

Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.

Estimation and Identifiability for a Dynamic Model of Maternal Nutrition and Fetal Growth in Sheep

A thesis presented in partial fulfilment of the requirements for the degree of

Master of Applied Statistics

at Massey University, Albany, New Zealand

Leiyan Wang

2012

Abstract

The optimal maternal nutrition intake is extremely important in the second half of pregnancy for fetal development in mammals. It affects the health and wellbeing of the offspring. The purpose of this study was to determine the optimal daily nutrition intake for sheep during the second half of their pregnancy, to achieve a pre-determined desirable birth weight for lambs. By achieving the optimal birth weight, the postnatal development of the animals is likely to be improved.

In this study, pregnant sheep carrying singletons or twins were considered. There were two levels of nutrition, low and high. Various dynamic mathematical models were proposed to obtain the optimal daily nutrition intake. The model parameters were estimated by weighted least-squares. Bootstrap simulations were used to check the reliability of each estimated parameter. Finally, the optimal daily nutrition intake was obtained by solving the boundary value problems, with pre-determined parameter values.

The results suggested that the optimal daily nutrition intake for sheep in the second half of their pregnancy was a constant. For the particular breed of sheep, with target weight 6.5 kg for singletons, the optimal nutrition intake was 1.36 kg of dry matter per day. For twins, with a target weight of 12 kg, the optimal nutrition intake was 1.93 kg of dry matter per day. In addition, a comprehensive and generic 'black-box' algorithm was produced using the software MATLAB. It could return the optimal daily nutrition intake for any type of mammals given a time series of fetal weight and maternal nutrition.

Acknowledgments

I would like to sincerely thank my supervisors, Professor Graeme Wake and Dr Barry McDonald for their constant guidance and support from beginning through the end of this project. Their encouragement enabled me to carry out this project successfully.

I would like to specially thank my family for their love, encouragement and support which enabled me to complete my thesis successfully.

In addition, I would like to thank the National Research Centre for Growth and Development for funding this project.

Table of Contents

Abstract.....	i
Acknowledgments.....	ii
List of Figures	v
List of Tables	vii
Glossary.....	viii
1. Introduction	1
1.1 Background	1
1.2 Description of data.....	2
1.3 Objective of this study	2
1.4 Thesis outline	3
2. Literature Review	4
2.1 Least squares estimation	4
2.2 Identifiability	6
2.3 Bootstrap resampling.....	9
2.4 Boundary value problems.....	12
3. Parameter Estimation	15
3.1 Background	15
3.2 Methodology.....	17
4. Results and Discussion	20
4.1 Grouped data – ordinary least squares	20
4.1.1 Full model.....	24
4.1.2 Cut-down model	27
4.1.3 Hybrid model.....	30
4.1.4 Summary	33
4.2 Model diagnostics – ordinary least-squares	34
4.2.1 Singletons – cut-down model	35
4.2.2 Twins – cut-down model.....	36
4.2.3 Twins – hybrid model.....	37
4.2.4 Summary	38
4.3 Model Improvement – Weighted Least-squares	39

4.3.1 Singletons.....	39
4.3.2 Twins	42
4.4 Model Diagnostics – Weighted Least-squares.....	45
4.4.1 Singletons – cut-down model	45
4.4.2 Singletons – hybrid model	46
4.4.3 Twins – cut-down model.....	48
4.4.4 Twins – hybrid model.....	49
5. Bootstrap Simulations.....	52
5.1 Methodology.....	52
5.2 Results.....	53
5.2.1 Cut-down model for singletons	54
5.2.2 Hybrid model for singletons.....	55
5.2.3 Cut-down model for twins	57
5.2.4 Hybrid model for twins	58
5.3 Summary	60
6. Optimal solutions	61
6.1 Cut-down model	62
6.1.1 Singletons.....	63
6.1.2 Twins	64
6.2 Hybrid model.....	66
6.2.1 Singletons.....	67
6.2.2 Twins	69
6.3 Simulations for optimal daily nutrition intakes	71
6.4 Summary	74
7. Conclusions and Future Study.....	76
7.1 Conclusions	76
7.2 Future Research Direction	77
Appendix	80
References	89

