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Integrating visualisation into the systems modelling toolkit: Applications to clinical and health process systems

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy

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DECLARATION

I certify that except where due acknowledgement has been made, the work is that of the author alone; the work has not been submitted previously, in whole or in part, to qualify for any other academic award; the content of the thesis is the result of work which has been carried out since the official commencement date of the approved research program; any editorial work, paid or unpaid, carried out by a third party is acknowledged; and, ethics procedures and guidelines have been followed.

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Summary

Many areas of modern society, including healthcare, can be thought of as process systems. Such systems can be understood in terms of a sequence of inputs, work activities and outputs which become difficult to understand and control as a result of complexity arising from interactions between components within these system. Such complexity can hamper the ability to make decisions relating to these process systems.

Operations Research/Management Science (OR/MS) has responded to this challenge with the development of systems models, which create a representation of the system under investigation that can be used to help make decisions about the process system. OR/MS literature has developed a wide variety of techniques for systems modelling, including computational, statistical and mathematical approaches to assisting decision-making. This suite of methods can be referred to as the "OR/MS toolkit" for systems modelling.

OR/MS practice often involves the use of visualisation to aid undertanding, interpret results from systems modelling, or otherwise assist OR/MS practitioners in working with systems. This widespread use of visualisation has occurred due to its ability to flexibly and intuitively represent large amounts of information.

However, there has been little discussion within OR/MS literature on the use of visualisation as a tool for systems modelling. Likewise, there is a lack of explicit knowledge on how visualisation should be applied in an OR/MS context, and a lack of reported, general knowledge on how to integrate visualisation with conventional OR/MS tools. Given that visualisation provides an intuitive means for understanding complex information, this presents an opportunity for OR/MS experts to better model process systems and provide support for decision-makers by making use of visualisation as a tool for systems modelling.

This thesis seeks to advance the use of visualisation in systems modelling by addressing these gaps. We provide a systematic review on the use of visualisation within OR/MS literature, and from this synthesise a series of general visualisation principles to guide

beneficial visualisation properties, and a series of general visualisation practices which suggest means of following these principles.

We then use the results of this synthesis to develop an original *Visual Systems Modelling Framework* which provides a method for integrating visualisation into the systems modelling toolkit. This framework draws from established OR/MS theory and practice by explicitly setting out a conceptual model describing the system, the intended purpose of modelling the system, and plans for any conventional OR/MS tools which will be used to model the system. It links these aspects of conventional OR/MS methodology to the visualisation principles identified by the systematic literature review.

The thesis provides illustrative case studies of this *framework* in action by applying it in the development of four models for clinical or health process systems. First, we describe several novel contributions to literature on the conventional OR/MS toolkit that were made in the development of these models. These include a novel dissimilarity measure that can be used to compare and group sequences of ordinal data where sequence length can vary, and systematic validation of a method of clustering survival data using Coxian Phase-Type distributions. These contributions are then used in the case studies which follow the *Visual Systems Modelling Framework*.

The first case study is in the context of the care of Traumatic Spinal Cord Injury (TSCI). The care of TSCI involves several healthcare processes working together in unison to treat a patient who may have many different co-existing injuries resulting from the same event which lead to the spinal cord injury. This heterogeneity among patients results in organisational uncertainty regarding the specific care pathways taken by patients, making it almost impossible to make decisions which will improve care processes for this patient group. Before improvements to this system can be made, a greater understanding of the TSCI healthcare process is required. The *Visual Systems Modelling Framework* is applied in this system to generate new insights and promote discussion about TSCI healthcare processes.

The second case study is in the context of investigating the role of neurorehabilitative physiotherapy in the recovery of stroke survivors. There are open questions within clinical literature on stroke rehabilitation regarding what physiotherapy regimens lead to better patient outcomes. In this application, the *Visual Systems Modelling Framework* is used to

allow clinical researchers the ability to identify patterns in and explore the relationships between physiotherapy regimens and patient health, thereby developing an understanding which can improve the care provided in stroke rehabilitation.

The third case study is in the same neurorehabilitative system as the second case study. In this application, the *Visual Systems Modelling Framework* is used to develop a model which predicts patient outcomes based on their received physiotherapy regimen. This assists clinical researchers seeking to identify what physiotherapy regimens are likely to improve patient outcomes.

The final case study is in the context of planning an major clinical trial in stroke rehabilitation which uses an adaptive trial design. Adaptive clinical trials use prespecified rules to adjust the behaviour of the trial based on data as it is accrued by the trial. These rules can be used to address ethical concerns regarding giving patients experimental treatments which appear to be ineffective, enforce balancing of important prognostic factors across treatment arms, or any number of other desired features. However, such designs can lead to complex and counter-intuitive behaviour in the trial, requiring both careful planning and understanding of these behaviours. In this application, the *Visual Systems Modelling Framework* is used to model this clinical trial to assist planning and communicate the behaviours arising from the adaptive trial design.

Through these four case studies, this thesis provides illustrations of how the *Visual Systems Modelling Framework* can be used across multiple systems, each with their own requirements and modelling purpose. This thesis demonstrates how visualisation can be integrated in the OR/MS systems modelling toolkit, and contributes to OR/MS literature by providing a method for applying visualisation as a systems modelling tool.

“ *A picture is a key to understanding. Scientific breakthroughs often build upon the successful visualisation of objects invisible to the human eye.* ”

Press Release announcing the 2017 Nobel Prize in Chemistry
(Nobel Media AB, 2017)

Chapter 1

Introduction

Operations Research/Management Science (OR/MS) is "a scientific approach to decision making that seeks to best design and operate a system, usually under conditions requiring the allocation of scarce resources" (Winston and Goldberg, 2004, p. 1). This approach to decision-making has seen adoption in many applications, including healthcare where it has been used in contexts ranging from broader health policy to management of health systems and down to applications assisting individual clinical decision-making (Brandeau, Sainfort, and Pierskalla, 2004).

Chapter 1 serves to introduce the research presented in this thesis by providing an overview of OR/MS and visualisation, as well as identifying gaps within OR/MS literature. It responds to these gaps by posing three research questions which are addressed in the thesis. This chapter then describes the research setting in which these questions were addressed, followed by the outcomes and contributions resulting from this research.

1.1 Process Systems, OR/MS, and Visualisation

Many aspects of healthcare can be understood as *process systems*, meaning that these aspects can be described both as a process or as a system. This thesis adopts the definitions of processes and systems according to Davenport (1993) and Daellenbach (1994) respectively:

> A *process* is "a specific ordering of work activities across time and place, with a beginning, an end, and clearly identified inputs and outputs: a structure for action" (Davenport, 1993, p. 5).

In contrast to this focus on sequences, inputs and outputs, a system focuses on the behaviours arising from interactions between components.

> A *system* can be defined as follows (Daellenbach, 1994, p. 27):
>
> 1. "A system is an organised assembly of components. 'Organised' means that there exist special relationships between these components."
> 2. "The system does something, i.e., it exhibits a type of behaviour unique to the system."
> 3. Each component contributes to the behaviour of the system and is affected by being in the system. No component has an independent effect on the system. The behaviour of the system is changed if any component is removed or leaves."
> 4. "Groups of components within the system may themselves have properties 1,2, and 3. i.e., they may form subsystems"
> 5. "The system has an outside - an environment - which provides inputs to the system and receives outputs from the system."
> 6. "The system has been identified by someone as of special interest"

An example of a *system* is patient's body, which satisfies all of these criteria. However, a patient's body is not a *process*, as it lacks a clear beginning, end, inputs or outputs or work activities. However, certain sub-systems of the can be considered processes (e.g. processes enabling digestion), as these sub-systems have the properties of a process.

This thesis defines a *process system* as follows:

> A *process system* satisfies the definition of being both a *process* and a *system*: A *system* which contains clearly defined inputs, outputs and work activities, or a *process* which exhibits systemicity.

The *process systems* discussed in this thesis focus on the care of patients with neurological diseases and injuries. These can be considered *processes* which begins when a patient enters (is input) into a care process, is treated (has work performed on them), and then ends when the patient is discharged (output). Likewise, this can be considered a *system*, as health care is complex and requires the coordination and organisation of a large number of interacting logistical and medical components in order to function.

By their nature, *process systems* are complex and understanding or interacting with them is challenging. OR/MS applications address this by developing models, which are then used to help guide decision-making. In this thesis we adopt the definition that a *model* is "an external and explicit representation of part of reality as seen by the people who wish to use that model to understand, to change, to manage and to control that part of reality" (Pidd, 2003, p. 12). This definition emphasises that a model is always a simplification which does not encapsulate the full system (representation of a part of reality), and that the model was developed by someone for some purpose.

As a result of differences in which parts of reality are to be modelled, as well as what exactly is intended to be understood, changed, managed or controlled, the function and purpose of a model can vary from application to application. These differences have been discussed in OR/MS literature, including taxonomies of model use laid out by Pidd (2010) and Bayer et al. (2014).

Under Pidd's (2010) taxonomy of model use, models are described as falling on a spectrum between *Routine Use* and *Human Interaction*, across which they are used for: *Decision Automation*, completely replacing human decision making; *Routine Decision Support*, used by humans to assist decision-making; *Investigation and Improvement*, gaining understanding of complicated situations and investigating potential improvements; and *Providing Insights for Debate*, fostering discussion which can lead to decisions being made. In comparison, Bayer et al.'s (2014) taxonomy provides focuses on the social role that a model fulfils, using two independent measures for classifying models. The first of these draws a distinction between *Technical* models, which represent existing knowledge,

and *Epistemic* models, which create new knowledge. The second of these distinguishes between *Representative* models, whose function is to represent reality, while a *Boundary* model's primary role is to facilitate communication.

The variety of model uses in OR/MS practice has lead to the development of many different mathematical and statistical techniques which are collectively known as the "OR/MS toolkit" (Pidd, 2004, p. 796). These methods include but are not limited to simulation, optimisation and statistical methods, each of which are active research areas in and of themselves. This variety of methods provides many approaches by which decision makers can understand, change, manage and control a modelled system. Despite the ongoing development of mathematical and statistical techniques which can be used for systems modelling, there has been little attention in OR/MS literature paid to the role of visualisation in systems modelling (Jääskeläinen et al., 2016).

Visualisation is an effective way to present and comprehend information, and "requires no understanding of complex mathematical or statistical algorithms or parameters" (Keim, 2002, p. 100) As visualisation provides a means for representing a system in a manner which decision-makers can comprehend without a formal background in OR/MS practices, it has the potential to support decision-makers in their use of methods within the systems modelling toolkit by assisting their comprehension of the system and techniques used in the modelling process.

The opportunity to better incorporate visualisation into OR/MS methodology was noted by Zhu and Chen (2008, p. 716), who argued that "when it comes to decision support, the focus should not only be on the development of more advanced technology but also on the creation of a framework to guide the applications of existing visualisation systems to the task of domains of decision making". Integrating visualisation into the systems modelling toolkit, a task this thesis terms *visual systems modelling*, will provide OR/MS experts with the opportunity to better represent, understand, change, manage and control reality.

1.2 Research Gaps

The research gaps in OR/MS literature regarding the use of visualisation in systems modelling can be summarised as follows:

Gap 1: Existing discussion within OR/MS literature on the use of visualisation has been narrow in scope, with limited attention paid to how visualisation can be integrated into the systems modelling toolkit. While visualisation technologies are available in a variety of commercial and noncommerical packages, there are only a "handful of success stories" that have been published on their use (Jääskeläinen et al., 2016, p. 716). What studies have been carried out have been disconnected from real-world systems. To date, "few studies on information visualization have been carried out" in the context of OR/MS. (Jääskeläinen et al., 2016, p. 13).

Gap 2: There is a lack of explicit knowledge about guiding principles and procedures used in the development and application of visualisation within OR/MS literature. Visualisation covers a wide body of methods, practices and techniques for representing and information (for a review, see Keim (2002)). However, there has been very little discussion on how such techniques can be applied in OR/MS practice, which lead to Zhu and Chen's (2008) call to action.

Gap 3: There is a lack of reported, general knowledge on how visualisation can be used in conjunction with mathematical and analytical techniques within the OR/MS toolkit. Where the use of visualisation and analytical approaches to systems modelling is discussed, it is in the context of standardised approaches to visualising specific analytical OR/MS tools, such as conventional process animations in provided by many discrete event simulation platforms (Swisher et al., 2001a)). Such approaches to visualisation are not readily generalisable to other methods within the systems modelling toolkit, inhibiting the development and refinement of OR/MS methodology.

1.3 Research Objective and Questions

This thesis seeks to address these research gaps and contribute to OR/MS literature by investigating the use of visualisation within the systems modelling toolkit. These gaps will be addressed, specifically in the context of clinical and health *process systems*, by answering the following research questions:

1. How is visualisation currently used in quantitative OR/MS?
2. How does model use across Pidd's (2010) and Bayer et al.'s (2014) taxonomies influence how systems visualisation can be used?
3. How can visualisation as a systems modelling tool be used in conjunction with conventional methods within the OR/MS toolkit to enhance decision support, specifically:
   (a) How can conventional OR/MS tools (such as k-nearest neighbours or clustering methods which use Coxian Phase-type distributions or novel dissimilarity measures) be integrated into *visual systems modelling* of clinical and health process systems?
   (b) How can visualisation help validate conventional OR/MS tools such as those described in question 3(a)?

1.4 Research Setting

This PhD was undertaken in close collaboration with The Florey Institute of Neuroscience and Mental Health (The Florey) and The Institute for Safety, Compensation and Recovery Research (ISCRR). The Florey is the largest brain research group in the Southern Hemisphere, supporting research in stroke, epilepsy, Alzheimer's and other serious neurological diseases (The Florey Institute of Neuroscience and Mental Health, 2018). ISCRR is a partnership between Monash University, Work Cover and the Transport Accident Commission, seeking to "facilitate research and best practice in the areas of injury prevention, rehabilitation and compensation" (ISCRR, 2018). All data used in this thesis was

supplied by ISCRR and The Florey, who provided feedback throughout the model development process. This close collaboration continued into model validation, strengthening links between this research and real-world OR/MS applications.

1.5 Outline of Thesis

This thesis is organised as follows. Chapters 2 and 3 contain theoretical and methodological contributions to OR/MS literature.

Chapter 2 provides a review of published literature on the use of visualisation in OR/MS, reporting on the principles and best practices which drive applications in the area. It then suggests a *Visual Systems Modelling Framework* for better integrating visualisation within the OR/MS toolkit by arguing that the "systems thinking" approach to OR/MS practice is equally applicable to visualisation. The use of the framework is demonstrated through case studies in Chapters 4-7.

Chapter 3 describes two analytical methodological contributions to OR/MS literature which are used in conjunction with the framework proposed in Chapter 2 in later chapters. The first of these contributions is validation of an existing method of clustering survival data by modelling it as the time taken to complete a process consisting of one or more sequential stages, as well as a generalisation of this method to other process types. The second contribution in this chapter is a novel dissimilarity measure for identifying homogeneous groups in sequences of observations, with varying sequence lengths. These are used in Chapters 4 and 5.

Chapters 4 to 7 contain case studies which apply contributions made in Chapters 2 and 3 to real-world systems.

Chapter 4 applies the *Visual Systems Modelling Framework* to develop a model for understanding process flow among patients who have suffered Traumatic Spinal Cord Injury (TSCI). TSCI is a debilitating condition which can lead to severe, lifelong disability. While there is evidence that improving care processes could lead to better outcomes for patients with TSCI, the complexity of the condition and the care processes required had

led to a great deal of uncertainty, which makes improvements difficult. The purpose of model presented in this chapter is to aid understanding of the TSCI care process system, and provide decision-makers with new insights for information to foster discussion and debate. The model achieves this by presenting systems data from the TSCI care process, using clustering techniques based on resource usage and length of stay to reduce the perceived complexity of the system. This model integrates visualisation with conventional OR/MS tools in a way which promotes customisablility, allowing users to either use clustering techniques as a tool for navigating the *visual systems model*, or to or to control the visual aspects of the model. As this allows several approaches to combining visualisation with conventional OR/MS tools, it can be considered a *User-Driven* approach to *visual systems modelling*.

Chapter 5 applies the *Visual Systems Modelling Framework* to develop a model for investigating patterns in treatment and patient health in stroke rehabilitation. Stroke is a common illness and a leading cause of death and disability worldwide. Improved care in this area can therefore lead to widespread improvements in patient wellbeing around the world. The model presented in this chapter helps clinical researchers to investigate the relationship between physiotherapy and patient outcomes in stroke rehabilitation by presenting graphical summaries of each individual patient's full care pathway, including therapy received on each day, the patient's changing health, and any adverse events that may have impacted their recovery. Conventional OR/MS tools such as cluster analysis are used to identify patterns in physiotherapy regimen and patient recovery to assist users in navigating this visualisation. These clusters can be used to navigate the developed visualisation of the model, and can be described as *analytically-driven visualisation*.

Chapter 6 applies the *Visual Systems Modelling Framework* to develop a counterpart model to the one presented in Chapter 5. While the model discussed in the previous chapter was focused on investigating dose-response relationships in stroke rehabilitation, the model presented in this chapter seeks to identify potentially beneficial physiotherapy regimens for the treatment of stroke. The developed *visual systems model* uses a conventional OR/MS predictive model which predicts patient outcomes based on the physiotherapy regimen they received, and uses visualisation to provide transparency to

the logic of the model and access to its outputs. As this model integrates visualisation with conventional OR/MS tools by using visualisation to navigate a conventional OR/MS tool, that can be considered *visualisation-driven analysis*

Chapter 7 presents models supporting the planning and implementation of an adaptive clinical trial in stroke rehabilitation. Two models are presented in this chapter, intended to be used in parallel to support the development and implementation of the trial. The first of these models focuses on communicating the mechanics of the trial to clinical researchers, and focuses on demonstrating concepts used in the trial rather than for decision-making. The second of these models is a simulation model which assists in the planning of the trial by predicting trial outcomes by providing assumptions and rules governing the trial behaviour. This application integrates visualisation with conventional OR/MS tools by separating these tasks, and can be considered *Parallel Model Design*

Chapter 8 summarises the work presented in this thesis, provides further discussion of its novelty and contributions to OR/MS literature, and identifies limitations in the research contributions made by this thesis. It presents suggestions for future research on the use of *visual systems modelling* in OR/MS practice.

1.6 Novelty and Contribution of Thesis

The contributions made by this thesis to OR/MS literature can be summarised as follows.

1. **Review of reported visualisation practices in OR/MS literature**. Chapter 2 reviews published literature on visualisation practices in OR/MS, and synthesises from it a list of foundational principles and common practices in approaching visualisation. It also identifies several research gaps in how visualisation is applied to OR/MS, and highlights the need for additional research and discussion in OR/MS literature.

2. **New knowledge on how to integrate visualisation into the OR/MS toolkit**. Chapter 2 addresses the research gap identified in the literature review by developing a *Visual Systems Modelling Framework* to guide the application of visualisation

as a systems modelling tool. The use of this framework is illustrated by developing a series of OR/MS models, each demonstrating a different approach to how visualisation can be integrated into the OR/MS toolbox. Comparisons between these models highlights:

(a) **How Visualisation can be used across the spectrum of model use**. Chapter 4 provides an example of how *visual systems models* can be used to *Provide Insights for Debate* in an *Epistemic Representative* fashion. Chapter 5 describes an *Epistemic Representative* model which has elements of both *Providing Insights for Debate* and assisting *Investigation and Improvement, while 6 illustrate how visual systems models can be used to Investigate and Improve in an Epistemic Representative fashion.* Chapter 7 shows how *visual systems models* can be used for *Routine Decision Support*, in both a *Technical Representative* and a *Technical Boundary* fashion.

