td>
<td>mmol/min</td>
</tr>
<tr>
<td>LAP</td>
<td>Lactic acid pool</td>
<td>mmol</td>
</tr>
<tr>
<td>VFAP</td>
<td>Proportion of LAP converted to VFAs</td>
<td>mmol</td>
</tr>
<tr>
<td>ALAC</td>
<td>Amount of lactic acid converted to VFAs</td>
<td>mmol/min</td>
</tr>
<tr>
<td>TA</td>
<td>Total amount of lactic acid and VFAs produced in 5-liter rumen</td>
<td>mmol</td>
</tr>
<tr>
<td>TAPL</td>
<td>Total acid concentration per liter (TA/5)</td>
<td>mmol acids/L</td>
</tr>
<tr>
<td>B</td>
<td>Buffer ‘intake’</td>
<td>g/min</td>
</tr>
<tr>
<td>BC</td>
<td>Buffering capacity for 1 g NaHCO3</td>
<td>mmol acids</td>
</tr>
<tr>
<td>OP</td>
<td>Osmotic pressure</td>
<td>mmol/kg</td>
</tr>
<tr>
<td>AR1</td>
<td>Absorption rate 1 (pH effect on VFAs absorption rate)</td>
<td>% of VFAP/min</td>
</tr>
<tr>
<td>AR2</td>
<td>Absorption rate 2 (Osmotic pressure effect on VFAs absorption rate)</td>
<td>% of VFAP/min</td>
</tr>
<tr>
<td>AR</td>
<td>Absorption rate of VFAs</td>
<td>% of VFAP/min</td>
</tr>
<tr>
<td>AB</td>
<td>Absorption of VFAs</td>
<td>mmol/min</td>
</tr>
<tr>
<td>OFR</td>
<td>Outflow rate of LA and VFAs in rumen fluid</td>
<td>mmol/min</td>
</tr>
<tr>
<td>OLA</td>
<td>Outflow of lactic acid in rumen fluid</td>
<td>mmol/min</td>
</tr>
<tr>
<td>OVFA</td>
<td>Outflow of VFAs in rumen fluid</td>
<td>mmol/min</td>
</tr>
</tbody>
</table>

The following description of the model involves the three parts shown in Fig. 1: 1) nutrition input; 2) acid conversion, absorption and outflow; and 3) regulation.

**Nutrition input**

The ‘diet’ in the model can be set for any ingredients and the period over which the model runs can be set for any duration. However, basically, dietary nutrients entering the ‘rumen’ included grain and hay, and running time was normally 24 h (1440 min). The iteration interval was set at 1 min. Therefore, all flows of material are described in g/min or mmol/min. ‘Intake’ levels for the basic investigation of the model were set at 300 g/d grain and 700 g/d hay. The pattern of ‘intake’ of grain (G) and hay (H) can be altered in the model. For basic model, the grain component of the ration of 300 g/d was ‘fed’ separately and ‘consumed’ over a 3 h period and therefore entered the ‘rumen’ at a constant rate of 1.667 g/min during this time.

The hay ration of 700 g/d entered the ‘rumen’ over the full 24 h period at a constant rate of 0.486 g/min.

The grain and hay in the rumen are ‘fermented’ and converted to metabolites, such as acids (VFAs, lactic acid etc.). These ‘precursors’ or ‘products’ are described as follows:

\[
FSG = G \times PFG \quad \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldOTS
by rate of fermentation and pH (Tilley et al., 1963; Leng & Leonard, 1965; Leng & Brett, 1966; Weston & Hogan, 1968). Lactic acid does not normally accumulate in the rumen of a sheep fed hay (Gall et al., 1953; Jayasuriya & Hungate, 1959; Nakamura et al., 1971). However, in sheep fed grain-based diets, lactic acid can accumulate with rapid fermentation and reduced rumen pH (Rowe, 1997; Rowe et al., 1991). The relationship between lactic acid production and pH is an inverse one, where increases in lactic acid production lead to a reduction in pH (Dunlop, 1972; Rowe, 1983, 1997; Rowe et al., 1991, 1993). The relationship between lactic acid production and pH used in the model can be seen in Fig. 2.

