AALBORG UNIVERSITET

Institut for medicin og sundhedsteknologi

Registrering af kandidatspeciale

Uddannelse: Sundhedsteknologi

Specialeemne/titel: Modelling of cardiopulmonary interactions for non-invasive estimation of pleural pressure from pulse pressure variation

Afleveringsdato: 2/1-2024

(Kun For MedIS: TM ☐ MMA☐ BM☐)

Ved indlevering af specialeblanketten attesterer alle studerende i gruppen, at de er bekendt med AAU's regler for persondatabeskyttelse (GDPR) samt retningslinjer om god skik i akademiske og videnskabsetiske anliggender (https://www.studerende.aau.dk/gdpr/).

Baggrund for projektet (foreløbig problemformulering)

(Her beskrives det problem, projektet tager udgangspunkt i; hvorfor er det et problem, hvad er formålet med specialet og for hvem og hvad er konsekvenserne?).

Estimating pleural pressure (P_{pl}) requires the complicated and resource intensive esophageal manometry maneuver to be performed. Therefore, P_{pl} estimations are rarely available for patients undergoing mechanical ventilation.

Pulse pressure variation (PPV) is a reliable predictor of fluid responsiveness in patients undergoing mechanical ventilation, as long as no cardiac arrythmia or spontaneous breathing occurs.

During the respiratory cycle, a number of cardiopulmonary interactions occur. The physiological mechanisms underlying the cardiopulmonary interactions are the same in positive- and negative pressure ventilations (PPV, NPV), but the outcome on relevant state variables is reversed between the two.

In mechanical ventilation, the respiratory cycle is most often controlled by PPV. The exceptions are when spontaneous breathing occurs, or by negative pressure mechanical ventilation, which is rarely used in clinical practice. In PPV, the pressure supplied by the ventilator inflates the lungs, while the diaphragm is relaxed. By Boyles law, the decrease in volume of the pleural space increases P_{pl}.
The cyclical changes in increased P_{pl} affect the cardiovascular system, by e.g. reducing systemic venous return (SVR), increasing right ventricular (RV) afterload and reducing RV preload.

These cardiopulmonary interactions are reflected in the PPV signal, thus adding a second signal of cyclical changes to the PPV signal.

Based on the understanding of cardiopulmonary interactions, the hypothesis for this project is that it is possible to estimate P_{pl} from the PPV signal.

Thus, the problem statement is:

"*How can the cardiopulmonary interactions be modelled, in order to estimate pleural pressure from pulse pressure variation?"*

Overordnet metodisk tilgang til projektet

(Her beskrives de metoder, der forventes anvendt i projektet. På tidspunktet for aflevering af specialekontrakten kan der naturligvis ikke gives mange detaljer, men metoderne kan angives på stikordsniveau, fx "litteraturreview", "laboratorieforsøg", "observationer", "algoritmeudvikling" osv.).

Se bilag 1
Tidsplan[1]
(Her angives en tidsplan for projektet samt særlige tidsmæssige opmærksomhedspunkter. Tidsplanen kan indeholde foreløbige milepæle, fx i et Gantt-diagram, der vedhæftes. Hvis projektet kræver godkendelser, fx fra videnskabsetisk komité, skal status for tilladelse angives, og hvis der tages udgangspunkt i data, som ikke indsamles i projektet, skal status for adgang til data anføres.) **Se bilag 2**

Hovedvejleder:		**Bi-vejleder:**
Navn:	Stephen Edward Reese	
Mail:	sr@hst.aau.dk	

Aftaler om vejledning
Beskriv kort de foreløbige aftaler, du/I har med vejleder og eventuel bi-vejleder, fx vedr. hyppighed og form på vejledermøder samt ansvarsfordeling mellem vejleder og eventuel bi-vejleder.

Hvilken afleveringsform forventer I:

Artikel med appendix ☐ Projektrapport ☐

Sprog i projektrapporten:

Dansk ☐

Engelsk ☒

Sprog til eksamen:

Dansk ☒

Engelsk ☐

Gruppens medlemmer:	
Fulde navn:	**Studienummer:**
Lasse Henrik Bech Leuchtman	20184208

Udarbejdes specialet i samarbejde med en ekstern partner:

Ja ☐ Nej ☒

<u>Hvis ja:</u>

Udfyld formularen vedrørende det eksterne samarbejde via linket her:

[1] Bemærk: Selvom studieordningen ikke specifikt nævner muligheden for at aflevere en artikel, kan man godt aflevere speciale i form af en artikel, hvis man kan dække alle læringsmål, men man skal være meget opmærksom på hvordan man udformer artikel og arbejdsblade, så man imødekommer alle læringsmål i studieordningen. Tal med vejleder om hvordan projektet kan formidles så der ikke er tvivl om at du/I lever op til læringsmål.

https://forms.office.com/r/tNnz3V8mry

Specialebeskrivelsen er godkendt af hovedvejleder[2] ______ ______________________________
Dato Underskrift

Vejleder udfylder:

Censorkvalifikationer (gælder ikke for ST og KVT): Klik eller tryk her for at skrive tekst.