(b) **How Visual and analytical components of OR/MS models can be integrated in different manners**. Each case study in this thesis illustrates a different approach to integrating visualisation with conventional OR/MS tools to develop visualisations of systems. Chapter 4 demonstrates how visualisation and analytical OR/MS methods can be integrated in a highly-customisable manner which allows users to specify how they want visual model components to interact with analytical components. In contrast, Chapters 5 and 6 exemplify a rigid approach to integrating visualisation, where conventional OR/MS tools are used to navigate visualisation, or visualisation is used to navigate analytical OR/MS tools. Chapter 7 illustrates an alternative approach by separating visualisation and modelling into two parallel models which support one another.

(c) **How visualisation can assist validation of conventional OR/MS tools**. Chapters 4 and 5 both make use of clustering, and use visualisation to interpret these clusters. Visualisation allows these clusters to be understood in terms of the system being modelled, thereby assisting validation of these clusters. Chapter 6 uses weighted k-nearest neighbours to predict patient outcomes. Visualisation is used to provide transparency to how predictions are made, thereby assiting validation of the model.

3. **Development of conventional OR/MS methods particularly suitable for application to process systems**

   (a) **A novel measure of dissimilarity for clustering sequences of ordinal records** Chapter 3 presents a novel measure for quantifying the dissimilarity between two or more sequences of ordinal records, where the length of these sequences can vary. Chapter 5 uses this measure.

   (b) **Validation of a method of clustering survival data using phase-type distributions** Chapter 3 presents comprehensive validation for clustering survival data using Coxian-phase type distributions, providing guides for when the method works as intended versus when it does not. Chapters 4 and 5 use these guides.

4. **Development of systems models in applications that are underserviced by the OR/MS community**. There has been little published OR/MS work performed in the context of caring for patients with either stroke rehabilitation or traumatic spinal cord injury. As a result, the challenges and potential benefits of applications in these areas are not well understood. The case studies presented in Chapters 4, 5, 6 thesis provide examples of how OR/MS methodologies can be applied in these areas.

5. **New Knowledge on the behaviour of adaptive clinical trial designs**. The design and application of adaptive clinical trials is a research area with the potential to improve ethical considerations around clinical trials. The case study presented in Chapter 7 supports research in this area by providing examples of how such a trial can be implemented.

Figure 1.1 summarises how each chapter of this thesis relates to each research question, and the contributions this thesis makes to OR/MS literature.

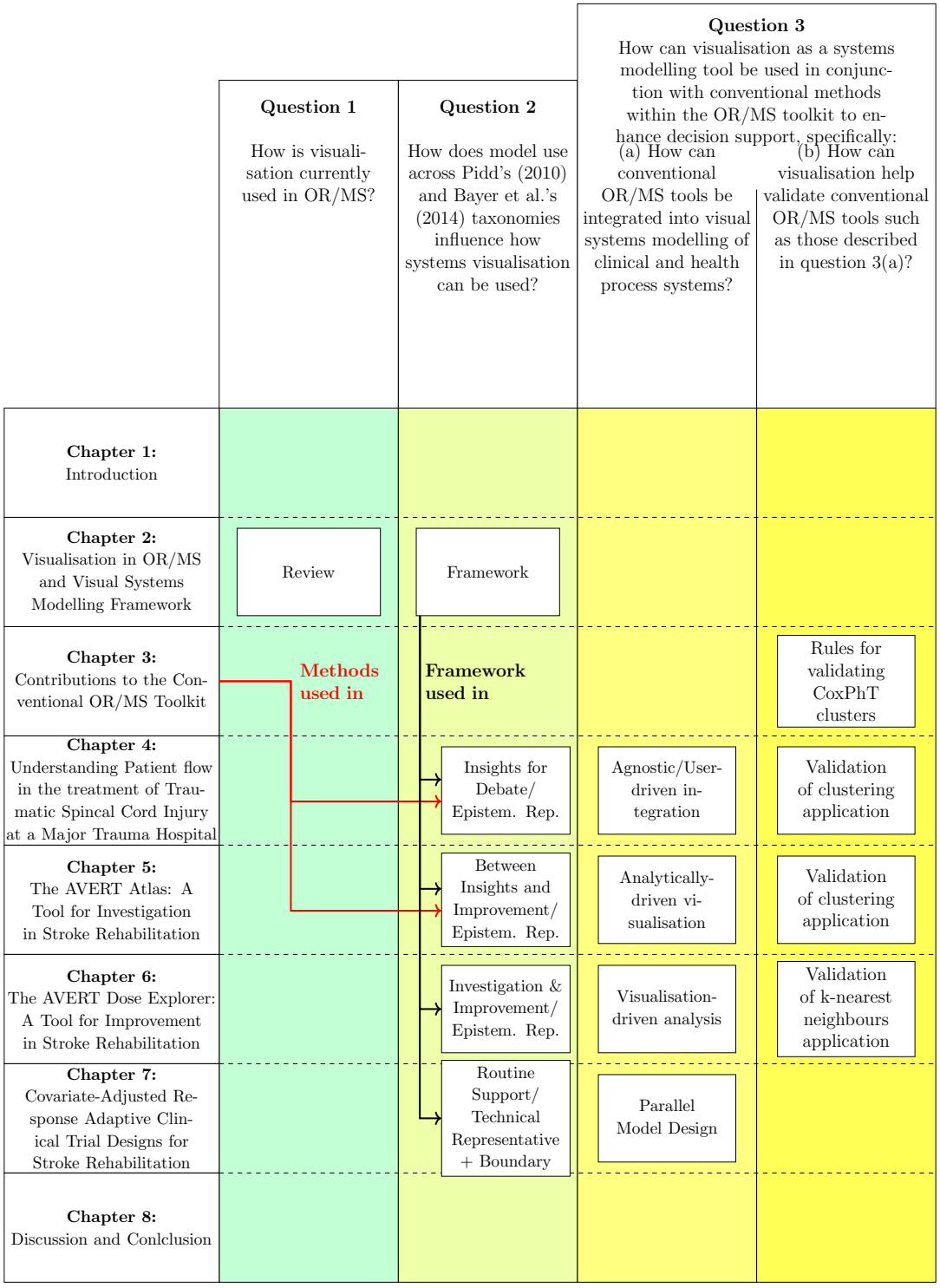


Figure 1.1: Outline of structure and contributions made by thesis

1.7 Summary and Conclusion

This chapter outlined the context and objective of this thesis by identifying gaps in the OR/MS literature, and formulated research questions to respond to this gap. The contributions made by this thesis to OR/MS literature are novel because visualisation is an area where there has been little discussion, and the *Visual Systems Modelling Framework* presented in this thesis is the first reported structured framework for integrating visualisation into the development of OR/MS models.

Chapter 2

Visualisation in OR/MS and Visual Systems Modelling Framework

2.1 Introduction

This chapter addresses Research Question 1 proposed in Section 1.3 by conducting a review of published OR/MS literature discussing the use of visualisation. It then synthesises the results of this review into a series of recommendations on the design and application of visualisation in OR/MS, and then uses these recommendations to develop a *Visual Systems Modelling Framework* to support *Visual Systems Modelling*. The *Visual Systems Modelling Framework* is applied in Chapters 4, 5, 6 and 7, with Section 2.4 of this chapter providing an overview of how each of these chapters apply visualisation across different modelling purposes, thus addressing Research Question 2.

2.2 Review of Data Visualisation, Animation and Interactivity in OR/MS

This section describes a systematic literature review on the use of visualisation within OR/MS literature, focusing on OR/MS applications which involve data. This focus was chosen to remove "Soft" OR/MS methods such as Soft Systems Methodology (Checkland, Scholes, and Checkland, 1990) from the review, as this has been extensively discussed and reviewed elsewhere (Forrester, 1994; Checkland, 2000; Platt and Warwick, 1995).

OR/MS literature on the use of visualisation was found by searching Scopus for any article where either of the following conditions were met, with no restrictions placed on time of publication:

1. Title, abstract or keywords matched the search term *("operational research" OR "operations research" OR "management science") AND ("visual*" OR "animat*" OR "interact*") AND "data"*

2. Source title matched the search term *("operational research" OR "operations research" OR "management science")*, and title, abstract or keywords matched the search term *("visual*" OR "animat*" OR "interact*") AND "data"*

Due to the lack of discussion within OR/MS literature which focuses on the use of visualisation for process systems modelling, this review treats the topic of visualisation broadly in order to include incidental discussions of visualisation. As the use of visualisation in the context of simulation is well understood, there was no attempt made to include simulation journals within this search.

A total of 1734 results were returned, and after reading the abstracts, a total of 141 papers were selected for full-text reading. Of these, 34 were excluded as duplicates or due to irrelevance, with reasons given in Appendix A.2, leaving 107 relevant papers, listed in Appendix A.1. Figure 2.1 summarises this process.

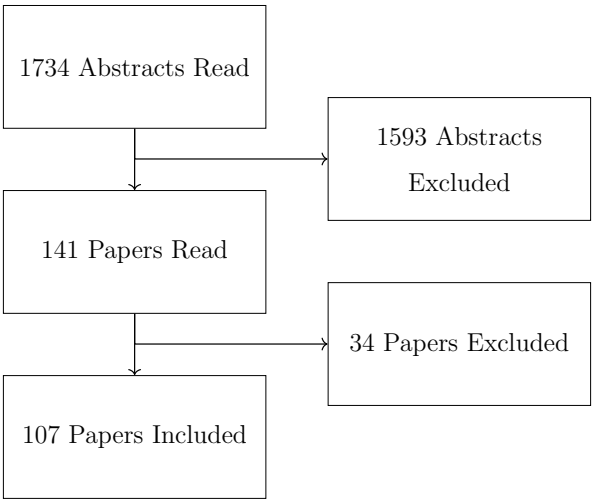


Figure 2.1: Summary of Literature Inclusion/Exclusion Process

Two of these papers provided an overview of the use of data visualisation in OR/MS: Andreinko et al. (2007) summarised the results of a 2006 workshop on methods of visu-

alising spatial and temporal data in geospatial sciences, which they refer to as "geovisual analytics for spatial decision support". They make a call for action for researchers to develop methods and tools to promote understanding of poorly defined and complex systems using visualisation. Jääskeläinen et al. (2016) reviewed OR/MS literature and identified three common approaches to information visualisation for Performance Measurement Systems: Soft Systems approaches, where user understanding of the system is diagramised; Data Visualisation, where data is visualised using standard visualisation techniques such as scatter plots and histograms; Dashboards, which organise and display data visualisations, allowing the user to see multiple system characteristics at once, with the ability to zoom in and focus on particular details as suits their investigative needs. However, the review concluded that OR/MS literature into the use of information visualisation as an OR/MS tool is limited, encouraging researchers to investigate visualisation in OR/MS.

Additionally, three other papers discussed the relationship between analytics and OR/MS methodology: France and Ghose (2018) reviewed the intersection between OR/MS practice, expert systems and statistics in the context of marketing analytics, and provided a historical overview of visualisation techniques used within marketing. Mortenson, Doherty, and Robinson (2015) reviewed the field of analytics, discussed how it relates to Operations Research and proposed a research agenda for OR/MS practitioners, noting that "OR/MS, a discipline closely focused on decision making, can see genuine benefits from visualisation such as improving the ease of model validation and increased buy-in from stakeholders" (p. 593) before encouraging further studies into the use of visualisation in OR/MS. Hindle and Vidgen (2018) demonstrated that analytics methodology can be applied in the context of OR/MS practice, and proposed a Business Analytics Methodology to guide the use of both conventional OR/MS techniques and data science methodologies in OR/MS practice, focusing on first on describing the system and its components, eliciting important contextual information, identifying opportunities for analytics, then using the selected analytics methods.

We classified the remaining papers into one of three categories:

1. Visualisation Concepts, Principles and Practices (16 papers),

2. Visualisation of numeric data either used or produced by a system of interest (35 papers), and

3. Visualisation of systems components and their relationships through the prism of conventional OR/MS tools and techniques (53 papers)

2.2.1 Visualisation Concepts, Principles and Practices

Five papers discussed visualisation as a general concept, highlighting how visualisation can be used to facilitate communication and understanding.

Wark and Lambert (2007) argued that presenting information as a visual narrative can improve system understanding by providing structure to the information provided. Eppler, Mengis, and Bresciani (2008) discussed ambiguity in how graphics are interpreted, and argues that conflicting interpretations of visualisations can facilitate discussion by recognising and preserving differing viewpoints. Wolf, Simpson, and Zhang (2009) demonstrated that experts are more likely than novices to take full advantage of visualisation tools that are available to them, and recommends that training procedures be modified to encourage novice users to fully utilise available visualisation tools. However, Bacic and Henry (2012) cautioned that visualisation is not always the most appropriate method for addressing problems, and recommends that it should only be used if it leads to a "perception of lower information uncertainty and complexity." This reflects earlier work done by Remus (1987), who compared the effectiveness of visual summaries of data against tabular summaries and found that visual summaries are better at representing complex data while tables are better at presenting low complexity data.

Eleven papers identified the importance of *user control*, allowing users to quickly change the direction of their investigation across *levels of abstraction*, *variables of interest*, and *time*. Eick and Wills (1995) discussed the benefits of interactive visualisation and discussed how interactivity could aid in data analysis. Chan, Keeton, and Ma (2010) promoted an *iterative approach* to visualisation, where investigators would begin by examining an isolated component of interest, slowly adding complexity and relationships to other system components as the model develops. Bieber (1995) and Morin, Jenvald, and Thorstensson (2000) both described tools for linking information consisting of *different formats and media*, arguing that by presenting summaries of data, along with relevant media such as images, video and accounts of events, users are better equipped to understand *complex processes*. Heer, Außem, and Wörzberger (2009) organised multidimen-

sional data as a hypercube (with each dimension corresponding to a variable) allowing the user to *interactively* visualise subsets of the dataset by making cross-sections and viewing "sides" of the cube. The remaining papers detailed applications where *interactivity* proved beneficial, with applications in domains such as managing military housing (Forgionne, 1997), product development (Matsatsinis and Siskos, 1999), management of ski safety (Radovanovic et al., 2019), construction management (Ye and Froese, 2009) computer network management (Dos Santos et al., 2000) and patient flow in hospitals (Jensen, Boyle, and Khanna, 2012).

In summary, these papers discussed visualisation in a theoretical sense or provided case studies which demonstrated common principles on how visualisation should be used. These papers agreed that user control added value to visualisations, and suggested that visualisation is most beneficial when it leads to a reduced perception information complexity.

The focus on reducing information complexity mirrors Pidd's (2003) definition of a model as a simplified representation of a part of reality. *It can therefore be argued that visualisation of a system can be considered a model of that system, as it is a representation of a part of reality, developed for some purpose within that system.* Like the conventional OR/MS modelling toolkit, there are many approaches to using visualisation to reduce perceived complexity. Example techniques to reduce perceived complexity include, but are not limited to, the use of interactivity, presenting information in a narrative which imposes a context-preserving structure, and by limiting the used visualisation techniques to those which decision-makers are familiar with.

2.2.2 Techniques for Visualising Data Used or Produced by a System

Two papers provided classifications for data visualisation techniques. Tan and Benbasat (1990) classified 2-dimensional data visualisation according to the type of question addressed by the visualisation and whether horizontally-aligned and vertically-aligned components correspond to elements which are discrete and clearly demarked, or are continuous and blend into each other. Keim (2002) followed a more general approach, classifying data according to the type of data, the technique with which data is visualised, and how these

visualisations can be manipulated to emphasise particular aspects.

Visualisation was heavily discussed in the context of process modelling, with five papers discussing the use of visualisation in this domain. Delias, Zoumpoulidis, and Kazanidis (2018) discussed visualisation in the context of process mining, and provided examples of how process sequence rules can be automatically identified and visualised. Burattin, Cimitle, and Maggi (2004) showed how animation could be used to show how process structure changes over time. these rules could be discusses method for visualising outputs from Bachhofner et al. (2017) discussed visualisation in the context of Business Process Analytics, and demonstrates how colour, size, and other visual cues can be used to represent process data. Bolt, Leoni, and Aalst (2018) used colour to highlight differences in event logs, which can then be interactively expanded for additional detail. Gulden (2016) developed a novel technique called "rhythm-eye" for visualising process event data.

Additionally, seven papers discussed the use of visualisation in business intelligence, specifically focusing on the use of *information dashboards* to present details about a system's properties. (Fradi et al., 2017) noted that dashboards provide easy access to information when making decisions, while two papers suggested approaches to dashboard design that could reduce the time and cost of data analysis: One promoting automated report generation (Pieterse, 2012), and one suggesting that the visual design for dashboard elements should be *decoupled* from data analysis, with analysts using a series of predeveloped templates instead (Nowak et al., 2012). Three papers highlighted the importance of *interactivity* and *customizability*. Neumayr, Schrefl, and Linner (2011) argued that the common dashboard approach poorly captures important environmental and contextual information that should guide more in-depth analysis, and suggests the use of a "semantic cockpit" to assists analysis by providing a means to progressively customise information displayed based on contextual information that has been gained through previous analysis, while Dau and Andrews (2014) used customisation to allow users to "explore their data in new ways, discovering hidden meaning and solving hitherto difficult problems". Wasser and Lincoln (2010) discussed the importance of representing in multiple ways to meet the needs of multiple types of users. Shamsuzzoha et al. (2017) provided an example of the application of a dashboard, but did not discuss the method in detail.

The majority of papers classified as techniques discussed specific visualisation tech-

niques for representing data.

Nine of these papers discussed novel data visualisation methods. Cano et al. (2013) described a technique for drawing multiple symbols on crowded visualisations which maximises the visibility of all symbols. Liiv et al. (2012) discussed the use of table row and column reordering techniques for visually organising and summarising data. Carrizosa, Guerrero, and Morales (2017) generalised the treemap visualisation technique to allow for complex shapes to be used beyond rectangles Feiner and Beshers (1990) and Abbiw-Jackson et al. (2006) described techniques for flattening of hyperdimensional data into a lower number of dimensions which can then be visualised. Rose et al. (2005) examined how electronic medical records are presented to clinicians, and proposed changes to how information is presented, and made suggestions such as increasing screen resolution or changing colour schemes to aid visual navigation. Suntinger et al. (2008) discussed a data visualisation method for visualising process data, representing event data in a 3-dimensional cylinder. Lee and Rojas (2013) developed methods for visualising project progress in construction management. Hazır and Shtub (2011) ran laboratory experiments comparing several method for visualising dynamic cost information for project management.

