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Modelling and Optimisation of Mechanical Ventilation for Critically Ill Patients

Submitted by **Anup Das**, to the University of Exeter as a thesis for the degree of Doctor of Philosophy in Engineering,
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I certify that all material in this thesis which is not my own work has been identified and that no material has previously been submitted and approved for the award of a degree by this or any other University.

Signature: ---------------------------------

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 multiobjective 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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