List of Figures

Figure 4. 1: $u(t)$ function with quadratic fitting for singletons.....	21
Figure 4. 2: $u(t)$ function with cubic fitting for singletons.....	21
Figure 4. 3: $u(t)$ function with quadratic fitting for twins	22
Figure 4. 4: $u(t)$ function with cubic fitting for twins	22
Figure 4. 5: The process flow chart for parameter estimation of full model.....	23
Figure 4. 6: Residuals vs. Fitted values (singletons – cut-down model).....	35
Figure 4. 7: QQ plot (singletons – cut-down model).....	35
Figure 4. 8: Residuals vs. Fitted values (twins – cut-down model)	36
Figure 4. 9: QQ plot (twins – cut-down model).....	37
Figure 4. 10: Residuals vs. Fitted values (twins – hybrid model)	37
Figure 4. 11: QQ plot (twins – hybrid model)	38
Figure 4. 12: Modified residuals vs. fitted values (singletons – cut-down model - WLS).....	45
Figure 4. 13: QQ plot (singletons – cutdown model - WLS).....	46
Figure 4. 14: Modified residuals vs. fitted values (singletons – hybrid model - WLS)	46
Figure 4. 15: QQ plot (singleton – hybrid model - WLS)	47
Figure 4. 16: Modified residuals vs. fitted values (twins – cut-down model - WLS).....	48
Figure 4. 17: QQ plot (twins – cutdown model - WLS)	48
Figure 4. 18: Modified residuals vs. Fitted values (twins – hybrid model - WLS)	49
Figure 4. 19: QQ plot (twins – hybrid model - WLS)	50
Figure 5. 1: Histogram of parameter R of cut-down model for singletons.....	54
Figure 5. 2: Histogram of parameter Lt of cut-down model for singletons	54
Figure 5. 3: Histogram of parameter k_1 of cut-down model for singletons	54
Figure 5. 4: Histogram of parameter x_0 of cut-down model for singletons	54
Figure 5. 5: Histogram of parameter R of hybrid model for singletons	55
Figure 5. 6: Histogram of parameter Lt of hybrid model for singletons	55
Figure 5. 7: Histogram of parameter A of hybrid model for singletons.....	55
Figure 5. 8: Histogram of parameter Lt_0 of hybrid model for singletons.....	55
Figure 5. 9: Histogram of parameter x_0 of hybrid model for singletons	56
Figure 5. 10: Plot of bootstrapped parameter Lt versus bootstrapped parameter Lt_0 of hybrid model for singletons.....	56
Figure 5. 11: Histogram of parameter R of cut-down model for twins	57
Figure 5. 12: Histogram of parameter Lt of cut-down model for twins.....	57
Figure 5. 13: Histogram of parameter k_1 of cut-down model for twins	57
Figure 5. 14: Histogram of parameter x_0 of cut-down model for twins.....	57
Figure 5. 15: Histogram of parameter R of hybrid model for twins	58
Figure 5. 16: Histogram of parameter Lt of hybrid model for twins.....	58
Figure 5. 17: Histogram of parameter A of hybrid model for twins	59
Figure 5. 18: Histogram of parameter Lt_0 of hybrid model for twins.....	59
Figure 5. 19: Histogram of parameter x_0 of hybrid model for twins.....	59
Figure 5. 20: Plot of bootstrapped parameter Lt versus bootstrapped parameter Lt_0 of hybrid model for twins.....	59