Twelve of these papers discussed how specific visualisation techniques could be used for specific applications. Network visualisation was discussed for understanding relationships in customer airline data (Farrugia and Quigley, 2009), organisational structure among nurses (Shafiei, Azar, and Esmaielpour, 2018) and differences in biomedical innovation across countries (Owen-Smith et al., 2002), as well as identifying anomalous network traffic for IT security threat detection (Wang, 2018). Likewise, scatter plots were discussed for applications in traffic flow monitoring (Kusakabe, Iryo, and Asakura, 2010) and monitoring of mental health among patients suffering from depression (Haspeslagh and Delesie, 1998). The remaining six case studies shared no common themes. Park et al. (2016) used visualisation to interpret results from crowdsourced decision-making in diagnosing colon cancer, using a dashboard containing word clouds, parallel coordinates and a colour-coded matrix to visualise demographics and decisions among people contributing to the crowdsourced results. Liu and Liu (2009) applied treemaps to structure understanding of banking data. Ieva and Paganoni (2015) discussed the use of funnel plots to detect outliers

among patients with acute myocardial infarction. Thomas et al. (2018) used visualisation to monitor the ecological impact of a hydro-electrical power plant, making use of "traffic light" colour coding intuitively highlight when ecological changes fall outside of accepted limits. Osekowska, Axelsson, and Carlsson (2013) used visualisation of potential fields to describe maritime traffic flow through bodies of water. Crowe et al. (2017) demonstrated the visualisation of two-dimensional cumulative proportions to identify patient groups who experienced a disproportionate number of adverse events, assisting decision-making in prioritising healthcare improvements

These papers focused on presenting novel methods for visualising data, or discussed methods for visualising data in specific contexts. Visualisation was used throughout these papers as a tool for understanding and interacting with real-world systems, but there was little discussion on how this ties into OR/MS methodology.

2.2.3 Visualisation for Conventional OR/MS Tools

Where the reviewed papers explicitly discussed OR/MS methodology, it was in the context of using visualisation as an interface for conventional OR models, either in model development and use, or in the advantages it brings in fulfilling the model's purpose.

Thirteen papers discussed visualisation in terms of how it can complement simulation-based OR applications. Sargent (2005) discusses how visualisation of simulation models can assist in the validation and verification of discrete-event simulation models. Likewise, Hamad and Al-Hamdan (2007) discusses how visualisation can be used in the validation of metamodels. Benke, Papasimeon, and McDonald (2018) extended traditional simulation visualisation methods using augmented reality, and discussed how this approach could be applied to simulations of military operations. Akhavian and Behzadan (2012) discussed how a combination of real-time process monitoring, discrete event simulation and 3D systems representations can assist decision makers in construction management. Of these, nine papers provided simulation case studies, in fish farming (Halachmi, 2006), medical clinics (Paul and Kuljis, 1995; Swisher et al., 2001b; Schaumann et al., 2017), military operational planning (Schubert et al., 2015), modelling craniofacial growth (Starke, Rübel, and Lux, 2003), trade flows and freight traffic (Velichko, Gribova, and Fedorishchev, 2016), port shipping processes (Koch, 2007), and production planning (Gravel et al.,

1994). These papers discussed the value added by visualisation by assisting model users with comprehending model mechanisms, and guiding trouble-shooting when the model behaves unexpectedly.

Additionally, three papers (Osekowska, Axelsson, and Carlsson, 2012; Grignard and Drogoul, 2017; Ingram and Brooks, 2018) made use of simulation environments for data visualisation. In these cases, the simulation environment was used as a convenient platform for developing complex animated, interactive visualisations of data. Rather than develop explicit rules for model behaviour, they instead fed data directly into the model to control the behaviour of simulation components.

Eight papers identified value in using visualisation to complement optimisation tools. Rather than being used for verification and validation as was the case in simulation visualisation, visualisation was seen here as an interface between users and "equation-heavy" optimisation routines. Collaud and Pasquier-Boltuck (1994) and Murphy and Stohr (1989) describe systems for visually describing and constructing linear programming models. Ardito et al. (2009) used optimisation routines to pre-optimise staff schedules, which would then be visualised and presented to a manager who could then review and alter recommendations made by the optimisation routine. This allowed expert human oversight of the model, where users could easily overrule recommendations made by the decision support tool that experience or additional knowledge suggests would be unfeasible or sub-optimal. El-Fattah (2012) developed a "traffic light model" for university capacity that would allow a user to visually compare current KPIs with predicted measures under recommendations made by an optimisation tool. Visualisation allowed for quick, low-detail interpretation of the results. Draman et al. (2002) described a system that opened the model-building process up to system practitioners by effectively treating optimisation routines as a black box model component that users can directly build around. Visualisation was seen here as a method for including users in model development, rather than as a tool for interpretation and application of final results. Gazmuri and Arrate (1995) presented an interactive, graphical system for optimisation in production planning Deasy et al. (2006) presents a tool for aiding research into radiotherapy treatment planning by providing an interactive software platform with visualisation capability for testing new approaches to the optimisation of radiotherapy dose. Tsiflakos and Owen (1993) discusses

the benefits of visualisation in the design of railway systems, using both simulation and optimisation.

Fourteen papers discussed the use of visualisation for multicriteria decision-making. Most of these papers discussed methods for visualising multicriteia optimisation outputs. Genest and Zhang (1996) discussed the use of Gower plots to represent relative values of solutions in multicriteria decision-making. Weber and Desai (1996) and Di Matteo, Dandy, and Maier (2017) discussed the use of parallel coordinates to visualise outputs from multi-criteria optimisation where there are multiple stakeholders with conflicting priorities, while Kasanen, Östermark, and Zeleny (1991) discussed the use of spider plot to display the same information. Trinkaus and Hanne (2005) suggested using arrows in conjunction with a spider plot to represent whether each variable should be maximised or minimised. Roselli, Almeida, and Frej (2019) compared spider plots and bar graphs by using eye-tracking technology to investigate how decision-makers interacted with these two methods. In contrast, rather than attempting to preserve all detail about potential solutions, Vetschera (1992) used a modified form of principle components analysis to reduce the dimensionality of multi-criteria optimisation problems which preserves preference information, thereby making it easier to visualise. Likewise, Miettinen et al. (2009) discussed how box indices could be used to visualise outputs from multi-objective optimisation. Frej, Almeida, and Costa (2019) uses networks to rank potential solutions where there is no clear information about priorities for each criteria. Hudec and Vujošević (2010) attempts to rank municipalities based on multiple criteria using fuzzy sets, and then uses visualisation to help interpret these rankings. Agarwal et al. (2019) used colour to interpret multicriteria performance rankings for police organisations, using hue to represent criteria performance. Siskos, Spyridakos, and Yannacopoulos (1999), Costa et al. (1999), and Mareschal and Brans (1991) present an interactive, graphical systems intended for practical use, in both cases using visualisation to understand the results of underlying OR/MS methods.

Six papers discussed the use of visualisation as a tool in the application of Data Envelope Analysis (DEA). El-Mahgary and Lahdelma (1995) and Førsund, Kittelsen, and Krivonozhko (2009) discussed 2D methods for visualising outputs of DEA, while Seidl and Sommersguter-Reichmann (2011) presented a 3D visualisation method. Yang, Xu, and

Yang (2012) suggested that visualising outputs from DEA could help when interactively adjusting the model. The rest of these papers discussed the use of visualisation to interpret outputs of DEA in evaluating hospital performance (Ozcan et al., 2010), or the electricity sector (Lins et al., 2007).

Twelve papers discussed how visualisation could be used for interpretation and validation of statistical methods. Bernatavičienė et al. (2006) and Dzemyda and Kurasova (2006) discussed techniques for visualising results returned by Self-Organising Maps, while four other papers applied the statistical method to analyse and visualise key performance indicators collected by organisations (Cattinelli et al., 2012), support clinician decision-making in ordering pathology tests (Zhuang et al., 2009), and identify profiles of customers who are targets for marketing campaigns (Seret et al., 2012). Lai et al. (2014) used visualisation to inspect and interpret clusters of patients with breast cancer that were identified with semi-supervised fuzzy c-means clustering. Likewise, Powell et al. (2017) discussed the use of parallel coordinates plots to interpret clusters which were identified using hierarchical clustering. Visualisation was also discussed in terms of model validation by visually comparing fitted distributions to real data (Alderman and Mense, 2007; Christodoulou and Taylor, 2001; Marshall and Shaw, 2014; Riihimäki, Sund, and Vehtari, 2010) or using visualisation to interpret and interrogate statistical models (Au et al., 2010)

With the exception of three papers which exploited simulation environments for data visualisations, visualisation was seen as an "add-on" to an underlying conventional OR/MS model. Where the visual component of this model was discussed in detail, it was in terms of the added value that it brought to the existing OR/MS model. There was no discussion of the use of visualisation as a standalone OR/MS systems modelling tool.

2.2.4 Synthesis of Literature

With the exception of a relatively small number of papers discussing visualisation as a general concept, the reviewed literature is limited to discussing either specific techniques for visualising systems data or visualisation in conjunction with conventional OR/MS tools. Where the reviewed literature discussed how visualisation can be used as a tool in OR/MS practice, it commented on lack of explicit knowledge within the OR/MS literature on the use of visualisation as a systems modelling tool (Jääskeläinen et al., 2016;

Andreinko et al., 2007).

Despite this, the reviewed literature described several common attitudes towards visualisation, which this review has synthesised into two categories: *Visualisation Principles*, or recommendations around what general properties of and approaches to systems visualisation are beneficial in communicating information, and *Visualisation Practices*, or recommendations about what specific techniques are effective at applying these Visualisation Principles.

2.2.4.1 Visualisation Principles

Visualisation Principles refer to recommendations about what visualisation should aim to achieve. These principles are fundamentally aimed at reducing information complexity and improving a decision-maker's ability to understand and interact with the system being modelled.

Principle 1: Model Users should be able to control what information is shown and level of detail to which it is shown. This was a common feature in the reviewed papers, either working from a low-detail overview of the full system with additional detail being pulled up as required (a top-down approach), or working from a single point, progressively adding additional information to get a bigger picture of the system (a bottom-up approach). For example, papers which took a a top-down "information dashboard" approach to visualisation (e.g. Dau and Andrews (2014), Wasser and Lincoln (2010)) followed the Visual Information-Seeking Mantra (Shneiderman, 1996), which states that the best approach to visualisation is "overview first, zoom and filter, then details on demand". In contrast, Chan, Keeton, and Ma (2010) demonstrated a bottom-up approach to visualisation where analysis incrementally adds more detail to provide more information. In both approaches, the ability to control how much information is presented at once was integral to the systems visualisations.

Principle 2: Contextual information should be preserved, and dimensionality and scale should be respected. Two papers (Neumayr, Schrefl, and Linner, 2011; Wark and Lambert, 2007) emphasised a need to interpret results of analysis in the light of broader contextual information, and this need was embedded into the methodology

proposed by (Hindle and Vidgen, 2018). Simplifying a system to improve human comprehension risks misrepresenting the reality being modelled. Care should therefore be taken to balance the need for reducing information uncertainty and complexity with the need to present information in an appropriate context. This was handled in the literature through the use of visualisation approaches which preserved natural heirarchical/multi-scale features (following systems criteria 4 of Daellenbach (1994) i.e. systems can be made up of subsystems) in a system (Liu and Liu, 2009; Dos Santos et al., 2000; Wasser and Lincoln, 2010), and handling hyperdimensionality by allowing users to interactively "swap out" what variables are used in a visualisation (Eick and Wills, 1995; Ardito et al., 2009; Dau and Andrews, 2014; Feiner and Beshers, 1990; Lee and Rojas, 2013; Wolf, Simpson, and Zhang, 2009). Other papers highlighted such contextual information by automatically displaying relevant information from prior analysis tasks (Neumayr, Schrefl, and Linner, 2011), providing structured access to additional relevant information outside the scope of the system representation (Bieber, 1995; Morin, Jenvald, and Thorstensson, 2000), or by presenting this information as a narrative to decision-makers (Wark and Lambert, 2007).

Principle 3: Static and dynamic system components should remain distinguishable. Reviewed literature demonstrated an approach to visualisation where temporal features of the system were treated separately to static features, either through the use of animation (discussed in Section 2.2.4.2 below), or in the case of static visualisations providing either a time-series approach to visualisation (Farrugia and Quigley, 2009; Halachmi, 2006; Morin, Jenvald, and Thorstensson, 2000) where one spatial dimension is devoted to represent time, or through interactivity where the model user can easily shift the visualisation to correspond to different time points (Radovanovic et al., 2019). This largely complements a focus on providing information in context as a priniciple for minimising the chance of misrepresenting a system.

Principle 4: Visual navigation should be facilitated and made intuitive. Several papers encouraged a user to "virtually navigate"(Akhavian and Behzadan, 2012) a system, or designing a solution in such a way that insights could be gained by "simply looking"(Halachmi, 2006) at the visualisation. Dos Santos et al. (2000) takes the idea

of virtual navigation literally, building an interactive 3D "world" that users can explore, making use of real-world structures (e.g. rooms inside buildings inside districts inside cities) to represent strongly hierarchical, multidimensional data. Numerous studies set up visualisations consisting of multiple panes that displayed different types of information in a side-by-side manner (Suntinger et al., 2008; Morin, Jenvald, and Thorstensson, 2000; Dau and Andrews, 2014; Ye and Froese, 2009) minimising the need for interruption caused by additional configuration of the visualisation. Minimising distractions in the form of excessive time navigating menus may promote faster understanding of the system being investigated by allowing users to better focus on the system they are investigating.

These *Principles* aim to improve the usability of a given systems visualisation, and through it, improve the chances of modelling leading to systems improvement. Given the relatively small amount of discussion in OR/MS literature on systems visualisation, these *Principles* should be updated and expanded on as further research in the area is published.

2.2.4.2 Visualisation Practices

Visualisation Practices refer to recommendations about the means by which *Visualisation Principles* can be applied. The practices outlined here are recommended because of their utility in *visual systems modelling*; in a given application, if a recommended practice does not assist in achieving a *Visualisation Principle*, it should not be used. Two *Visualisation Practices* make recommendations about the method that should be used when developing visualisation:

Practice 1: Build visualisations iteratively. Several papers (Ardito et al., 2009; Chan, Keeton, and Ma, 2010; Lee and Rojas, 2013) documented an iterative process to building visualisations, where a solution would begin either with a prototype or small in scope and then be expanded upon according to feedback from decision makers. This was used to ensure that the final solution suited the needs of decision-makers. This is reflective of an iterative approach to any OR Modelling task where decision-makers are involved in the development of a model.

Practice 2: Decouple "design" and "analysis" steps in visualisation development. Many studies discussed the design of a visualisation as a separate planning step prior to analysis. In addition to possible savings in time and cost (Nowak et al., 2012; Morin, Jenvald, and Thorstensson, 2000; Neumayr, Schrefl, and Linner, 2011), this approach also complements the previous two principles: This decoupling allows for more rapid prototyping of a solution (Ardito et al., 2009; Lee and Rojas, 2013), and provides a framework for aspects of a visualisation to respond in predefined ways according to instructions provided by the user (Ye and Froese, 2009; Suntinger et al., 2008; Akhavian and Behzadan, 2012; Lee and Rojas, 2013).

In addition, four practices focused on general visualisation techniques:

Practice 3: Provide user control for interactivity and customisation. This allows users to adapt their line of questioning, and can allow a user to "gain a better visual perspective"(Akhavian and Behzadan, 2012, p. 754) of subsystems, and provide a "better understanding" (Bacic and Henry, 2012, p. 3) to users. Interactivity was commonly discussed or demonstrated in the context of managing information complexity by indicating what information is important to a user at a given time. This was used to control visualisations of data (Ardito et al., 2009; Bieber, 1995; Burattin, Cimitle, and Maggi, 2004; Chan, Keeton, and Ma, 2010; Dau and Andrews, 2014; Heer, Außem, and Wörzberger, 2009; Jensen, Boyle, and Khanna, 2012; Liu and Liu, 2009; Liiv et al., 2012; Neumayr, Schrefl, and Linner, 2011; Dos Santos et al., 2000; Suntinger et al., 2008; Wasser and Lincoln, 2010; Wolf, Simpson, and Zhang, 2009; Ye and Froese, 2009). Additionally, this flexibility likely provides some degree of robustness against decision-makers asking a partially incorrect question, or against the need to ask follow-up questions. This may also promote model trust, thereby increasing the chance of adoption of insights gained.

Practice 4: Take advantage of animation. Animation intuitively allows for temporal features to be represented in a visualisation, and was commonly used for this purpose in reviewed literature (Farrugia and Quigley, 2009; Akhavian and Behzadan, 2012; Halachmi, 2006; Wark and Lambert, 2007; Farrugia and Quigley, 2009; Sargent, 2005; Osekowska, Axelsson, and Carlsson, 2012; Grignard and Drogoul, 2017; Ingram and Brooks,

2018) It also provides a means of representing a variable in hyperdimensional data (Feiner and Beshers, 1990), or for attracting attention to a particular point via a "flickering" motion Lee and Rojas, 2013.

Practice 5: Use static visual cues to represent multi-dimensional data. Visualisation aspects such as colour and size were both frequently used or discussed as a method of representing additional information (Burattin, Cimitle, and Maggi, 2004; Farrugia and Quigley, 2009; Feiner and Beshers, 1990; Jensen, Boyle, and Khanna, 2012; Liu and Liu, 2009; Lee and Rojas, 2013; Nowak et al., 2012; Suntinger et al., 2008; Wolf, Simpson, and Zhang, 2009; Hindle and Vidgen, 2018; Agarwal et al., 2019; Hindle and Vidgen, 2018; Bachhofner et al., 2017), or to highlight related information across multiple simultaneous data representations (Liiv et al., 2012; Ye and Froese, 2009). This provides a method for preserving additional, multidimensional information in a visualisation.

Practice 6: Automate repetitive tasks. Visualisation benefits model users by providing a method for quickly and intuitively interpreting models. Where a model user has to engage in repetitive tasks which distract from visual inspection of the developed model, this benefit may be reduced. Minimising the amount of time spent on repetitive tasks therefore allows for more time and mental energy to be devoted to analysis (Nowak et al., 2012; Neumayr, Schrefl, and Linner, 2011; Pieterse, 2012). If a user spends a significant amount of time manually performing a repetitive task, automating this process will allow for more time spent performing tasks requiring human attention.

2.2.4.3 Summary

While there is consensus in the reviewed literature about what features of and approaches to visualisation are desirable, visualisation has either been treated as a complementary addition to simulation or optimisation models, or in the case of data visualisation, the focus has been on the use of visualisation as a tool for analysing data either generated or used by a system.

In both cases, visualisation appears to have been treated somewhat differently to more conventional OR/MS tools, where the focus has been on how to effectively present specific data or model outputs as opposed to discussing the use of visualisation as a tool

for *Systems Modelling*. This presents an opportunity for OR/MS experts to better inform, communicate and promote understanding when working with domain experts by treating visualisation in the same manner that methods from the conventional OR/MS toolkit are treated.

2.3 A Visual Systems Modelling Framework

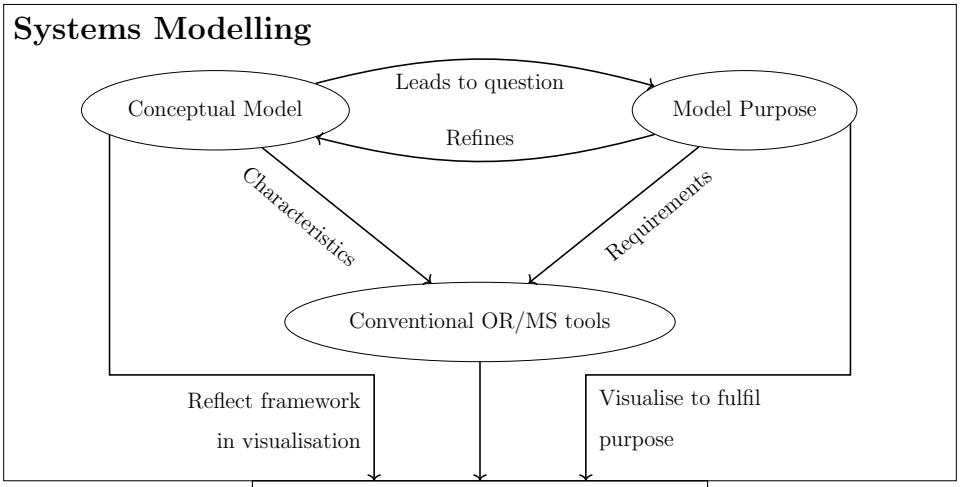
This section presents an original framework which facilitates the integration of *Visualisation* into the OR/MS systems modelling toolkit. At its core, the framework is based on the premise that *Visualisation* is no different to any other tool used in OR/MS, and should be treated as such. This premise is demonstrated by discussing how to integrate *Visualisation* into OR/MS methodology, described here in terms of the development of:

1. A *Conceptual Model*, which identifies an understanding of the system and its components;

2. A *Model Purpose*, which specifies what a systems modelling tool aims to achieve and the associated requirements associated with that;

3. Any *Conventional OR/MS tools* which are applied to model or simplify the system or any of its components.

The interactions between these three aspects of OR/MS methodology lead to a series of systems components and requirements for systems modelling. Methods of visualisation are then selected and developed to meet these systems requirements while following the Principles and Practices of Visualisation identified in Section 2.2.4. This approach to linking *Visualisation* with conventional OR/MS methodology is summarised in Figure 2.2.