Equations 4a and 4b describe the production of lactic acid from grain and hay, respectively (Tilley et al., 1963; Weston & Hogan, 1968; Rowe, 1983; Rowe et al., 1991, 1992).

\[
\text{LAG} = \text{PFSG} \times \text{LAR} \quad \quad (4a)
\]

\[
\text{LAH} = \text{PFSH} \times 0.01 \quad \quad (4b)
\]

where \( \text{LAR} \) is the proportion of the pool of fermentable substrate from grain (PFSG) converted to lactic acid and varies depending on pH. \( \text{LAG} \) (mmol/min) is the amount of lactic acid produced from the pool of fermentable substrate from grain (PFSG) and is mostly influenced by pH via LAR. LAG is calculated by multiplying PFSG by LAR. However, LAH (mmol/min) is the amount of lactic acid produced from the pool of fermentable substrate from hay (PFSH) and is not affected by pH. LAH produced from PFSH was negligible and constant at 0.01 (1%) (Jayasuriya & Hungate, 1959; Nakamura et al., 1971). The remaining PFSG and PFSH are converted to VFAs using Equations 5a and 5b, respectively (Weston & Hogan, 1968; Rowe, 1983; Rowe et al., 1991; Ding, 1997).

\[
\text{VFAG} = \text{PFSG} \times (1- \text{LAR}) \quad \quad (5a)
\]

\[
\text{VFAH} = \text{PFSH} \times 0.99 \quad \quad (5b)
\]

where VFAG (mmol/min) is the amount of VFAs produced from the pool of fermentable substrate derived from grain (PFSG) and is most influenced by pH via LAR which depends on pH. VFAH (mmol/min) is the amount of VFAs from the pool of fermentable substrate produced from hay (PFSH). A further two state variables, namely LAP (LA pool, mmol) and VFAP (VFAs pool, mmol), are used in the model and their initial values were 0 and 500 mmol, respectively (Rowe, 1983; Rowe et al., 1991; Ding, 1997). However, their values at any time (t) are expressed as:

\[
\text{LAP}(t) = \text{LAP}(t - dt) + \left( \text{LAG} + \text{LAH} - \text{OLA} - \text{ALAC} \right) \times dt \quad \quad (6a)
\]

\[
\text{VFAP}(t) = \text{VFAP}(t - dt) + \left( \text{VFAH} + \text{VFAG} + \text{ALAC} - \text{AB} - \text{OVFA} \right) \times dt \quad \quad (6b)
\]

where t is time in min from the beginning of the simulation and dt is the time step (1 min). LAG and LAH have been defined in Equations 4a and 4b, respectively. OLA (mmol/min) and OVFA (mmol/min) are the amount of outflow of lactic acid and VFAs from the rumen in the fluid phase, respectively (Weston & Hogan, 1968; Ding, 1997). ALAC (mmol/min) is the amount of lactic acid converted to VFAs and is calculated as follows:

\[
\text{ALAC} = \text{LAP} \times \text{LAPR} \quad \quad (7)
\]

where LAP has been defined above and LAPR (\% of LAP) is the proportion of lactic acid pool converted to VFAs. Again the LAPR value depends on pH (Jayasuriya & Hungate, 1959; Patra et al., 1996; Pitt & Pell, 1997; Nikолов, 1998) and is calculated according to the relationship shown in Fig. 3.
Acid absorption

VFAs are mainly absorbed from the rumen; however, lactic acid is apparently not absorbed from the rumen (DING et al., 1998; DING & XU, 2003). Lactic acid is either converted to VFAs or flows out of the rumen. Absorption (AB) (mmol/min) of VFAs is calculated using Equation 8 where VFAP (mmol) is the VFAs pool. AR (% of VFAP) is the absorption rate and is mainly influenced by pH and osmotic pressure (OP) (WESTON & HOGAN, 1968; GODFREY et al., 1992; ROWE, 1997; DING, 1997; DING & XU, 2003). The calculation of AR, pH and OP are described more fully in Equation 13 of the regulation section.

\[ AB = VFAP \times AR \]  \hspace{1cm} (8)

Acid outflow

In addition to fermentation and absorption in the rumen, some nutrients flow to the omasum, abomasum and the small intestine. The outflow of VFAs and lactic acid from the rumen depends on the VFAs pool (VFAP), the lactic acid pool (LAP) and outflow rate (OFR). According to the work of WESTON & HOGAN (1968), about 24% of VFAs produced in the rumen flowed out of the rumen in the fluid phase. Therefore, a value of 0.4%/min for VFAs and lactic acid was taken as the outflow rate (OFR) in Equation 9 used in the model. Again this value was dependent on the pH and osmotic pressure (WESTON & HOGAN, 1968; GODFREY et al., 1992; ROWE, 1997; DING, 1997; DING & XU, 2003).