Blanketten afleveres eller sendes pr. mail til studiesekretæren senest 9 hverdage efter semesterstart.

Studiesekretæren sender blanketten videre til studielederen.

Specialebeskrivelsen er godkendt af studieleder _________ ______________________________
Dato Underskrift

[2] Vær opmærksom på at det ikke er muligt for eksterne samarbejdspartnere at være hovedvejleder. Hovedvejleder skal være PLA (professor, lektor, adjunkt) på HST medmindre andet er aftalt med viceinstitutleder.

Bilag 1

Contents

Projektphases

Phase 1- Domain Analysis

Milestones

- **Clinical Problem**
- **Physiological Mechanisms**
- **Motivation for physiological modelling**
- **SOTA**
- **Problem Statement**

- **Foundational cardiopulmonary model**

Phase Description

In the domain analysis phase, the problem will be analyzed based on its relevant aspects.

The clinical aspect investigates how the instance of the healthcare sector is affected by the issue - how does it affect the clinician's workflow, what is the effect on variables of interest in patient outcome and other significant factors.

The physiology will be described at a level of detail which encapsulates the effect on the patient's physiological systems in a clear and concise manner, without introducing unnecessary complexity with insignificant influence on outcome.

The motivation section investigates the necessity for creating physiological models in the context of researching clinical phenomena.

The state of the art (SOTA) section will investigate the performance and architecture of current non-invasive physiological models used for researching the clinical problem. The SOTA section will have high influence on the requirements for the final system, as it bridges the gap between the previously described theory, and current scientific/clinical application of the theory.

Methods applied for reaching milestones

Method	**Description**	**Associated Milestone**
Unstructured Literature Search	Conducted based on initial curiosity, without formal research questions, search process and literature review process.	*All*
Structured Literature Search	Formally investigates a set of research questions, conducted	*All*

	through a well defined search process in peer reviewed databases. Found literature is filtered based on inclusion/exclusion criteria, and reviewed based on standardized review schemes.	
Interview	A semi-structured interview, wherein a clinician or similar expert in the field shares their expert knowledge on the problem in a formal setting, documented for future usage.	*Clinical Aspect SOTA*
Algorithm Development	Through the domain knowledge acquired in the domain analysis phase, a foundational cardiopulmonary model will be developed. This model will be implemented as a set of differential equations describing the cardiopulmonary interactions, and will serve as a proof of concept of feasibility.	*Foundational Cardiopulmonary model*

Phase 2- Requirement Engineering

Milestones

- **Requirement Elicitation**
- **Requirement Analysis**
- **Requirement Specification**

Phase Description

The requirement engineering phase defines a set of constraints to which the system must adhere.

Elicitation defines the needs of the clinician/researchers which the system will support, based on the research conducted in the domain analysis phase

System requirements constrain the system on a technical- and user experience level, without necessarily impacting the core support provided for the clinician/researchers.

Requirements analysis filters the identified requirements, based on available resources. Resources can include manpower, allocated project time and economical aspects, among others.

Methods applied for reaching milestones

Method	**Description**	**Associated Milestone**
Structured literature search	See Domain Analysis phase	*Requirement Elicitation*
Interview	See Domain Analysis phase	*Requirement Elicitation*

MoSCOW	MoSCOW is an acronym for must-, should-, could- and would- have. Requirements are given a priority level based on their relevance for the project. The priority level is used as a threshold when subsequently filtering requirements.	*Requirements Analysis* *Requirements Specification*

Phase 3- Solution Analysis

Milestones

- **Data Source**
- **System Description**
- **Physiological Modelling**
- **System Architecture**
- **Implementation Methods**

Phase Description

The Solution Analysis phase aims to identify a suitable solution to the problem statement, in accordance with constraints posed by the system- and user-requirements.

The data source section describes the clinical trials from which the trials originate. Furthermore, the data relevant to the problem solution is described in detail.