Link to Visual Systems Modelling							
	Visualisation Principles						
System Features	*					*	*
		*		*	*		
	*						
		*	*		*		
						*	*

Figure 2.2: Overview of framework

2.3.1 Conceptual Model

The conceptual framework describes the view of the system under investigation as understood by decision makers and stakeholders, capturing all system components, their relationships and system behaviours. This reflects first and second systems criteria defined by Daellenbach (1994) and presented in Section 1.1. For the remainder of this thesis, the set of components, relationships and behaviours are termed *system features*.

Articulating an external, explicit conceptual model provides a list of *system features* that are considered important and why they are important. This list can then be used to formulate questions and thus define the *model purpose*. Additionally, the list of *system features* helps identify what *conventional OR/MS tools* could be applied.

Not all systems features are necessarily as important as one another, and may not need to be captured in the same level of detail in a model. Developing a conceptual model and set of *system features* allows for decisions of this nature to be made in an explicit fashion.

This framework does not suggest a method for developing a conceptual model. This

could be done in an ad-hoc fashion based on informal discussions with decision-makers, or through a more formalised process. Such processes for developing conceptual models are a conventional part of Problem Structuring approaches, designed for managing extremely complex situations with multiple, often conflicting, stakeholders and actors (Mingers and Rosenhead, 2004). The choice of a particular "Soft" OR/MS method (mentioned at the start of Section 2.2) for this purpose, or the decision to develop a conceptual model in a more ad-hoc way, comes from the judgement and personal preferences of the OR/MS practitioner developing the model.

The process of developing an explicit conceptual model is also valuable in simpler systems, as eliciting a list of *system features* provides an explicit set of important components and relationships that can be used to assist model development.

The *systems features* elicited from the conceptual model provide an explicit description of what perspectives and potentially conflicting priorities should be built into the model. This provides a guide for the development of visualisations, thereby ensuring that the final model is representative of the underlying system.

2.3.2 Model Purpose

The development of a conceptual framework for the system under investigation clarifies the purpose of the modelling exercise. Focusing on the purpose of the OR application both refines the conceptual framework being used and clearly outlines what users expect to get out of the modelling exercise, which leads to the specific requirements regarding the function and validation of any developed model.

Under the Pidd (2010) approach to classifying model purpose, models are considered to fall on a spectrum between *Decision Automation* and *Providing Insights for Debate*.

As visualisation is fundamentally a tool for aiding human comprehension, its use at the *Decision Automation* end of this spectrum is limited to the monitoring of the behaviour of other models, taking advantage of its utility for validation and verification in other modelling contexts (Sargent, 2005).

When humans retain oversight and decision-making of a model for *Routine Decision Support*, visualisation can be used to interpret other OR/MS tools such as optimisation models (Ardito et al., 2009) and simulation models (Akhavian and Behzadan, 2012), with

visualisation serving to make other systems models more approachable.

As human interaction becomes more important and models are used for *System investigation & Improvement*, the focus of modelling tasks begins to focus on developing "understanding of a very complex situation". This emphasis on gaining understanding of a complex situation reflects the need for data visualisation to lead to "a perception of lower information uncertainty and complexity"(Bacic and Henry, 2012). As in the case of *Routine Decision Support*, systems visualisation may be used to interpret other OR/MS models (e.g. the use of animation in Discrete Event Modelling (Halachmi, 2006) or optimisation for production planning (Draman et al., 2002)), but in this mode data visualisation in and of itself can be used as a tool for exploring a system with the intention of achieving a particular goal. For example, Jensen, Boyle, and Khanna (2012) discusses the development of an interactive data visualisation tool for exploring patient flow data in a hospital.

Lastly, where modelling is undertaken for the purpose of *Providing Insights for Debate*, the aim of modelling is on developing consensus and a shared view of a system. Most of the specific visualisation techniques discussed in Section 2.2.2 were examples of this modelling approach, where in contrast to using *Visualisation* as a tool for *Investigation and Improvement*, the primary focus is on understanding a system, rather than in attempting to examine a particular problem.

With the exception of automated models running without any human oversight, *Systems Visualisation* can be used across Pidd's (2010) spectrum of model use. Likewise, the role of visualisation can be understood in terms of the the "interfaces" described by Bayer et al. (2014), differentiating between knowledge (*Epistemic* vs. *Technical*) and social (*Boundary* vs. *Representative*) roles (discussed in Section 1.1).

Models which serve as *Epistemic Boundary Objects* focus on the communication and development of joint understanding between stakeholders. Such tasks are the focus of the developing research area of *Collaborative Visualisation*, which formed in response to analysis tasks "becoming increasingly large and complex, not to mention uncertain, ill-defined, and broadly scoped." (Isenberg et al., 2011) Visualisation in this mode seeks to address challenges which can be described as wicked problems by establishing common ground from which decision-makers can "share, negotiate, and discuss their views and interpreta-

tions on a dataset and contribute unique perspectives on a given problem."(Isenberg and Carpendale, 2007).

Rather than emphasising communication, *Epistemic Representative Objects* focus on representing a system with the aim of developing new knowledge. This is the view of data visualisation as described by Keim (2002), where "visual data exploration processes can be seen as a hypothesis generation process: The visualisations of the data allow the user to gain insight into the data and come up with new hypotheses"

A model which serves as a *Technical Boundary Object* focuses on the communication of already existing information. The use of guided visualisation is an example of visualisation in this mode, such as in the narrative-based visualisation discussed in Wark and Lambert (2007).

As the focus shifts away from communication, such models become *Technical Representative Objects*, which simply provide outputs to other models. The use of visualisation to provide Monitoring of other OR/MS models falls into this category.

The actual visualisation approaches used across these roles may be very similar. A visualisation tool which was developed for visual data exploration (an *Epistemic Representative* role) could be just as easily used for guided exploration (a *Technical Boundary* role) by retracing the steps taken to uncover insights. Likewise, visualisations of conventional OR/MS tools may fall into more than one of these categories, depending on the purpose of the visualisation. For example, visualisation which focuses on *OR Model Interpretation* is *Technical* in nature, as the visualisation does not generate new knowledge, but could be either a *Representative* or *Boundary* object depending on if the visualisation is intended to communicate with others, or to simply provide access to model outputs. Likewise, visualisation for *OR Model Exploration* is an *Epistemic* activity, as the goal of model exploration is the development of new knowledge. This can either be performed in a *Representative* context (where a system representation is explored and experimented on as in "what if" analysis), or in a *Boundary* context (where exploration sits in the larger context of discussion and negotiation among decision-makers).

The *Technical/Epistemic* axis of this taxonomy roughly aligns with that of Pidd's (2010) taxonomy of model use, as a model designed for more automated use necessarily focuses on applying existing knowledge rather than generating new knowledge. The link

between these two taxonomies, and examples of how *Systems Visualisation* can be used as an OR/MS tool across this spectrum, can be found in Figure 2.3

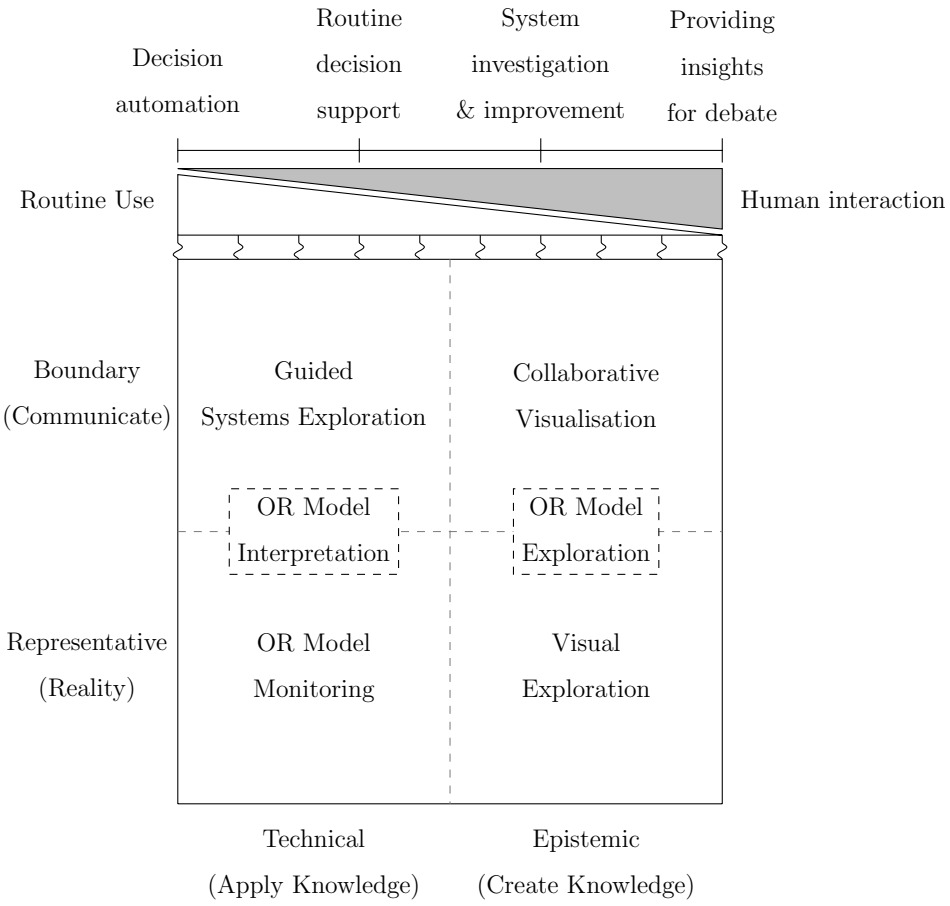


Figure 2.3: Pidd's and Bayer's combined taxonomies of model use (Pidd, 2010, p. 16), (Bayer et al., 2014, p. 128), applied to potential modes of data visualisation in OR/MS

Determining the purpose of the planned systems model creates a feedback loop with the *Conceptual Model*. Determining which *system features* are relevant for the model's purpose refines the conceptual model by potentially adding or removing features not previously captured, or by imposing different levels of importance on particular *system features*. Likewise, determining why a particular feature is important leads to the identification of the purpose of the systems model. This cycle can continue until both the *Conceptual Model* and *Model Purpose* are well-defined and consistent.

2.3.3 Applied OR/MS Tools

Finally, if it is sensible to apply conventional OR/MS tools in analysing the system, these should be selected and applied. Visualisation synergises well with many other analysis methods, as demonstrated in Section 2.2, meaning that these tools can be leveraged for the purposes of visualisation to uncover or highlight patterns (e.g. via clustering), provide readily interpretable results (e.g. via projections and predictive modelling), or otherwise simplify the system. The selection of specific OR/MS tools is inherently subjective and based on the conceptual model and model purpose, and as such this framework makes no recommendations regarding specific conventional OR/MS techniques. If an OR/MS expert believes the application of a given conventional OR/MS tool is beneficial to a given system, it is included in this framework.

2.3.4 Linking Systems Modelling and Visualisation

After the *Conceptual Model* and *Model Purpose* have been articulated, and any *Conventional OR/MS tools* have been chosen, the final step in developing a *Visual Systems Model* is to draw links between the identified list of *systems features* and the *visualisation principles* outlined in Section 2.2.4.1.

Drawing these links is achieved by explaining how to represent each *System Feature* in a manner which fulfils the listed *Visualisation Principles*. This can be achieved by using the *Visualisation Practices* outlined in Section 2.2.4.2, or by some other method. It is not necessary for all *features* to be linked to all *principles*, as some *principles* may be considered more important in a given application. Likewise, the *Model Purpose* may identify some *features* as more important than others; important *features* will be the focus of the model, and therefore will be more likely to be linked to additional *principles*.

This process can be simplified through the use of the selected *conventional OR/MS tools*. Rather than drawing links directly between *system features* and *visualisation principles*, links may be drawn between *features* and *OR/MS tool* inputs, then between *OR/MS tool* outputs and *principles*. In this case, *coventional OR/MS tools* serve to simplify the *visual systems model*, effectively reducing the number of *features* which need to be encapsulated in the *visual systems model*.

These links between *systems features* and *visualisation principles* can be represented

as a table, where each row represents a *feature*, each column represents a *principle*, and each cell represents the link between these components. Populating these individual cells with *how* each *principle* is met for each *feature* generates a matrix of *Desirable Properties* for the development of the *visual systems model*, and provide an evaluable set of criteria for use in model development.

2.3.5 Summary of Framework and Procedure for Implementation

The framework developed in this section provides a method for *Visual Systems Modelling* by using conventional OR/MS methodology (development of a conceptual model, identification of a model's purpose, selection of conventional OR/MS tools), and linking this to *Visualisation Principles*. The application of this framework can be performed procedurally with the following steps:

Procedure for using visualisation as an OR/MS systems modelling tool		
1	Develop conceptual framework for the system	
2	For each component of the conceptual framework:	
	2.1	Identify its relationship to other components
	2.2	Identify what model requirements it is associated with
	2.3	Identify the possible approaches that can be taken to address this requirement, identifying: • If it can be reasonably simplified with conventional OR/MS tools • What visualisation approaches are appropriate
	2.4	Justify decision about approach in terms of *Visualisation Principles*
3	Examine the mapping created between *System Features* and *Visualisation Principles*	
4	For any *features* which are not adequately visually represented:	
	4.1	Re-examine the *feature*, following step 2
5	If all *features* are adequately represented:	
	5.1	Build visualisation according to decisions set out in this process
6	If required, iterate this process according to feedback from decision makers	

2.4 Examples of Visual Systems Modelling Framework in this Thesis

Depending on the area of application and the purpose of the model, the result of the application of this framework may appear very different. Chapters 4 – 7 of this thesis describe the application of this framework in a variety of contexts, each focusing on an application which fulfils a different modelling purpose. This section provides an outline of how each chapter applies the *Visual Systems Modelling Framework*, and demonstrates how the structure of the matrix of *desirable properties* varies from application to application.

2.4.1 Traumatic Spinal Cord Injury

This application of the *Visual Systems Modelling Framework*, documented in Chapter 4, focuses on understanding patient flow in the treatment of traumatic spinal cord injury (TSCI) in a major trauma hospital, with the aim of facilitating discussion of challenges to the system.

Patient flow through this system is multifaceted and dynamic. In addition to *Patient Details* (e.g. age, sex), *Injury Circumstance* (circumstances of injury), *Injury Details* (injury severity and co-existing injuries), and *Clinical Outcomes* (complications, survival rate, destination upon exit from hospital), there are distinct process-focused components such as the *Clinical Pathway* that patients take (the order and frequency with which departments are visited) and *Destination upon Departure*.

These process-focused systems components are heavily driven by a patient's *Clinical Requirements* (type of care needed) and *Available Resources* (type of care available), and a patient's treatment will cause *Resources to be Blocked* for other patients. In summary, TSCI is an complex condition with extreme heterogeneity in patient needs, driven by the prevalence of numerous trauma injuries resulting from a single event. As a result of this, patient flow for these patients is poorly understood.

Before process improvements can be made to this system, the system must first be understood. According to Pidd's (2010) and Bayer et al.'s (2014) combined taxonomies of model purpose, the purpose of this model is to *Provide Insights for Debate* in this area. As the intention of this model is to reflect reality and provide new information, and is therefore *Epistemic Representative* in nature.

Visualisation in this chapter takes a "dashboard" approach to presenting information, where different aspects of patients or patient groups are displayed at once. A user can filter patients according to various characteristics, and organise them into clusters identified through pre-developed conventional OR/MS tools. Each patient's journey through the hospital is animated, allowing users to visually track the details of their hospital stay. Table 2.1 outlines the structure of the matrix of *Desirable Properties* (discussed in Section 2.3.4) for this case study. Cells which are coloured blue indicate where a link between a systems feature (row) and a *Visualisation Principle* (column) has been made. The first column of this matrix indicates if a conventional OR/MS tool has been used in modelling

that systems feature.

Table 2.1: Structure of matrix of desirable properties in Chapter 4

	Conventional OR/MS tool used?	Principle 1	Principle 2	Principle 3	Principle 4
Patient Details					
Injury Circumstance					
Available Resources					
Injury Details					
Clinical Pathway					
Clinical Requirements					
Clinical Outcomes					
Destination upon Departure					
Resources Blocked					

2.4.2 The AVERT Atlas

This application of the *Visual Systems Modelling Framework*, documented in Chapter 5, focuses on investigating dose-response relationships in stroke rehabilitation.

In comparison to the application of the *framework* in the context of TSCI (Section 2.4.1), the health care process for stroke rehabilitation is far simpler. A patient who has had a stroke enters rehabilitation in a particular *Care Setting* (such particular geographic region) with particular *Patient Baseline Information* (such as age, stroke type and stroke severity), and receives a *Physiotherapy Regimen* (frequency and duration of neurorehabilitative physiotherapy). A *Dose-Response Relationship* (patient response to physiotherapy) leads to changes in the *Patient's Health Progression* (day-to-day health state), which may in turn lead to changes in the *Physiotherapy Regimen*. Eventually, this

patient experiences a long-term *Patient Outcomes* (such as standard clinical measures and functional milestones such as the ability to walk) as a result of the *Dose-Response Relationship*.

Unlike the model discussed in Chapter 4, there is a clear goal in this process system with relatively little ambiguity within the system. Under Pidd's (2010) and Bayer et al.'s (2014) combined taxonomies of model purpose, the purpose of this model is somewhere between *Providing Insights for Debate* and aiding *Investigation and Improvement* care processes in stroke rehabilitation. This is achieved by developing new understanding of how stroke survivors respond to physiotherapy. It is therefore *Epistemic Representative* in nature.

The *visual systems model* developed in this case study, coined the *AVERT Atlas*, represents each individual patient with a static image tile. Each tile shows all information relating to each individual patient, including their dynamic therapy and health state information. These tiles are arranged in a grid. Users can filter out patients from this grid based on any combination of criteria, as well as by using conventional OR/MS tools which identified homogeneous patient groups prior to visualisation. Table 2.2 outlines the structure of the matrix of *Desirable Properties* for this case study.

Table 2.2: Structure of matrix of desirable properties in Chapter 5

	Conventional OR/MS tool used?	Principle 1	Principle 2	Principle 3	Principle 4
Patient Baseline Information					
Care Setting					
Patient Health Progression					
Physiotherapy Regimen					
Dose-Response Relationship					
Patient Outcomes					

2.4.3 AVERT Dose Explorer

This application of the *Visual Systems Modelling Framework*, documented in Chapter 6, focuses on identifying promising physiotherapy regimens for improving outcomes for stroke rehabilitation patients.