Figure 6. 1: Optimal solution for the hybrid model of singletons ($xb=6.0$ kg)	68
Figure 6. 2: Optimal solution for the hybrid model of singletons ($xb=6.5$ kg)	68
Figure 6. 3: Optimal solution for the hybrid model of singletons ($xb=7.0$ kg)	68
Figure 6. 4: Optimal solution for the hybrid model of singletons ($xb=7.5$ kg)	68
Figure 6. 5: Optimal solution for the hybrid model of singletons ($xb=8.0$ kg)	69
Figure 6. 6: Optimal solution for the hybrid model of singletons ($xb=8.5$ kg)	69
Figure 6. 7: Optimal solution for the hybrid model of twins ($xb=11.0$ kg).....	70
Figure 6. 8: Optimal solution for the hybrid model of twins ($xb=11.5$ kg).....	70
Figure 6. 9: Optimal solution for the hybrid model of twins ($xb=12.0$ kg).....	70
Figure 6. 10: Optimal solution for the hybrid model of twins ($xb=12.2$ kg).....	70
Figure 6. 11: Optimal solution for the hybrid model of twins ($xb=12.5$ kg).....	71
Figure 6. 12: Histogram of bootstrapped daily nutrition intake for singletons	72
Figure 6. 13: Histogram of bootstrapped daily nutrition intake for twins (after removing one extreme outlier)	73
Figure 6. 14: Histogram of bootstrapped daily nutrition intake for twins with feasible range between 0 and 3 kg/day	74
Figure A. 1: The logical process flow chart for Black-box algorithm.....	80

List of Tables

Table 4. 1: Parameter estimation for full model of singletons	24
Table 4. 2: Parameter estimation for full model of twins (quadratic fitting of nutritional function) .	25
Table 4. 3: Parameter estimation for full model of twins (cubic fitting of nutritional function).....	26
Table 4. 4: Parameter estimation for cut-down model of singletons.....	28
Table 4. 5: Parameter estimation for cut-down model of twins (quadratic fitting of nutritional function)	28
Table 4. 6: Parameter estimation for cut-down model of twins (cubic fitting of nutritional function)	29
Table 4. 7: Parameter estimation for hybrid model of singletons.....	31
Table 4. 8: Parameter estimation for hybrid model of twins (quadratic fitting of nutritional function)	32
Table 4. 9: Parameter estimation for hybrid model of twins (cubic fitting of nutritional function)...	32
Table 4. 10: Parameter estimation for full model of singletons with WLS.....	40
Table 4. 11: Parameter estimation for cut-down model of singletons with WLS.....	41
Table 4. 12: Parameter estimation for hybrid model of singletons with WLS.....	41
Table 4. 13: Parameter estimation for full model of twins with WLS.....	43
Table 4. 14: Parameter estimation for cut-down model of twins with WLS	44
Table 4. 15: Parameter estimation for hybrid model of twins with WLS	44
Table 6. 1: The optimal solution for the cut-down model of singletons.....	63
Table 6. 2: The optimal solution for the cut-down model of twins	65
Table 6. 3: The optimal solution for the hybrid model of singletons.....	67
Table 6. 4: The optimal solution for the hybrid model of twins	69
Table 6. 5: Summary of the best optimal solutions	75

Glossary

BLUE	Best linear unbiased estimate	
BVP	Boundary value problems	
GLS	Generalised least squares	
ODE	Ordinary differential equation	
PCA	Principal component analysis	
QQ Plot	Quantile-Quantile plot	
SSE	Sum of squares of errors	
WLS	Weighted least squares	
a	A factor which influencing the ‘carrying capacity’ on historical intake	kg
b	The discount factor, which indicates that the cumulative intake is influenced by the past	day ⁻¹
k_0	The basic component of the ‘carrying capacity’	kg
L	The value of nutrition intake at which the per unit mass growth rate is half of the maximum	kg/day
L_0	The value of cumulative intake at which the influencing factor is half of its maximum	kg
r	The maximum per unit mass growth rate	day ⁻¹
t	Time	day
u	The daily maternal nutrition intake	kg/day
x_0	The initial fetal weight at the start of the second half of pregnancy	kg
y	A cumulative nutrition intake	kg