The system description bridges the gap between domain analysis, requirement engineering and clinical implementation, by providing the context for the clinicians' usage of the system in their workflow.

Physiological modelling provides the architecture of the systems data processing engine at a unit- and module level.

The system architecture encapsulates the full system at relevant levels of detail. This includes database connectivity, user interfaces, interactions between modules and other relevant factors.

The implementation method section contains a description of the tools applied in building and testing the system.

Methods applied for reaching milestones

Method	**Description**	**Associated Milestone**
Bioelectrical modelling	Bioelectrical modelling (BE) identifies the circuit diagram analogues of the relevant physiological mechanisms. BE provides a high level architecture of the physiological models, assisting as a useful tool for stakeholder communication and guiding implementation.	*Physiological Modelling* *System Architecture*
Compartment modelling	Compartment modelling structures the physiological mechanisms into encapsulated	*Physiological Modelling* *System Architecture*

	compartments. They contain more detail than BE, describing state variables as well as independent variables and interactions between these. This provides a level of the architecture which is closer to the physiology than BE, allowing for the same communicative and implementational benefits as BE, but from a different perspective.	

Phase 4- Solution Implementation and testing

Milestones

- **Individual Compartment Implementation**
    - **Individual Compartment Testing**
- **Module Implementation**
    - **Module Testing**
- **System Implementation**
    - **System Requirement Testing**
    - **User Requirement Testing**

Phase Description

This phase is a distillation of the work performed in the previous phases. First, the individual compartments will be implemented and tested according to the tests designed in the test plans.

The same process will be conducted at the module level of the architecture. In this case, modules are defined as a coherent collection of compartments, influencing a common module state variable. E.g. the heart consists of six compartments, with the modules state variable being pulse pressure.

Finally, the individual modules will be assembled into the full system, which is then tested on the system- and user- requirements.

Methods applied for reaching milestones

Method	**Description**	**Associated Milestone**
Mathematical Toolbox	Depending on the available data, different methods can be applied for computing the systems state	*Individual Compartment Implementation* *Module Implementation*

	variables. Thus, ODE Solvers, optimization algorithms, integration and differentiation etc. can be applied, depending on the context.	*System Implementation*
Test Design	Depending on the requirements and physiological constraints of the system, tests will be designed to test its capabilities of handling different usability scenarios.	*Individual Compartment Testing* *Module Testing* *System- and user-requirement testing*

Phase 5- Report Writing

Milestones

- **Problem Analysis**
- **Problem Statement**
- **Solution Analysis**
- **Methods**
- **Results**
- **Discussion**
- **Conclusion**

Phase Description

The report writing phase consists of disseminating the research conducted in the previous phases.

The report is structured into different sections, which aid in disseminating the results of the work in a structured and scientific manner.

Bilag 2

Speciale	**0h**	**10%**
Domain Analysis	**0h**	**48%**
Structured literature search	**0h**	**30%**
Clinical Problem	0	100%
Physiological Mechanisms	0	100%
Motivation for Physiological Modelling	0	100%
SOTA	0	0%
Problem Statement	0	100%
Build foundational cardiopulmonar...	**0h**	**13%**
Model the heart	0	50%
Test and evalute heart model	0	0%
Model the respiratory system	0	0%
Test and evalute respiratory system...	0	0%
Combine models	0	0%
Test and evaluate cardiopulmonary i...	0	0%
Requirement Engineering	**0h**	**0%**
Solution Analysis	**0h**	**0%**
System Description	0	0%
Modelling	**0h**	**0%**
Bioelectrical Modelling	0	0%
Compartment Modelling	0	0%
Physiological Modelling	0	0%
Architecture components	**0h**	**0%**
UX	0	0%
Database Connectivity	0	0%
Physiological Model Engine	0	0%
System Architecture	0	0%
Method Description	**0h**	**0%**
Python	0	0%
ODE Solvers	0	0%
Optimization Algorithms	0	0%
Test scenarios	0	0%
Implementation Methods	0	0%
Solution Implementation and Testi...	**0h**	**0%**
Individual Compartment Implementat...	0	0%
Individual Compartment Testing	0	0%
Module Implementation	0	0%
Module Testing	0	0%
System Implementation	0	0%
System Requirement Testing	0	0%
User Requirement Testing	0	0%
Report Writing	**0h**	**0%**
Problem Analysis	0	0%
Problem Statement	0	0%
Solution Analysis	0	0%
Methods	0	0%
Results	0	0%
Discussion	0	0%
Conclusion	0	0%