While the system that is the target of this case study is the same as that described in Section 2.4.2, the conceptual model which is used in this chapter is simpler. In this view of the system, a patient enters the system with *Patient Baseline-Characteristics* (age, stroke type, stroke severity), receives physiotherapy and responds to this through *Dose-Response Behaviour*, then has *Clinical Outcomes* as a result of this physiotherapy.

According to Pidd's (2010) and Bayer et al.'s (2014) combined taxonomies of model purpose, this is a model for *Investigation and Improvement* that is *Epistemic Representative* in nature. However, in this case the emphasis is on *Improvement* rather than *Investigation*, falling closer to the *Decision Automation* end of Pidd's (2010) spectrum.

The *visual systems model* developed in this case study, coined the *AVERT Dose Explorer*, uses conventional OR/MS tools to predict patient outcomes based on baseline information and physiotherapy regimens, then uses visualisation to interpret and contextualise the predictions made by the applied conventional OR/MS tool. Table 2.3 outlines the structure of the matrix of *Desirable Properties* for this case study.

Table 2.3: Structure of matrix of desirable properties in Chapter 6

	Conventional OR/MS tool used?	Principle 1	Principle 2	Principle 3	Principle 4
Patient Baseline-Characteristics					
Dose-Response Behaviour					
Clinical Outcomes					

2.4.4 AVERT-DOSE: A Stroke Rehabilitation Trial with Adaptive Randomisation

The final application of the *Visual Systems Modelling Framework* focuses on the planning of a stroke rehabilitation trial using a Multi-Arm Multi-Stage Covariate-Adjusted Response-Adaptive (MAMS-CARA) trial design.

MAMS-CARA trial designs use prespecified *Trial Rules* to control a range of dynamic *Trial Behaviours* in the trial, including dropping experimental treatments which are ineffective and adjusting the probability of a patient being sent to a given *Treatment* arm (Rosenberger, Sverdlov, and Hu, 2012). This adjustment of probability can occur to ensure that important *Patient Baseline Information* (prognostic variables which could influence a patient's response to a treatment) are balanced across treatment groups (covariate-adjusted randomisation), or to send more patients to treatments which appear effective, thereby maximising the number of trial participants who have positive *Clinical Outcomes* (response-adaptive randomisation). The results of this trial (*Trial Outcomes*) are then used to improve stroke care.

Unlike the three previous case studies, this application makes use of multiple models of the system for different purposes. Under Pidd's (2010) taxonomy of model use, both of these models are used for *Routine Decision Support*, throughout the trial planning process.

- Communicating system behaviours to clinical researchers. The aim of this model is to demonstrate the dynamic properties of this clinical trial design to clinicians who do not have a statistical background. Under Bayer et al.'s (2014) taxonomy, it is therefore a *Technical Boundary Object*, as it is used to transmit pre-existing information.

- Planning and making decisions about the details of the mathematics which underpins the adaptive randomisation, aiming to maximise statistical power (probability of seeing a significant result, assuming one exists) and precision (probability of selecting the best treatment arm). Under Bayer et al.'s (2014) taxonomy, it is therefore a *Representative Boundary Object*, as it is used for fine-detail calculations in a well-defined and understood system.

The first model uses an animated Discrete-Event Simulation model to demonstrate the dynamics of the clinical trial, focusing on how the probability of sending particular patients to particular treatment arm updates over time. Individual patient covariates and clinical outcomes are represented through the appearance (shape and colour) of entities within the animation, while randomisation decisions are visualised as processes within the model. The current balance of covariates and response-adaptation is tracked with a series of charts that dynamically update as the model runs. Table 2.4 outlines the structure of the matrix of *Desirable Properties* for this model.

The second model is an unanimated Discrete-Event Simulation model that simulates many iterations of a clinical trial to examine its expected behaviour and final outcomes. In this case, visualisation is used to examine outputs of the model, and interpret relationships between trial outcomes and decisions about the behaviour of the adaptive randomisation. Visualisations used in this case are conventional, two-dimensional plots used in everyday data analysis. Table 2.5 outlines the structure of the matrix of *Desirable Properties* for this model.

Table 2.4: Structure of first matrix of desirable properties in Chapter 7

	Conventional OR/MS tool used?	Principle 1	Principle 2	Principle 3	Principle 4
Patient Baseline Information					
Trial Rules					
Patient Treatment					
Trial Behaviour					
Clinical Outcomes					

Table 2.5: Structure of second matrix of desirable properties in Chapter 7

	Conventional OR/MS tool used?	Principle 1	Principle 2	Principle 3	Principle 4
Patient Baseline Information					
Trial rules					
Patient Treatment					
Trial Behaviour					
Clinical Outcomes					
Trial Outcomes					

2.5 Conclusion

This chapter provided a systematic review of OR/MS literature on visualisation and synthesised from it a series of *Visualisation Principles* and *Visualisation Practices*, but identified a lack of discussion within the OR/MS literature on the use of visualisation as a systems modelling tool. This addresses Research Question 1 proposed in Section 1.3. This chapter then proposed and developed the *Visual Systems Modelling Framework* to guide the use of visualisation as a systems modelling tool, and provided a procedure for applying it. This partially addresses Research Question 2 proposed in Section 1.3. The *Visual Systems Modelling Framework* is used in Chapters 4 - 7, and the application of this framework was briefly outlined within this chapter.

Chapter 3

Contributions to Conventional OR/MS Toolkit

3.1 Introduction

This chapter contains methodological contributions, which are used in Chapters 4 and 5, and addresses Research Question 3(b) proposed in Section 1.3. Two contributions to the literature on conventional OR/MS tools are contained in this chapter. The first contribution is a novel dissimilarity measure for quantifying the differences between sequences of observations, allowing for sequence length to vary, and is introduced in Section 3.2. The second contribution is systematic validation of an existing method of clustering survival data using Coxian Phase-Type Distributions. This contribution is discussed in Section 3.3.

3.2 Distance-based clustering of Multiscale Data with varying record lengths

3.2.1 Introduction

Using dissimilarity as a basis for modelling a system is intuitive and appealing as a result of its conceptual simplicity (Dudani, 1976). Quantified measures of of dissimilarity (often called *distance*, provided they are metric) are used as the basis of several popular sta-

tistical methods such as agglomerative hierarchical clustering (Ward Jr, 1963), k-means clustering (MacQueen, 1967), and predictive models such as k-nearest neighbours (Cover and Hart, 1967). For example, agglomerative hierarchical clustering identifies homogeneous groups among a series of observations by measuring the distance, or dissimilarity, between each pair of observations. Distances among observations are represented by a *dissimilarity matrix*, where row i column j of this matrix contains the distance between observations i and j. This matrix is then used to identify clusters within the data by grouping observations with relatively small distances together.

Many distance-based methods can be used independently of the choice of distance measure, making them flexible enough to apply to many different systems. Likewise, there are many different possible ways of defining distance for applications in systems modelling. A comprehensive overview of these can be found in Deza and Deza (2009). In data analysis, the most common family of distance measures is the Minkowski, or p-norm family of distances, including Euclidean and Manhattan Distances. Under this approach, the distance between two observations $\mathbf{A} = (a_1, a_2, \ldots, a_n)$ and $\mathbf{B} = (b_1, b_2, \ldots, b_n)$ is defined as:

$$D_{Minkowski}(A, B, p) = \left(\sum_{i=1}^{n} |a_i - b_i|^p \right)^{1/p} \tag{3.1}$$

Process Systems are often strongly hierarchical in nature, with system components often being systems themselves (Systems Definition 4 (Daellenbach, 1994), discussed in Section 1.1). Additionally, processes can often vary in length based on the specific work activities that need to be performed. This gives rise to systems with complex structures that, where sequences of work activities can occur, these sequences may be of different lengths, making it difficult to compare them using conventional dissimilarity measures. For example, consider the following system structure: A patient enters a health care system with specific *prognostic factors* related to their health state. Their health state changes from day to day in response to treatment, and they eventually leave the system with a final health state. The length of both sequences of health states and treatment received, across this time period is a function of the length of stay of this patient. This presents a challenge in measuring the dissimilarity between two patients with different lengths of stay. Figure 3.1 summarises this problem

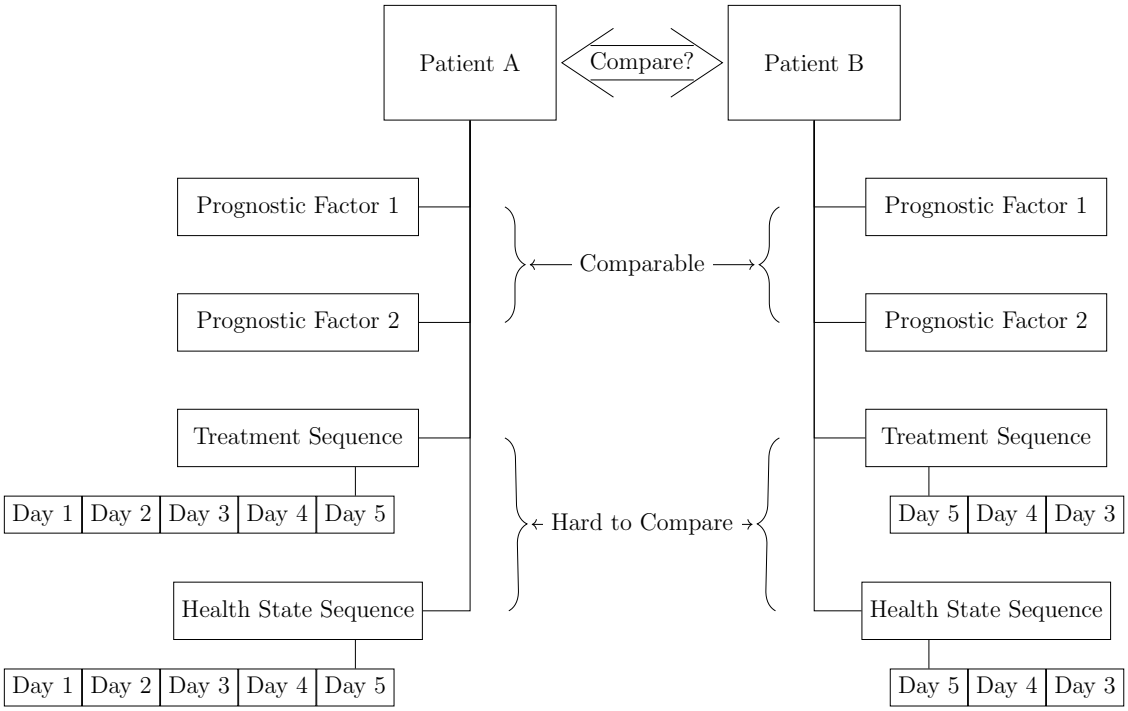


Figure 3.1: Summary of structure and challenges in drawing comparisons between patients

If treatment is a numeric dose, the differences in treatment sequence length can be addressed by assuming that treatment (work activity) does not occur after the end of the process. This allows treatment sequence length to be standardised by appending zero values (no treatment) to the end of each sequence. Such assumptions are harder to make regarding a patient's health state, as this relates to a dynamic property of a system component, rather than a work activity imposed upon the component. Therefore, conventional dissimilarity methods cannot be used to examine this system feature, and new approaches are needed.

3.2.2 A novel dissimilarity measure

This section presents a novel dissimilarity for comparing two sequences of ordinal values. Consider two sequences of ordinal observations **A** and **B** such that

$$\mathbf{A} = (a_1, a_2, \ldots, a_n) \tag{3.2}$$

$$\mathbf{B} = (b_1, b_2, \ldots, b_m) \tag{3.3}$$

where each a_i, b_j is an observed score on a predefined ordinal scale. Unless $n = m$, the distance between **A** and **B** cannot be measured using p-norm family approaches.

There are other approaches that can be used to measure distances between collections of objects. In the Computer Science discipline, the distance between two strings of characters can be measured using *Edit Distance*, or Levenshtein (1966) distance. Under this approach, the distance between two strings is given by the minimum number of operations to transform one string into the other, where allowed operations are:

- Insertion of a character anywhere in the string
- Deletion of a character anywhere in the string
- Substitution of any character for another character

A similar approach could be used to cluster variable-length sequences of ordinal observations. As arbitrary substitution does not consider the ranked nature of the data, and arbitrary insertion/deletion is inappropriate for addressing truncated days, we propose the following set of operations, following the same approach as Levenshtein (1966). *Ordinal Edit Dissimilarity* is defined as the minimum number of operations required to transform one sequence of observations into another sequence, where the allowed operations are:

- Append a value to the end of the sequence
  - The value of the new level is set as equal to the last observed level. This is similar to Last Operation Carried Forward, a common imputation approach used in clinical research for handing missing data resulting from patient drop-out (Shao and Zhong, 2003).
- Delete the last recorded value from the end of the sequence
  - To preserve symmetry, this operation can only be performed if the value to be removed is equal to the second last observed value.
  - If not, the value to be removed must be incremented/decremented prior to this operation (with additional cost).
- Increment or Decrement a level for a given day

- This must be performed after all Append/Delete operations, as it is more reasonable to assume that a patient's health state remains unchanged than it is to assume a miraculous recovery. This prevents the unrealistic transformation of a short-stay, unhealthy patient into a long-stay healthy patient by simply incrementing the last observed state "up" and then propagating this final state to the required observation length.
- Optionally, the number of increments used in this step can be raised to a power p to further penalise multiple increments.

The process of Appending/Deleting and Incrementing/Decrementing levels can be given different cost weights (the ratio between these given by r) to encapsulate their relative significance. The dissimilarity between two observed processes $\mathbf{A} = a_1, a_2, \ldots, a_n$ and $\mathbf{B} = b_1, b_2, \ldots, b_m$, is therefore defined as:

$$dist_{Edit}(\mathbf{A}, \mathbf{B}, r, p) = r|n-m| + \left(\sum_{i=1}^{\min(n,m)} |a_i - b_i|^p + \sum_{i=1}^{|n-m|} \begin{cases} |a_{m+i} - b_m|^p, & n > m \\ |b_{n+i} - a_n|^p, & n < m \\ 0, & n = m \end{cases} \right) \tag{3.4}$$

Where $n = m$, this reduces to $\sum_{i=1}^{n} |a_i - b_i|^p$, which is equivalent to Minkowski distance without the $\frac{1}{p}$ exponent. By not including this exponent, p can be chosen to emphasise differences in scores on an ordinal scale. For example, where $p = 2$, a single observational difference of 2 ranks would be considered as equally important as four observational differences of 1 rank. This is analogous to quadratically weighted Cohen's kappa (Cohen, 1968), a measure of inter-rater reliability commonly used in the context of ordinal data in clinical research that penalises disagreement based on the magnitude of that disagreement.

Where $p > 0$ and $r > 0$, $dist_{Edit}$ is semi-metric, as it obeys the following properties:

1. $dist_{Edit}$ is *symmetric*, i.e. $dist_{Edit}(A, B) = dist_{Edit}(B, A)$

   Proof. Where $n = m$, this measure reduces to Minkowski distance without the $\frac{1}{p}$ exponent, and this is trivially true. Without loss of generality let $X = (x_1, x_2, \ldots, x_n)$

and $Y = (y_1, y_2, \ldots, y_m)$ where $n > m$.

$$\begin{aligned} dist_{Edit}(X,Y) &= r|n-m| + \sum_{i=1}^{\min(n,m)} |x_i - y_i|^p + \sum_{i=1}^{|n-m|} |x_{m+i} - y_m|^p \\ &= r(n-m) + \sum_{i=1}^{m} |x_i - y_i|^p + \sum_{i=1}^{n-m} |x_{m+i} - y_m|^p \end{aligned}$$

$$\begin{aligned} dist_{Edit}(Y,X) &= r|m-n| + \sum_{i=1}^{\min(m,n)} |y_i - x_i|^p + \sum_{i=1}^{|m-n|} |x_{m+i} - y_m|^p \\ &= r(n-m) + \sum_{i=1}^{m} |y_i - x_i|^p + \sum_{i=1}^{n-m} |x_{m+i} - y_m|^p \\ &= r(n-m) + \sum_{i=1}^{m} |x_i - y_i|^p + \sum_{i=1}^{n-m} |x_{m+i} - y_m|^p \\ &= dist_{Edit}(X,Y) \end{aligned}$$

□

2. $dist_{Edit}$ is *non-negative*, i.e. $\forall A, B : dist_{Edit}(A,B) \geq 0$

Proof. Where $r > 0$, $r|n-m| > 0$, $\sum_{i=1}^{\min(n,m)} |a_i - b_i|^p > 0$ and $\left(\sum_{i=1}^{|n-m|} \begin{cases} |a_{m+i} - b_m|^p, & n > m \\ |b_{n+i} - a_n|^p, & n < m \\ 0, & n = m \end{cases} \right) > 0$ for any A, B.
Therefore, $\forall A, B : dist_{Edit}(A,B) \geq 0$. □

3. $dist_{Edit}$ obeys *the identity of indiscernibles*, i.e. $dist_{Edit}(A,B) = 0 \iff A = B$

Proof. $dist_{Edit}(A,A) = r|n-n| + \left(\sum_{i=1}^{n} |a_i - a_i|^p + \sum_{i=1}^{|n-m|} 0 \right) = 0$, therefore $A = B \Rightarrow dist_{Edit}(A,B) = 0$.

If $dist_{Edit} = 0$ then following statements must be true:

(a) $r|n-m| = 0$

(b) $\sum_{i=1}^{\min(n,m)} |a_i - b_i|^p = 0$

(c) $$\left(\sum_{i=1}^{|n-m|} \begin{cases} |a_{m+i} - b_m|^p, & n > m \\ |b_{n+i} - a_n|^p, & n < m \\ 0, & n = m \end{cases} \right) = 0$$

Where $r > 0$, $r|n-m| = 0 \iff n = m$. Part (c) is therefore trivially true, and $\sum_{i=1}^{\min(n,m)} |a_i - b_i|^p = 0 \iff p > 0$ and $\forall i \in \{1, 2, \ldots, n-1, n\} : a_i - b_i$. Therefore, $dist_{Edit} = 0 \Rightarrow A = B$.

As $dist_{Edit} = 0 \Rightarrow A = B$ and $A = B \Rightarrow dist_{Edit}(A, B) = 0$, $A = B \iff dist_{Edit}(A, B) = 0$. □

4. $dist_{Edit}$ does not obey *the triangle inequality*, i.e. $\exists A, B, C : dist_{Edit}(A, C) \geq dist_{Edit}(A, B) + dist_{Edit}(B, C)$

Proof. Let $A = (2, 2, 2, 2, 2)$, $B = (1, 2)$ and $C = (1)$, then for any r and p, $dist_{Edit}(A, B) = 3r + 1$, $dist_{Edit}(A, C) = 4r + 5$ and $dist_{Edit}(B, C) = 1r + 1$. As $dist_{Edit}(A, B) + dist_{Edit}(B, C) = 4r + 2 < dist_{Edit}(A, C)$, the triangle inequality does not hold. □

As the triangle inequality does not hold, algorithms which rely on this feature (for example k-means) can not be used with $dist_{Edit}$. However, agglomerative hierarchical clustering can use this measure to identify homogeneous groups of patients provided that single or complete linkage is used rather than centroid clustering (Lance and Williams, 1967).