\[ OFR = \frac{(1 - AR)}{155.6} \]  \hspace{1cm} (9)

where OFR (% of VFAP and LAP/min) is outflow rate of VFAP and LAP from the rumen. OFR is mainly affected by pH and osmotic pressure (OP) via absorption rate (AR) which varies depending on pH and OP. The constant 155.6 is calculated on the basis of AR described in Equation 13.

\[ OVFA = VFAP \times OFR \]  \hspace{1cm} (10)

where OVFA (mmol/min) is outflow of VFAs from the rumen and its value equals the product of the VFAs pool (VFAP) and the outflow rate (OFR).

\[ OLA = LAP \times OFR \]  \hspace{1cm} (11)

where OLA (mmol/min) is the outflow lactic acid from the rumen determined as the product of lactic acid pool (LAP) and outflow rate (OFR). OLA and OVFA change with pH since the formation of lactic acid (LA) and VFAs from the pool of fermentable substrate from grain (PFSG) is affected by pH (Equations 4a and 5a)

Regulation

The regulating system in the model includes buffer, pH and osmotic pressure (OP). There are many other factors, like substrate, recycling of microbial matter within the rumen, effects on digesting bacteria, affecting the regulating system (RUSSELL, 1984; JOUANY et al., 1988; ZIEMER et al., 2002; GALBRAITH et al., 2004), however, so far these informations are not fine enough to be included.

Buffer system is often included in the prevention of lactic acidosis (COUNOTTE et al., 1979; ROGERS & DAVIS, 1982; KOVACIK et al., 1986; CUMBY et al., 2001). The inclusion of additional buffer (B) is a decision variable in the model which can be altered over time Sodium bicarbonate (NaHCO₃) was used as a standard buffer in a series of experiments and was therefore chosen for use in this model. The buffering capacity (BC) used in the model was 15 mmol VFAs per gram of NaHCO₃. This is 76% of the theoretical value determined by titration in the experiments (DING, 1997; DING et al., 1996, 1997) (24% of additional NaHCO₃ was assumed to flow out of the rumen with the fluid or solid phase). In the experiments of DING (1997) and DING et al. (1996, 1997), it was shown that 1 g NaHCO₃ can buffer 20 mmol acetic acid at pH 6.

The total amount of lactic acid and VFAs present in the rumen directly affects pH. The total acids (TA, mmol) in 5 liters of the rumen were considered together with the amount of additional buffer (B) to calculate the total effective acid concentration (TAPL, mmol/L) as described in Equation 12.

\[ TAPL = \frac{(TA - B \times BC)}{5} \]  \hspace{1cm} (12)

where TA (mmol) is total acids, i.e. the sum of lactic acid pool (LAP) and VFAs pool (VFAP). If no additional buffer (B) is added, B * BC will be zero and TAPL will equal TA/5.

The relationships between TAPL (mmol/L), pH and OP are shown in Figs 4 and 5, respectively.
The pH and osmotic pressure (OP) were found to be very important factors affecting the absorption of VFAs both in the experiments of Ding et al. (1997) and the work of Williams & Mackenzie (1965). The effects of pH and osmotic pressure (OP) on the absorption of VFAs from the VFAP in the rumen are included in the model through absorption rate 1 (AR1) and absorption rate 2 (AR2), respectively. The absorption of VFAs depends on VFAP (VFAs pool) and VFAs absorption rate (AR). AR (% of VFAP/min) was calculated in the model using Equation 13.

\[
AR = AR1 \times AR2 / 31.25
\]

where AR1 (% of VFAP/min) is absorption rate 1 (pH effect on VFAs absorption rate), and AR2 (% of VFAP/min) is absorption rate 2 (Osmotic pressure effect on VFAs absorption rate). The constant 31.25 is calculated on the basis of outflow rate (OFR) described in Equation 9. Equation 13 represents base rate of absorption of approximately 76% of VFAs produced in the rumen of sheep, but it is mainly dependent on the pH, osmotic pressure and substrates (Weston & Hogan, 1968; Ding, 1997; Ding et al., 1997).

### SUMMARY OF THE MODEL

All aspects of the model are represented in Equations (1) to (13) and Figs 1 to 5. Table 1 lists the abbreviations used in the Fig. 1. The differential equations can be solved numerically for a given set of initial conditions and parameter values.

This model is a first step in the building of a rumen model suitable for exploring lactic acidosis. There is another continuous paper of this model, entitling 'a model for exploring lactic acidosis: 2. model valuation and validation' in the same issue of this journal, to validate the present model to key parameters and validate it by performance against experimental results in sheep.

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### REFERENCES


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