



Modelling and Optimisation of Mechanical Ventilation for Critically Ill Patients

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Abstract

This thesis is made up of three parts: i) the development of a comprehensive computational model of the pulmonary (patho)physiology of healthy and diseased lungs, ii) the application of a novel optimisation-based approach to validate this computational model, and iii) the use of this model to optimise mechanical ventilator settings for patients with diseased lungs.

The model described in this thesis is an extended implementation of the Nottingham Physiological Simulator (NPS) in MATLAB. An iterative multi-compartmental modelling approach is adopted, and modifications (based on physiological mechanisms) are proposed to characterise healthy as well as diseased states.

In the second part of the thesis, an optimisation-based approach is employed to validate the robustness of this model. The model is subjected to simultaneous variations in the values of multiple physiologically relevant uncertain parameters with respect to a set of specified performance criteria, based on expected levels of variation in arterial blood gas values found in the patient population. Performance criteria are evaluated using computer simulations. Local and global optimisation algorithms are employed to search for the worst-case parameter combination that could cause the model outputs to deviate from their expected range of operation, i.e. violate the specified model performance criteria. The optimisation-based analysis is proposed as a useful complement to current statistical model validation techniques, which are reliant on matching data from *in vitro* and *in vivo* studies.

The last section of the thesis considers the problem of optimising settings of mechanical ventilation in an Intensive Therapy Unit (ITU) for patients with diseased lungs. This is a challenging task for physicians who have to select appropriate mechanical ventilator settings to satisfy multiple, sometimes conflicting, objectives including i) maintaining adequate oxygenation, ii) maintaining adequate carbon dioxide clearance and iii) minimising the risks of ventilator associated lung injury (VALI). Currently, physicians are reliant on guidelines based on previous experience and recommendations from a very limited number of *in vivo* studies which, by their very nature, cannot form the basis of personalised, disease-specific treatment protocols. This thesis formulates the choice of ventilator settings as a constrained multi-

objective optimisation problem, which is solved using a hybrid optimisation algorithm and a validated physiological simulation model, to optimise the settings of mechanical ventilation for a healthy lung and for several pulmonary disease cases. The optimal settings are shown to satisfy the conflicting clinical objectives, to improve the ventilation perfusion matching within the lung, and, crucially, to be disease-specific.

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Table of Contents

Abstract	1
Acknowledgements	3
Table of Contents	4
List of Figures	7
List of Tables	11
Abbreviations and Nomenclature	13
Chapter 1: Introduction	16
1.1 Motivation.....	16
1.2 Thesis organisation	18
1.3 Main contributions of this study	20
Chapter 2: Modelling of pulmonary physiology	23
2.1 Pulmonary physiology – key concepts	23
2.1.1 Lungs.....	23
2.1.2 Lung volumes and capacities	24
2.1.3 O ₂ and CO ₂ movement across the alveolar membrane.....	27
2.1.4 The airways and the blood vessels	29
2.1.5 Distribution of ventilation and perfusion	30
2.2 Modelling and implementation of a pulmonary physiology simulator.....	32
2.2.1 Modelling of pulmonary systems - background.....	32
2.2.2 Simulation model initialisation	45
2.2.3 Program Structure	46
2.3 Model development and utilisation.....	48
2.3.1 Simulating a healthy lung.....	50
2.3.2 Simulating diseased lungs	51
2.3.3 <i>In silico</i> behaviour of diseased lungs	53
2.3.4 Simulating alveolar volumes.....	54
2.3.5 The effect of PEEP.....	58
2.3.6 Clinical validation of the modified model.....	61

Chapter 3: Validation of Pulmonary Physiology Models	64
3.1 Current methods.....	64
3.1.1 Disadvantages of current methods	68
3.2 Model validation using optimisation methods.....	71
3.2.1 Sequential Quadratic Programming	74
3.2.2 Mesh Adaptive Direct Search (MADS)	74
3.2.3 Genetic Algorithms (GA).....	76
3.2.4 Differential Evolution (DE)	79
3.3 Validation of pulmonary physiology simulator for clinical applications	81
3.3.1 Introduction.....	81
3.3.2 Modelling of uncertain parameters	82
3.3.3 Formulation of the model validation problem.....	83
3.3.4 Results.....	86
3.3.5 Discussion	95
Chapter 4: Optimising Mechanical Ventilator Settings	99
4.1 Introduction.....	100
4.1.1 Mechanical Ventilation	100
4.1.2 Ventilator Associated Lung Injury (VALI).....	103
4.1.3 Current approaches to deciding mechanical ventilation settings	104
4.2 Problem introduction	107
4.3 Multi-objective optimisation.....	108
4.3.1 Introduction.....	108
4.3.2 Methods for multi-objective optimisation.....	111
4.4 Problem description	117
4.4.1 Mechanical ventilator settings.....	117
4.4.2 <i>In silico</i> setup	119
4.5 Modelling healthy and diseased lung states.....	122
4.6 Multi-objective optimisation of mechanical ventilation	123
4.6.1 Weighted Aggregate Objective Function approach	125
4.6.2 Comparison of the WAOF approach to NSGA-II.....	126
4.7 Computing optimised ventilator settings	129
Chapter 5: Conclusions and Future Work	136
5.1 Conclusions.....	136

5.2	Future work.....	139
Appendix	143
A	– Pre and post-intervention ventilator settings to validate modified model.....	143
B	– Termination conditions for optimisation algorithms - TolFun and TolX.....	144
Bibliography	145