The selection of r and p plays a significant role in the structure of the final clusters. There are two potential strategies for handling this selection: One would be to select multiple values (potentially based on the structure of dendrograms prior to forming the final clusters), and perform analysis on each cluster to ensure robustness of results against selected settings. Alternatively, if it expected that there should be an association between identified clusters and some other system feature, r and p could be selected in order to

maximise the association between that system feature and clusters identified by using $dist_{Edit}$ with agglomerative hierarchical clustering.

An illustrative example of the second strategy is provided in Section 5.5.2.1, where this method is used to identify clusters in patient health states. These health states are are expected to be highly associated with a patient's level of independence post-stroke, and r and p were therefore chosen to maximise the association between patient level of independence and the clusters resulting from agglomerative hierarchical clustering based on $dist_{Edit}(.,.,r,p)$, where association was measured using Pearson's χ^2 statistic when identified clusters and independence level were cross-tabulated.

3.2.3 A method for understanding dissimilarity in the context of other systems features

This section describes a method for integrating dissimilarity measures like that outlined in Section 3.2.2 with other systems features. First, the set of systems features should be partitioned into subsets such that all features are in exactly one subset. If the dissimilarity resulting from these subsets can be quantified, the resultant dissimilarity matrices can be linearly combined to provide an overall measure of difference across scales and features D_{Grand}, defined as

$$D_{Grand} = \sum_i w_i \frac{D_i}{\max(D_i)} \tag{3.5}$$

where D_i is the ith dissimilarity matrix describing a subset of system features and w_i is a weight associated with feature subset $i, i < n$ where n is the total number of features. These subsets can occur at different scales within hierarchical system structures. For example, the structure summarised in Figure 3.1 could use three dissimilarity matrices: one capturing the two prognostic factors, one capturing a standardised version of the Treatment sequence, and one capturing the health sequence. These feature subsets can use different dissimilarity measures, allowing the specific methods used to be tailored to the application.

There are two potential ways to choose the value for each w_i. One would be to assign these manually, based on the perceived importance of each system feature. This would

allow for a flexible approach that allows a tailored definition of dissimilarity across a wide variety of system features.

Another approach to selecting these weights is to optimise the ability for the final weight to classify some target systems feature Var. For example, each w_1, w_2, ..., w_{n-1} could be chosen under cross-validation to maximise the accuracy of the dissimilarity between records $d(w_1, w_2, \ldots)$ as a predictive tool under weighted k-nearest neighbours (Dudani, 1976). To do this, a function controlling the relationship between distance and importance would first need to be formulated. One simple formula for this was given by Dudani (1976), letting this value be inversely proportional to the distance between two patients. That is, the relative importance v of each observed record is given by $v(d) = 1/d$. Once the function $v(d)$ is chosen, the predicted value of Var, $Var_{pred}(v(d(w_1, w_2, \ldots, w_{n-1})))$ can be determined based on $v(d)$ and the weights governing $d(w_1, w_2, \ldots, w_{n-1})$. Each individual weight w_i can then be chosen to maximise the agreement between Var and $Var_{pred}(v(d(w_1, w_2, \ldots, w_{n-1})))$. This process is summarised by Figure 3.2.

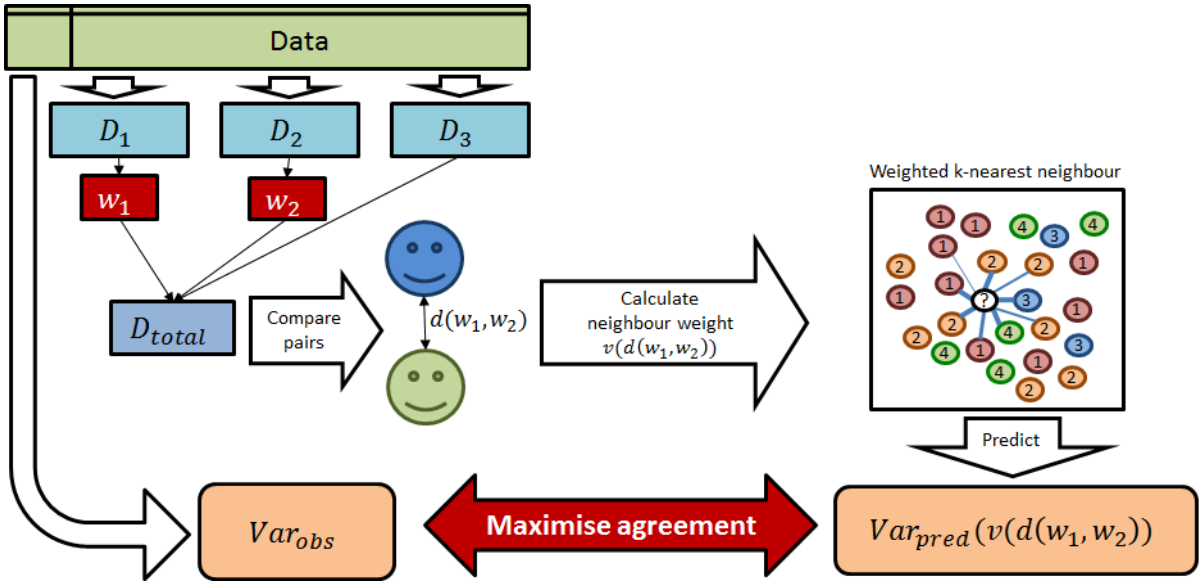


Figure 3.2: Process for selecting feature subset weights based on predictive ability

Selecting feature subset weights to maximise predictive ability allows for these weights to be interpreted as a measure of the relative importance of each feature subset in explaining the predicted variable. In this manner, $d(w_1, w_2, \ldots, w_{n-1})$ become comparable to the coefficients commonly returned by common linear regression models, where the rel-

ative magnitude of coefficients attached to a variable can be used to explain relationships within the modelled system.

As this approach is heavily dependent on the initial partitioning of systems features, care should be taken in selecting which partition is used. The chosen partitioning should logically follow the conceptual model for the system under investigation to improve interpretability.

One advantage of this approach is that it minimises the number of parameters used in optimisation algorithms which underpin methods which seek to maximise agreement (e.g. maximum likelihood methods) or minimise error (least squares regression). In the example summarised in Figure 3.1, if all sequences were of length 3, that would result in a total of 8 variables to be used in a model (2 prognostic factors, 3 health states, and 3 treatments). If this system is instead partitioned into Prognostic Factors, Treatment Sequence and Health Sequence, only three variables are needed. This results in maximising classification accuracy being a significantly easier optimisation problem under partitioning. Therefore, not only does this method handle complex systems structures, it also provides a means for handles highly dimensional data.

3.2.4 Conclusion

This section presented a novel measure for quantifying the dissimilarity between two sequences of ordinal observations, and proposed two methods of combining information captured by this in the context of larger structures. The statistical tools presented in this section are used in Chapter 5 to understand how patient health changes across their stay in physiotherapy

3.3 Validation and Generalisation of a clustering method based on Coxian Phase-Type Distributions

3.3.1 Introduction

A common approach to modelling health systems is through the analysis of time-to-event data, ranging from using it to identify excessive consumption of finite resources to

understanding patient health (Palmer, Fulop, and Utley, 2018).

One method of analysing time-to-event data is Phase-Type Distributions, developed by (Neuts, 1981). Phase-type distributions model time-to-event data as the time taken for entities to move through a continuous-time Markov process consisting of n transient states and a single absorbing state $n+1$ (Latouche and Ramaswami, 1999). This Markov process has initial state probability given by $\alpha = (\mathbf{p}, 0)$ and infinitesimal generator

$$Q = \begin{bmatrix} T & \mathbf{q} \\ \mathbf{0} & 0 \end{bmatrix} \tag{3.6}$$

where $\mathbf{q}$ and $T_{i,j\neq i}$, describe the rate of transition between states. The probability of transitioning from state i to j in the time interval δt is given by

$$P(X(t+\delta t) = j | X(t) = i) = T_{i,j}\delta t + o(\delta t) \quad i \neq j \tag{3.7}$$

$$P(X(t+\delta t) = n+1 | X(t) = i) = \mathbf{q}_i \delta t + o(\delta t) \tag{3.8}$$

Where $i, j \leq n$. The diagonal elements give the rate of exit from each phase irrespective of destination, and is calculated as sum of all rates out of a given phase. This can be written as:

$$T_{i,i} = \mathbf{q}_i + \sum_{j=1, j\neq i}^{n} Ti, j, i \leq n \tag{3.9}$$

The time taken for entities to reach the absorbing state $n+1$ of this Markov process is order n Phase-type distributed ($PH(\mathbf{p}, T)$, adopting the shorthand used in Latouche and Ramaswami (1999)) with probability density function

$$f(t) = \mathbf{p} \exp\{Tt\} \mathbf{q} \tag{3.10}$$

$$q = -T\mathbf{1} \tag{3.11}$$

Phase Type Distributions are extremely flexible and can be fit to a wide variety of distribution shapes. Phase-type distributions have seen adoption across a wide variety

of disciplines. A review of their applications in health contexts can be found in Fackrell (2009).

While Phase Type Distributions provide flexibility, in the general case, they suffer from overparameterisation. An order n Phase-type distribution has n^2+n-1 parameters (Fackrell, 2009). Not only does this lead to concerns around model generalisablility, it also leads to challenges in fitting these distributions to data.

As a result, structured subclasses of phase type distributions are often used instead. In a health care, Coxian Phase-type distributions are the most common phase structure for modelling length of stay (Fackrell, 2009). An order n Coxian Phase-type distribution has $2n-1$ parameters, and models a process consisting of n sequential phases, where at each step an entity can move from state i, $i \leq n$ to $i+1$ with rate λ_i, or move to absorption from state i, $i \leq n$ with rate μ_i. (Figure 3.3)

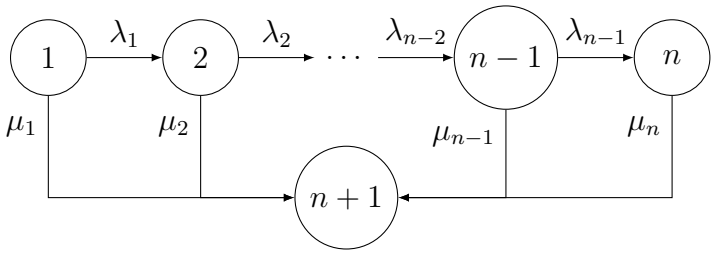


Figure 3.3: Coxian Phase-type structure

3.3.2 Clustering using Coxian Phase-type distributions

Marshall and McClean (2004) developed a method for clustering time-to-event data in the context of hospital length of stay. In this method, length of stay is modelled using a Coxian Phase-Type distribution, with the underlying Markov process modelling the hospital. The probability π_i, $i \leq n$ of a patient exiting the hospital from the ith phase is calculated from the probability density for transitioning in each individual state:

$$\pi_1 = \int_0^\infty \mu_1 e^{-(\lambda_1+\mu_1)}dt \qquad = \frac{\mu_1}{\mu_1+\lambda_1} \tag{3.12}$$

$$\pi_2 = \int_0^\infty \mu_2 e^{-(\lambda_2+\mu_2)}dt \int_0^\infty \lambda_1 e^{-(\lambda_1+\mu_1)}dt \qquad = \left(\frac{\mu_2}{\mu_2+\lambda_2}\right)\left(\frac{\lambda_1}{\mu_1+\lambda_1}\right) \tag{3.13}$$

$$\vdots$$

$$\pi_n = \left(\frac{\mu_n}{\mu_n+\lambda_n}\right)\prod_{i=1}^{n-1}\frac{\lambda_i}{\mu_i+\lambda_i} \tag{3.14}$$

Patients are then arranged by length of stay in ascending order. The first π_1 proportion are assigned cluster 1, the next π_2 proportion are assigned cluster 2, and so on (Marshall and McClean, 2004).

By clustering patients by exit phase, investigators can then compare these clusters to identify distinguishing patient characteristics. Clusters may be thought of as being associated with latent processes for moving through the modelled system. However, there is no published literature validating that this method results in clusters with correspond to the underlying process model. This section provides validation of Marshall and McClean (2004) clustering technique, and gives guidelines on when it can be used to reliably model some underlying process and when it cannot.

3.3.3 Validation of Coxian Phase-type Clustering

To measure the agreement between Marshall and McClean (2004) clustering and the underlying process being modelled by a Coxian Phase-type Distribution, we generated many Coxian Phase-Type distributions (of 2,3,4 and 5 phases) and simulated these processes, recording time-to-absorption and the phase from which simulated each data point exited the system. We then ran Marshall and McClean (2004) clustering as described by Marshall and McClean (2004) on the resultant simulation data, and compared this with recorded exit phase. The resultant dataset was then used to develop models that could predict the level of agreement between actual exit phase and Marshall and McClean (2004) clusters.

Each Coxian Phase-type (CoxPhT) process was simulated in R (R Core Team, 2017), with exponentially distributed delays separating decision points and absorption. At each potential chance of a patient choosing to exit at phase i, the probability was given by

$\frac{\mu_i}{\mu_i+\lambda_i}$ (derived in Marshall and McClean (2004)). Chosen exit phase, and total time-to-absorption, were recorded for each simulated entity.

We then performed Marshall and McClean (2004) clustering on these recorded times to in order to predict exit phase, and measured the level of agreement with actual exit phase using Cohen's kappa with quadratic weighting (κ).

The value of κ was recorded along with the original parameters for the CoxPhT structure $(\mu_1, \mu_2, \ldots, \lambda_1, \lambda_2, \ldots)$. The resulting data set was then used to develop develop predictive models (using CART and linear regression) to identify when CoxPhT clustering accurately predicted exit phase.

To improve computational feasibility, we fixed $\lambda_1 = 1$ when selecting parameter values for each CoxPhT structure. As a change in time scale $f(a \times t)$ has no effect on the shape of a distribution or on the proportion of patients exiting from each phase (as $\frac{a\mu_i}{a\mu_i+a\lambda_i} = \frac{\mu_i}{\mu_i+\lambda_i}, i \leq n$), scaling all parameters by a factor of $a = \frac{1}{\lambda_1}$ standardises the parameters and reduces the number of permutations of parameters to test.

As the number of phases increases, the number of parameter permutations grows exponentially. To manage this while maintaining diversity in the selected sets of parameters, all parameters but $\lambda_1 = 1$ were randomly chosen log-uniformally to fall between successive intervals on a log-uniform grid between 0.01 and 100. Once a parameter was chosen from each successive interval, the simulation and evaluation process would then repeat. Restricting the random selection of parameters in this way, ensured that the resulting dataset would be evenly distributed across parameter permutations. Every iteration of this process would generate an additional random data point in each interval. This maintained the evenly spread nature of the data while allowing each iteration to select different parameter combinations which were distinct from those of each previous iteration, thereby providing additional detail across parameters in the same way that deterministically selecting parameters from a fine grid would, without causing the computational time to become infeasible as the number of phases increased. This process was repeated until the data set contained results from the number of simulated Coxian Phase-Type processes given in Table 3.1.

For larger numbers of phases, this process was left to run for longer to account for increases in dimensionality. The exception to this was for the 2-phase system, which

completed iterations of this simulation significantly faster than higher order systems, resulting in a disproportionately large sample size in the time between simulation start and checking the size of the results.

Table 3.1: Sample Size for each model

2 phase	3 phase	4 phase	5 phase
9999	3328	53248	983040

From this data, we built models to predict if a given set of parameters μ_1, μ_2, ..., λ_1, λ_2, ... would correspond to a kappa value of at least 0.7, 0.75, 0.8 or 0.9, values which are indicative of good-to-excellent statistical agreement. For this purpose, we developed Classification and Regression Trees (CART) using Salford Systems (Salford Systems, 2019), and logistic regression models with Elastic-net regularisation, implemented in the *glmnet* package in R (Friedman, Hastie, and Tibshirani, 2010). Elastic-net regularisation is a method of fitting regression models which penalises extraneous model coefficients by using a combination of LASSO regression (L_1 penalty), and ridge regression (L_2 penalty), which in this case were equally divided. We allowed complete interaction between all parameters unless they were removed by the regression model. This process is summarised in Figure 3.4.

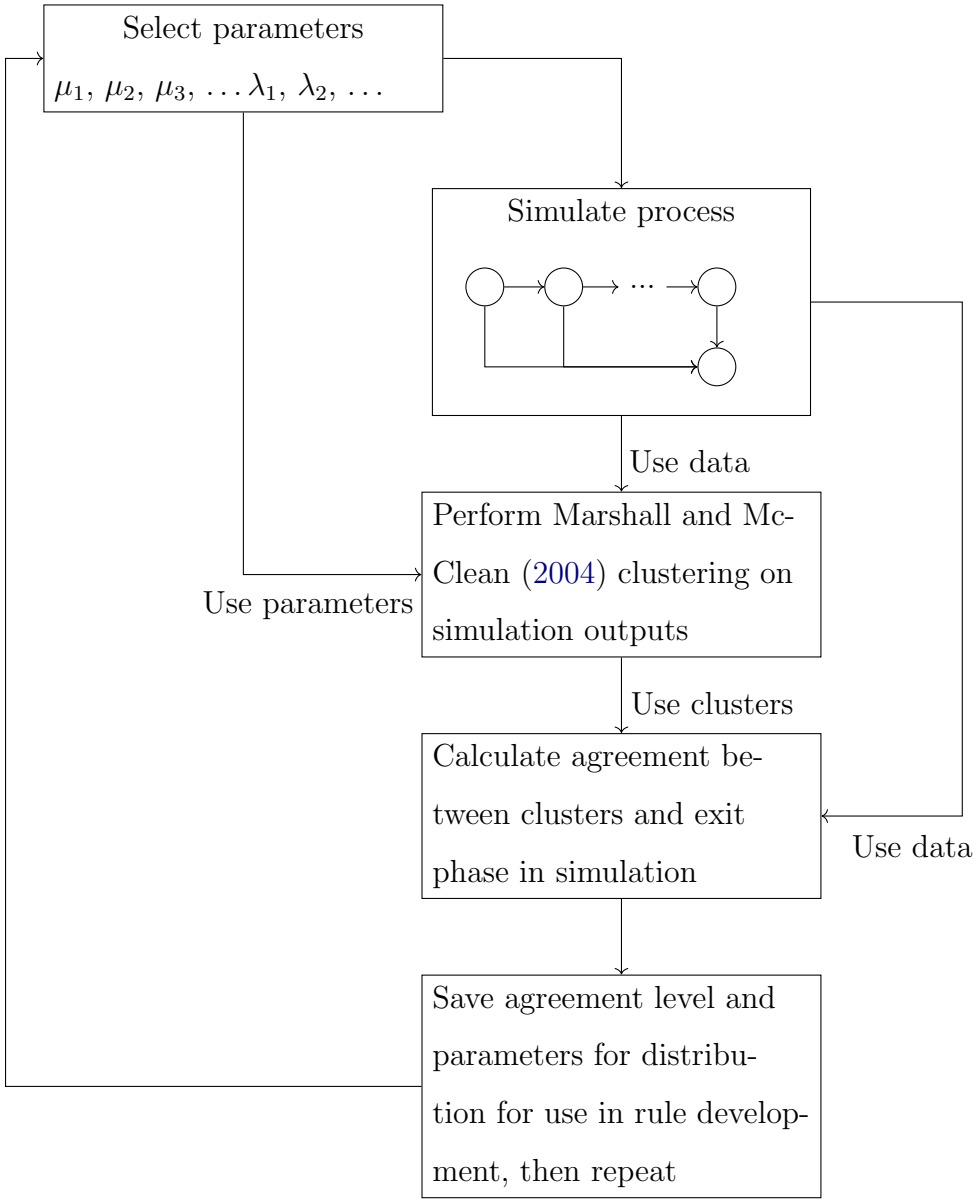


Figure 3.4: Summary of validation method for Marshall and McClean (2004) clustering

3.3.4 Rules for reliability of Coxian Phase-Type clustering

3.3.4.1 CART

In all cases, CART was able to identify rules for when the simulated Coxian Phase-Type Distributions reliably matched the simulated process, with no significant drop in accuracy under 10-fold cross validation. In all models, area under ROC curve was at least 0.9 for both training and testing evaluations of accuracy (Table 3.2). Full trees can be found in Appendix B.1

In all trees, the most important parameter for determining if the clustering mechanism agreed with the underlying process being modelled μ_1. Additionally, the first cut in μ_1 is similar across each threshold. For lower values of Cohen's weighted κ, this cut is sufficient to predict expected clustering behaviour. Table 3.3 summarises these thresholds, and the percentage of cases above them where clustering behaves as expected. Where $\frac{\mu_2}{\lambda_1}$ falls below this threshold, the technique can still work provided that μ_1 is not too small. This suggests that the method does not behave as expected when $\mu_1 \ll \lambda_1$, or when a "tunnel" or "holding" phase occurs (i.e. absorption can not be immediately reached) at the start of the process. Conversely, the technique also works best if the last phase's transition rate μ_n is relatively low. This corresponds to a greater time lag in exiting from the last phase, making it distinct and therefore more likely to be correctly classified by the method. All other parameters exist in relation to one another with no clear rules.

Table 3.2: Area Under Curve for CART Models

		Cohen's Kappa Threshold			
Number of Phases		$\kappa \geq 0.7$	$\kappa \geq 0.75$	$\kappa \geq 0.8$	$\kappa \geq 0.9$
2	train	0.99	0.98	0.98	0.98
	test	0.98	0.98	0.98	0.97
3	train	0.97	0.96	0.98	0.95
	test	0.96	0.95	0.97	0.94
4	train	0.97	0.97	0.95	0.93
	test	0.97	0.97	0.96	0.93
5	train	0.95	0.96	0.95	0.9
	test	0.95	0.95	0.95	0.9

Table 3.3: Initial threshold of $\frac{\mu_1}{\lambda_1}$ and percentage of cases above threshold where clusters agree with process

	Kappa Threshold			
Number of Phases	0.70	0.75	0.80	0.90
2	1.65 (81.5%)	1.65 (77.8%)	1.65 (72.7%)	1.65 (56.0%)
3	2.47 (84.8%)	2.47 (80.1%)	2.47 (74.5%)	4.19 (53.9%)
4	2.25 (83.5%)	2.42 (78.9%)	2.8 (72.5%)	4.21 (43.7%)
5	2.29 (83.3%)	2.42 (77.7%)	2.78 (70.4%)	5.14 (40.4%)

3.3.4.2 Logistic Regression

The majority of parameters in the logistic regression model can be removed without noticeable impact on model performance.

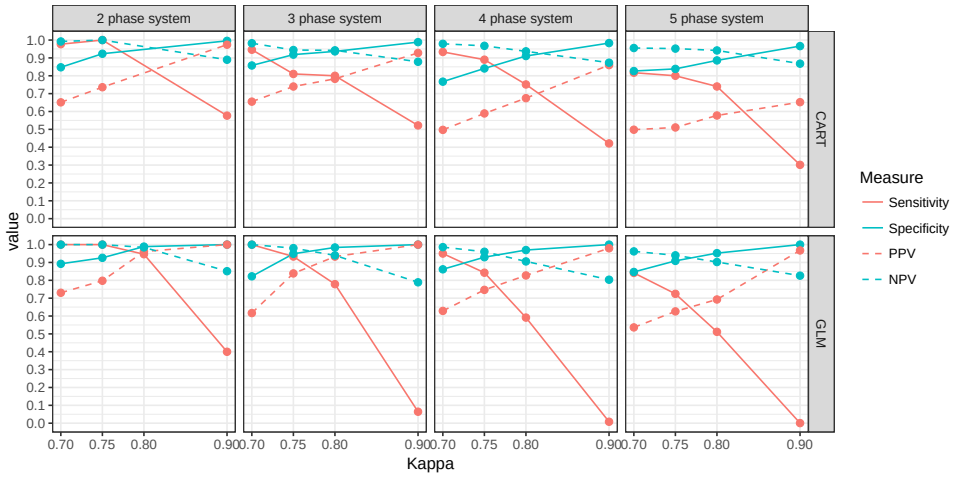


Figure 3.5: Tradeoff in number of parameters vs AUC for *glmnet* fit

In all cases, the most influential parameters were the exit rates μ_i with the most prominent parameter being μ_1. While these parameters cannot be taken in isolation, this is consistent with the results outlined in Section 3.3.4.1. The number of parameters chosen (nPars) and corresponding AUC, along with the leading 6 parameters for each model, can be found in Table 3.4. Full equations can be found in Appendix B.3.

Table 3.4: Area Under Curve for selected GLM Models

		Cohen's Kappa Threshold			
Number of Phases		0.70	0.75	0.80	0.90
2	nPars	3	3	3	3
	AUC	0.9996	0.9995	0.9987	0.989
	Leading Parameters	μ_1, μ_2, $\mu_1\mu_2$	μ_1, μ_2, $\mu_1\mu_2$	μ_1, μ_2, $\mu_1\mu_2$	μ_1, μ_2, $\mu_1\mu_2$
3	nPars	11	7	6	9
	AUC	0.9957	0.9952	0.9954	0.9703
	Leading Parameters	μ_1, μ_2, μ_3, $\mu_3\lambda_2$, $\mu_2\lambda_2$, $\mu_1\mu_3$, ...	μ_1, μ_2, μ_3, $\mu_3\lambda_2$, $\mu_2\lambda_2$, $\mu_2\mu_3$, ...	μ_1, μ_2, μ_3, $\mu_3\lambda_2$, $\mu_2\lambda_2$, $\mu_2\mu_3$	μ_1, μ_3, μ_2, $\mu_3\lambda_2$, $\mu_1\lambda_2$, $\mu_1\mu_2$, ...
4	nPars	16	16	9	21
	AUC	0.9901	0.9902	0.9807	0.9519
	Leading Parameters	μ_1, μ_2, μ_3, μ_4, $\mu_2\lambda_2$, $\mu_3\lambda_2$, ...	μ_1, μ_2, μ_3, μ_4, $\mu_2\lambda_2$, $\mu_3\lambda_2$, ...	μ_1, μ_2, μ_3, μ_4, $\mu_3\lambda_2$, $\mu_4\lambda_3$, ...	μ_1, μ_2, μ_3, μ_4, $\mu_3\lambda_2$, $\mu_1\lambda_2$, ...
5	nPars	11	13	9	26
	AUC	0.9803	0.9802	0.971	0.941
	Leading Parameters	μ_1, μ_2, μ_3, $\mu_2\lambda_2$, $\mu_3\lambda_2$, μ_4, ...	μ_1, μ_2, μ_3, $\mu_3\lambda_2$, $\mu_2\lambda_2$, μ_4, ...	μ_1, μ_2, μ_3, $\mu_3\lambda_2$, $\mu_4\lambda_3$, μ_4, ...	μ_1, μ_2, μ_3, $\mu_3\lambda_2$, μ_5, μ_4, ...

3.3.5 Validation of Rules

To validate these rules, we repeated the data generation process outlined in Section 3.3.3, this time varying all parameters including λ_1 between 0.1 and 10 (sample sizes given in table 3.5). We then compared simulated Cohen's Kappa with predicted agreement between clusters and underlying process following the the rules developed in Section 3.3.4.

Table 3.5: Number of Coxian Phase Type distributions generated to validate developed rules

2 phase	3 phase	4 phase	5 phase
579	9216	147456	2097152

All models had poor sensitivity when classifying models where $\kappa \geq 0.9$, but otherwise the predictive models perform well when used on unscaled PhT distributions, with both sensitivity and specificity of at least one model comfortably above 0.7. The regression models generally performed better for thresholds of $\kappa \geq 0.7$ and $\kappa \geq 0.75$. However, for $\kappa \geq 0.8$ the sensitivity was consistently higher for CART than it was for regression, though the regression models maintained the higher specificity. These rules are summarised in Figure 3.6, which shows a grid of plots identifying model quality for each order of Coxian Phase-Type distribution, and each type of rule (regression vs CART). Each line in these plots shows the value of a measure of rule quality (Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value) at each of the levels of agreement (κ) being used.

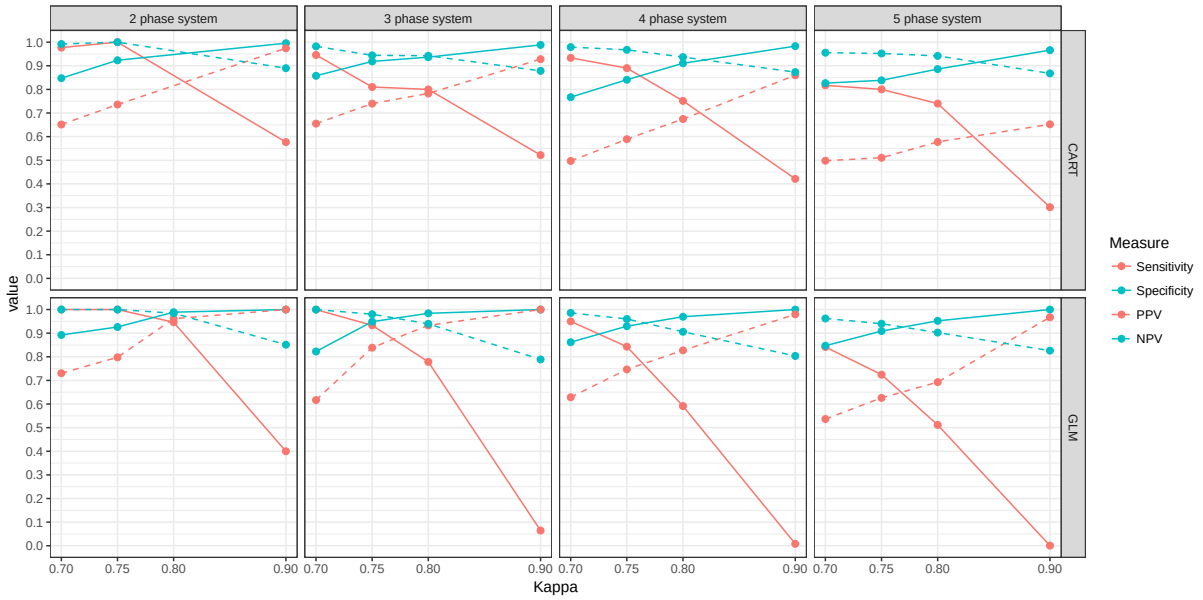


Figure 3.6: Validation results of rules for predicting quality

With the exception of models for predicting $\kappa \geq 0.90$, the models presented in Section 3.3.4 were robust when presented with new data where the distribution was not pre-scaled so that $\lambda_1 = 1$. These results therefore demonstrate that the developed predictive tools

can be reliably used to determine if CoxPhT clustering likely corresponds with the process being modelled by the PhT distribution. They therefore provide a means for determining if a given application of CoxPhT clustering leads to clusters which can be interpreted in terms of an underlying process.

3.3.6 Conclusion

This section presented rules for when Marshall and McClean (2004) clustering results in clusters matching the underlying process being modelled, which, under validation, reliably predict agreement up to a value of $\kappa \geq 0.8$. These rules are used in Chapters 4 and 5 to assist model development.

3.4 Conclusion

This chapter reported on two contributions to literature on conventional OR/MS tools which were made in the process of model development in the case studies described in this thesis. The contributions outlined in this chapter are used in Chapter 4 and Chapter 5 in their application of the Visual Systems Modelling Framework introduced in Section 2.3.

Chapter 4

Understanding Patient flow in the treatment of Traumatic Spinal Cord Injury at a Major Trauma Hospital

4.1 Introduction

This chapter discusses the first application of the *Visual Systems Modelling Framework* to a health system in this thesis. Section 4.2 summarises the clinical context in which this case study takes place, and Section 4.3 demonstrates how this context can be considered to be a process system. Section 4.4 describes how the *Visual Systems Modelling Framework* (developed in Section 2.3) was used in this case study, with Section 4.5 providing a matrix of *Desirable Properties* for the visual systems model resulting from the framework's use. Section 4.6 describes the final *visual systems model*, with Section 4.7 describing validation of both the developed model and the *Visual Systems Modelling Framework*.

4.2 Clinical Context

Traumatic Spinal Cord Injury is a debilitating condition that leads to severe lifelong disability. However, the care process for TSCI has a great deal of uncertainty in it, due to the rarity and heterogeneity which characterises the condition.

There is some uncertainty in clinical literature regarding what practices are benefi-

cial for patients with TSCI (Raslan and Nemecek, 2012). While animal studies have repeatedly shown that surgical decompression of the spinal cord leads to better clinical outcomes, there has been ongoing debate around how translatable this knowledge is (Fong and Eismont, 2007), with such translational benefits potentially being "impossible" to conclusively demonstrate similar efficacy in a human population (Ramer, Ramer, and Bradbury, 2014, p. 1241). In addition to being a rare condition (leading to challenges in gathering sufficient sample sizes for large-scale, high-quality clinical research), TSCI is highly associated with other traumatic injuries (known as polytrauma) which adds significant confounding factors to potential clinical trials (El Tecle, Dahdaleh, and Hitchon, 2016). Likewise, there is uncertainty over the timing of surgical intervention. Due to the underlying biomechanics of the condition (where neurons gradually die until pressure is relieved), any benefit from surgical decompression is likely to be time-sensitive, where such treatment is only beneficial within a certain window of time post-injury. There is no clear evidence to suggest where such a time window would end, adding an additional layer of uncertainty to this system.

While there is evidence that rapid surgical decompression of the spinal cord may lead to improved outcomes for patients with TSCI, there is a lack of strong evidence to support this belief. This uncertainty makes it extremely difficult to affect system change, as there is little concrete evidence from which to make decisions. This is reflected in the lack of published OR/MS applications in the area. To the best of our knowledge, the Access to Care and Timing project (Noonan et al., 2012) represents the only published account of OR/MS application to this clinical domain.

Despite this, there is growing interest among clinicians in examining the processes of care for patients with TSCI. Several studies have identified and measured system delays in the acute phase of care (Middleton et al., 2012; Battistuzzo et al., 2016; Furlan, Tung, and Fehlings, 2013), and an international survey of spinal rehabilitation units identified a consistent perception of delays in admission and discharge, where similar analysis could improve system processes and patient outcomes (New et al., 2013). However, the first step in improving patient outcomes in this area is to understand the current processes of care.

4.3 Traumatic Spinal Cord Injury Care as a Process System

The care of TSCI meets all the criteria required for it to be considered a *process system* according to the definition adopted in Section 1.1 of this thesis. It can be considered a process under the definition given by Davenport (1993, p. 5):

Inputs: The primary input into the TSCI care process are patients who have experienced TSCI. Additionally, the care process is constrained by what resources are available within the hospital.

Work Activities: Patients undergo various treatments in the care process at various times and locations. These treatments occur in response to the specific needs of each patient in terms of their individual injuries and injury severity.

Outputs: Patients are eventually discharged from the TSCI care system, ideally in a better health state than they were when they entered. Outputs in this system include clinical outcomes and the resources blocked during their stay.

Likewise, this care process meets all the criteria to be considered a System under Daellenbach (1994, p. 27):

1. A system is an organised assembly of components. 'Organised' means that there exist special relationships between these components. The care of TSCI involves numerous components involving patients and hospital resources (staff, beds, etc). A special relationship exists between patients and hospital resources, as patients utilise those resources to improve their health. A special relationship exists between hospital resources and other hospital resources as there exists a limited capacity for their use.

2. The system does something, i.e., it exhibits a type of behaviour unique to the system. The care of TSCI changes the health of patients within the system, repairing damage and improving their likelihood of long-term survival with minimal disability.

3. Each component contributes to the behaviour of the system and is affected by being in the system. No component has an independent effect on the system. The behaviour of the system is changed if any component is removed or leaves. The care of TSCI has numerous emergent systemic behaviours arising from heterogeneity among served patients, the uncertainty in what treatments are most beneficial, and resources shared with other care processes within the larger health care system. For example, access to operating theatres is limited by resources (availability of hospital staff and the theatre being free for use). This availability is influenced by the demands of patients entering the system, thereby causing indirect influences on the care pathways experienced by other patients.

4. Groups of components within the system may themselves have properties 1,2, and 3. i.e., they may form subsystems. A patient can be considered to be a subsystem in this context, as their health is an ever-changing system component based on underlying biological causes. Additionally, groups of hospital resources are divided into various departments, each of which may be considered a system in and of itself.

5. The system has an outside - an environment - which provides inputs to the system and receives outputs from the system. The environment for the care of TSCI consists of the broader population of people who can experience TSCI, thus entering the system (Input). Once their care is complete, they then leave the system (output). The larger healthcare system can also be considered part of the environment, as resource requirements in other parts of the care system will influence the resource capacity available for the care of TSCI (input). Likewise, the care of TSCI impacts on the resources available to other parts of the larger healthcare system (output).

6. The system has been identified by someone as of special interest. Patients who experience TSCI can have their long-term health improve as a result of medical treatment, leading to better quality of life and increased participation in society. The care of TSCI is therefore considered important not only to patients who have experienced TSCI, but also on both public health and economic grounds.

As the care of TSCI patients can be understood through the lens of process systems,

visualising this process system can be used to address the outlined challenges in the area.

4.4 Application of Visual Systems Modelling Framework

This section applies the *Systems Visual Modelling Framework* to the TSCI care process system. Section 4.4.1 describes the *Conceptual Model* uses by the framework, and Section 4.4.2 describes the *Model Purpose*. Section 4.4.3 describes the conventional OR/MS tools that are used in this case study.

The Conceptual Model and Model Purpose presented in this section were developed with the Institute for Safety, Compensation and Recovery Research (ISCRR). Model development took place in an iterative process, with the model being modified and improved in response to feedback. The final model was presented to ISCRR, where it was used to facilitate discussion. Additionally, this model was presented separately to a manager who was not involved in model development, with the intention of applying it to a purpose beyond the one it was developed to meet. The manager did not find this model useful for their purposes, which fell elsewhere on Pidd's (2010) spectrum of model use. While this model fulfilled its intended purpose, it was not suitable in a context beyond its original intention.

4.4.1 Conceptual Model

As discussed in Section 4.3, the care of patients with TSCI can be understood as a process system. As it meets the definition of a process, it can can be considered in terms of Inputs, Work Activities and Outputs.

Kreindler (2016) argues that the leading cause behind a health care process intervention failing to lead to improvements is a lack of focus on systemicity within these processes. The author suggests that interventions into health care processes should follow a Population-Process-Capacity model (health care seeks to link a population in need to a capacity to provide care through some care process). The population-process-capacity model of healthcare systems, combined with the inputs, work activities, and outputs identified above, provides the basis for the conceptual model used in this application. This

conceptual model is summarised in Table 4.1.

Table 4.1: Summary of Conceptual Model

	Population	Process	Capacity
Inputs	Patient Details	Injury Circumstance	Available Resources
Work Activities	Injury Type/Severity (Care Processes Needed)	Clinical Pathway	Clinical Requirements (Care Processes Used)
Outputs	Clinical outcomes	Destination upon departure	Resources Blocked

The *system features* resulting from this conceptual model are as follows:

Patient Details Details about a patient such as age, sex and health insurance status are inputs which may influence anticipated system behaviours before an injury even occurs. For example, a patient's type of health insurance (e.g. public health, private health, work cover, cover provided by the TAC) may influence the type of care provided and where a patient is discharged to.

Injury Circumstance Like patient details, the circumstances of an injury, such as the type of location where an injury takes place and the type of activity that was being performed at the time, are inputs to this system that may influence the behaviour of the system. For example, different types of injuries are more likely in different circumstances (e.g. Vehicle accidents likely lead to more complex trauma cases with many serious injuries; care for TSCI in a work environment is likely to be paid for by work cover).

Available Resources The care of TSCI sits within a larger health care system and shares common resources such as hospital beds, staff and equipment, all of which may be used elsewhere and therefore made unavailable. The available capacity to care for patients within the TSCI care process is therefore an input to this system.

Injury Type/Severity The type of and extent of injuries drives the care processes that a patient needs. For example, a patient with multiple life-threatening injuries across multiple body areas will require different care than a patient with an isolated spinal cord injury.

Clinical Pathway A patient's clinical pathway refers to the sequence of treatments which the patient undergoes through the TSCI care process, which can occur in different hospital departments (e.g. Emergency Department, Operating Theatre, General Ward, Intensive Care Unit, etc). For example, a patient who requires stabilisation to keep them alive may be sent directly into an operating theatre, while less life-threatening injuries may be treated later.

Clinical Requirements Clinical requirements refer to the care processes which a patient needs to improve their health. For example, an orthopaedic surgeon is required for broken bones, a neurosurgeon for the treatment of TSCI, and mechanical ventilation is required for patients who cannot breathe unassisted.

Clinical Outcomes Patient outcomes in this system are concerned with the health and expected life of patients after their hospital stay, including survival, impact of disability and the number of complications during their hospital stay.

Destination upon departure After a patient's stay in the hospital is complete, they are discharged to some other location such as home, a rehabilitation hospital or a nursing home. This can initiate other processes (such as TSCI rehabilitation) which occur outside of the scope of this system.

Resources Blocked While other parts of the health care system can influence the available resources in the care of TSCI, TSCI can use resources which are then unavailable to other parts of the health care system.

The care of TSCI is complex and multifaceted, with both process- and patient-driven factors which influence one another. The factors set out here, combined with the relative rarity of TSCI (and the resultant scarcity of data) lead to a great deal of uncertainty within this system, presenting significant challenges to improving this system. However, explicitly listing the features of this system provides a clear summary of what needs to be modelled, which can be used to guide the modelling process.

4.4.2 Model Purpose

The uncertainty within this system as discussed in Section 4.4.1 presents significant challenges to the improvement of care for patients with TSCI. Before any improvements can be made, this uncertainty must be reduced by improving understanding of the system's processes. Therefore, the systems modelling exercise presented in this chapter aims to *Provide Insights for Debate* under Pidd's (2010) taxonomy of model use. As it seeks to generate new information, it can be considered an *Epistemic Representative* object under Bayer et al.'s (2014) taxonomy of social roles. Both of these taxonomies are discussed in Section 1.1.

4.4.3 Conventional OR/MS Tools

The care of traumatic spinal cord injury is a system with a strong degree of heterogeneity among patient needs and a scarcity of data due to the rarity of the condition. These factors present significant barriers to the use to sophisticated statistical and analytic tools within the system. As such, the application of conventional OR/MS tools within this chapter is limited to clustering patients based on common features such as resource use or to projecting long-term economic outcomes among patients.

4.4.3.1 Clustering Patients according to Length of Stay

Length of Stay is a commonly-studied feature of health systems on account of its relevance both as a measure of patient outcomes and resource utilisation. This application models Length of Stay using Coxian Phase-Type Distributions (discussed Section 3.3), taking advantage of their ability to cluster patients according to the path taken through the model.

To achieve this, the EMPhT algorithm (Asmussen, Nerman, and Olsson, 1996) will be applied to fit Coxian Phase-Type Distributions to Length of Stay, sequentially increasing the number of phases in order to optimise Bayesian Information Criterion (BIC) (Schwarz, 1978). The fitted distribution will then be checked against the validity rules developed in Section 3.3.3 to confirm that the resultant clusters are interpretable in terms of the modelled process.

4.4.3.2 Clustering Patients according to care processes used

A patient's care pathway and the resources used by it can be examined by analysing which departments a patient's procedures took place in. Common groups of patients according to care processes used are identified by performing hierarchical clustering on the proportion of each patient's procedures which were performed in each department.

4.4.3.3 Projecting long-term economic outcomes

A patient's long-term health is the primary output of the TSCI care system, and therefore important to understand. In order to provide a common measure for patient outcomes, Disability-Adjusted Life-Years (DALYs) (Murray, 1994) are used to project long-term outcomes for patients. DALYs are a health economics measure describing the total years of life lost due to disability, calculated as the sum of years of life lost due to premature death (YLL), and the number of years lived with the disability (YLD), giving rise to the formula:

$$DALYs = YLD + YLL \tag{4.1}$$

where:

$$YLD = D\left\{\frac{KCe^{ra}}{(r+\beta)^2}\left[e^{-(r+\beta)(L_d+a)}\left[-(r+\beta)(L_d+a)-1\right]-e^{-(r+\beta)}\left[-(r+\beta)-1\right]\right]+\frac{1-K}{r}\left(1-e^{-rL_d}\right)\right\} \tag{4.2}$$

$$YLL = \frac{KCe^{r(a+L_d)}}{(r+\beta)^2}\left[e^{-(r+\beta)(L_e+a)}\left[-(r+\beta)(L_e+a)-1\right]-e^{-(r+\beta)}\left[-(r+\beta)-1\right]\right]+\frac{1-K}{r}\left(1-e^{-rL_e}\right) \tag{4.3}$$

where a is the age of disability onset, L_d is the life expectancy with disability and L_e is life expectancy had the patient not become disabled, r is a discount rate taking into account that being healthy in the near-term is considered more important than in the long-term, β is an age weighting factor, C is a constant correction for non-uniform age weighting and K is a parameter to remove non-uniform age weights. These values are set at $r = 0.03$, $C = 0.16243$, $K = 1$ and $\beta = 0.04$ (Murray, 1996, pp. 64–66).

The disability weights D were taken from Haagsma et al. (2015), and life expectancies L_d and L_e were calculated using the standardised mortality ratios reported in Frankel et al. (1998), combined with actuarial Life Tables published by the Australian Bureau of Statistics (Australian Bureau of Statistics, 2015).

4.5 Desirable Properties resulting from Application of Visual Systems Modelling Framework

Given the breadth of systems information to be captured, an interactive "Dashboard" approach to visualisation (discussed in Section 2.2.2) was chosen for its ability to present large amounts of disparate information at once while allowing a user the ability to easily filter information on a variety of system properties and call up increasingly detailed information as required (*Visualisation Practice* 3).

The heterogeneity of injury among patients should be presented in this model in a way which is easy to visually understand, encapsulating information about both injury location and severity.

As the primary focus of this application was to understand patient flow through the TSCI care system, this was emphasised by developing an animated representation of the process (*Visualisation Practice* 4), with patients entering, visiting departments, then exiting the system to the location where they were discharged. Contextual information (such as patient and injury details) should be linked to this using static visual cues such as colour and size (Visualisation Practice 5).

Table 4.2 summarises these desirable properties for the model, and provides the criteria which will be used in validating the final model. Rows of this table correspond to the *System Features* summarised in Section 4.4.1. The first column summarises the conventional OR/MS tools used to model these features. The remaining columns of this table correspond to the *Visualisation Principles* discussed in Section 2.2.4.1. This table is filled by summarising how each *System Feature* makes use of the *Visualisation Principles*.

Table 4.2: Desirable properties of model arising from framework

	Conventional OR/MS Tools	Visualisation Principles			
		Principle 1: Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Patient Details		Group or filter by details. Provide overview first, allowing users to "zoom in" for more detail as desired	Allow user to assign colour, size, etc to represent this information when representing patients		Present summaries of details in a dashboard format
Injury Circumstance					
Available Resources	No information available, outside of the scope of the developed model				
Injury Details		Provide overview first, allowing users to "zoom in" for more detail as desired	Provide detailed breakdown of the type of injuries that occurred		Present breakdown of injury details in a manner that allows for quick visual understanding
Clinical Pathway	Cluster based on department usage	Group or filter by department usage cluster. Provide overview first, allowing users to "zoom in" for more detail as desired	Allow user to assign colour, size, etc to represent this information when representing patients		
Clinical Requirements					Present summaries of details in a dashboard format
Clinical Outcomes	Project long-term health using DALYs	Provide overview first, allowing users to "zoom in" for more detail as desired	Show breakdown of DALYs in terms of YLL and YLD. Allow user to assign colour, size, etc to represent this information	End animated representation of patient journey with destination upon departure	
Destination upon departure		Group or filter by destination upon departure. Provide overview first, allowing users to "zoom in" for more detail as desired	Allow user to assign colour, size, etc to represent this information when representing patients		
Resources made unavailable	Model LoS using Coxian Phase Type Distributions	Group or filter by CoxPhT Cluster. Provide overview first, allowing users to "zoom in" for more detail as desired		Use LoS to control speed of animation, representing its dynamic nature	

4.6 Developed Model

This section describes the model which was developed using the *Visual Systems Modelling Framework*. Section 4.6.1 outlines the data which was used in the development of the model. Section 4.6.2 outlines the application of the conventional OR/MS methods discussed in Section 4.4.3. Section 4.6.3 outlines the specific visualisation methods chosen to represent each systems component. Finally, Section 4.6.4 describes the fully developed model itself.

4.6.1 Data

The data used in the development of this model came from anonymised, routinely collected hospital records for patients with both permanent and transient spinal cord injury from July 2011 to July 2014 provided by ISCRR (Alfred Health Ethics Committee Number 337/14). This constituted a total of 342 admissions, where available information included sociodemographics, injury severity and location, as well as the times and locations for all treatments received by the patient during their hospital visit.

4.6.2 OR/MS Tools

There were three analytical methods applied to this system: clustering based on Length of Stay, clustering based on department usage, and projecting long-term patient outcomes.

4.6.2.1 Clustering Patients according to Length of Stay

A Coxian Phase-Type Distribution was fitted to Length of Stay as set out in Section 4.4.3.1. Model selection using Bayesian Information Criterion would lead to an exponential distribution (with no clustering mechanism available). As a result, model selection was conducted to minimise Akike Information Criterion instead. This resulted in a 3-phase Coxian Phase Type Distribution with parameters given in Table 4.3.

Table 4.3: Fitted CoxPhT Models Length of Stay

					Phase number i				
Number of phases	log-likelihood	AIC	BIC		1	2	3	4	5
1	-1160.77	2323.54	2327.38	μ_i	0.09125739				
2	-1157.69	2321.37	2332.87	μ_i	0.10156483	0.04523229			
				λ_i	0.01012991				
3	-1154.71	2319.42	2338.58	μ_i	0.05153455	0.57685808	0.05372556		
				λ_i	0.09010786	0.20299872			
4	-1154.61	2323.22	2350.04	μ_i	0.06256131	0.11050986	0.81180769	0.05434444	
				λ_i	0.08121606	1.06104437	0.39817386		
5	-1154.36	2326.72	2361.2	μ_i	0.07290420	0.02586292	0.20456782	0.10369925	0.05063056
				λ_i	0.77284174	0.82896343	0.66837699	0.02086352	

The validation rules developed in Section 3.3 were applied to the selected 3-phase CoxPhT model. The CART model was applied by identifying the appropriate nodes in the trees supplied in Appendix B.1, while the Regression model was applied by using the formulas supplied in Appendix B.2, with a positive value required for the model to be considered likely to result in clusters which correspond to the underlying process being modelled.

Table 4.4 summarises the results of applying these validation rules to the 3-phase system, providing details of if clusters agree with the underlying process model with minimum κ of 0.70, 0.75, 0.80 or 0.90 along with the output from the model (either the node within CART corresponding to the classification, or the calculated value of the regression model).

According to the rules developed in Section 3.3, the clusters resulting from Marshall and McClean (2004) clustering will not lead to clusters which correspond to the underlying markovian process being modelled. As a result, these clusters were not investigated further.

Table 4.4: Results of validation of CoxPhT Clusters

	CART		Regression	
κ value	Pass?	Node	Pass?	Value
70	No	1 (2.2%)	No	-3.57282
75	No	1 (4.4%)	No	-2.8523
80	No	4 (1.3%)	No	-2.82761
90	No	1 (0.3%)	No	-2.85047

4.6.2.2 Clustering Patients according to Care Processes Used

Clustering according to care processes used (outlined in Section 4.4.3.2) resulted in 5 major homogeneous groups split by where the majority of medical procedures for each patient took place: Emergency Department (ED), General Operating Theatre (GOR), Intensive Care Unit (ICU), Referring Hospital (Ref Hosp), and hospital wards (Ward). Figure 4.1 shows the dendrogram for these clusters, while Figure 4.2 shows a "radar plot" where each radial axis represents the proportion of procedures performed on a patient and each coloured line around these axes represents a patient, with cluster given by colour.

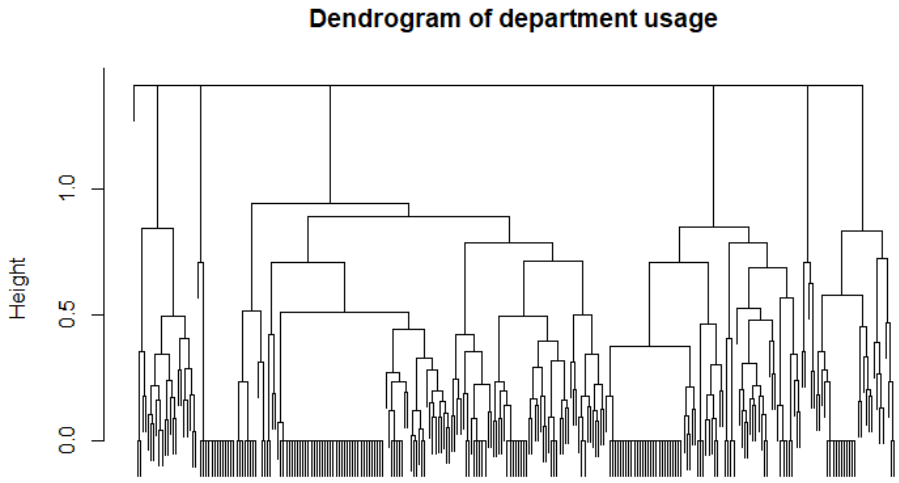


Figure 4.1: Dendrogram of care processes used

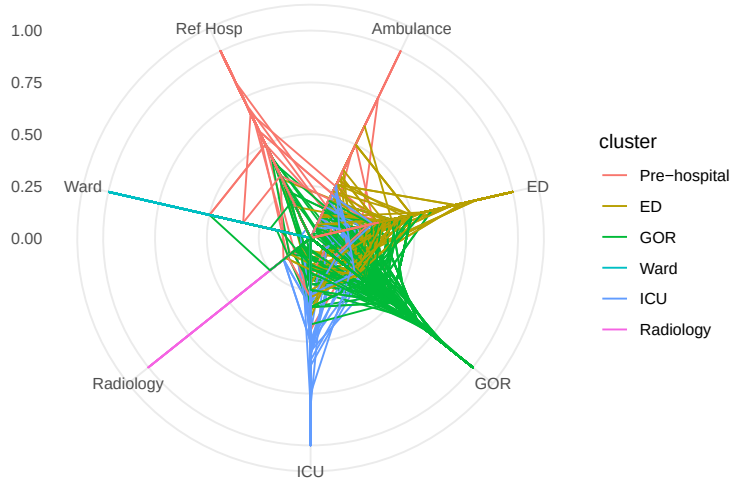


Figure 4.2: Radar plot showing resource usage across resource clusters

Notably, patients in the GOR and ED clusters appear to have more disparate hospital usage than patients in the ICU cluster, suggesting that there are multiple pathways through the system beyond simply being sent to a single primary department. These clusters simplify this aspect of this system and provide a simple means of understanding patient pathway through the TSCI care system. However, these clusters must be understood in terms of how they relate to the broader health care system.

4.6.2.3 Projecting long-term Economic Outcomes

Disability-adjusted life years were calculated for each patient using the available data in combination with the method outlined in Section 4.4.3.3. This information was incorporated into the *Visual Systems Model*, resulting in it being able to present projections of long-term outcomes for patients and patient subgroups.

4.6.3 Visual Components of Model

The chosen dashboard approach to visualisation provided flexibility in how each system component would be represented. This section outlines the visual techniques chosen to represent each system component within the final model.

Patient Details such as age, sex, and type of health insurance are represented using conventional data visualisation techniques. The distribution of Age is given by a

histogram, while Sex and Payment Class are both given using pie charts. In animated components of the visualisation (discussed below), the user can modify size and colour within the animation to represent Age or Sex/Payment Class respectively. Additionally, users can group records according to Sex and Payment Class, allowing for drilling down into patient subgroups.

Injury Circumstance such as the place of injury and activity at the time are represented in the same manner as Sex and type of health insurance as described above. Pie charts give the distribution of patients with each characteristic, users can modify animated entity colour to represent these components, and can also group records according to them.

Injury Details are presented in two primary ways: The distribution of Injury Severity (given by Injury Severity Score, a medical score measuring trauma severity (Baker et al., 1974)) and the Total Number of Injuries is given by histograms. Injury location is represented with a diagrammed breakdown of the human body, with histograms representing distribution of the number of injuries in each body region.

Additionally, details of the most severe injury in each body area is given by Abbreviated Injury Scale (AIS) codes, a standardised code which encapsulates an injury's type, location and severity (Gennarelli and Wodzin, 2008). These codes are coloured according to their severity, ranging through black, blue, green, orange, red and gray as injuries become increasingly severe.

Clinical Pathway is represented with a detailed process animation which reproduces the sequence of operations and procedures performed in each department. This animation is customisable to allow a representation of other system components through this process, as discussed above.

Clinical Requirements are represented by a series of histograms showing the number of procedures performed in each department on each patient. Additionally, the department utilisation clusters discussed in Section 4.6.2.2 can be used in a similar fashion to either group patients by department usage or using colour to represent this in the process

animation giving the clinical pathway.

Clinical Outcomes are represented in terms of DALYs as outlined in 4.4.3.3 and the number of complications each patient has during their time in the TSCI system. The distribution of DALYs and number of complications are both given by histograms. The proportion of patients who died in hospital is given by a pie chart.

Destination Upon Departure is represented as the final component of the process animation that describes a patient's clinical pathway. The distribution of patient destination is also given with a pie chart.

Resources Made Unavailable is represented by the amount of time that a patient makes use of patient resources. The distribution of Length of Stay (both hospital and in the emergency department), as well as the number of hours spent in ICU or on mechanical ventilation, are given in histograms. These values can also be used to control the size of patients within the process animation described above. Additionally, movement speed within this process animation can be linked to Length of Stay.

These visualisation components are combined in a dashboard environment to build the final model.

4.6.4 Developed Visual Systems Model

The *visual systems model* developed for this application was built in the modelling environment Anylogic 7 (The Anylogic Company, 2015). This consisted of four main views (Figure 4.3), each displaying sequentially more information. Figures 4.7, 4.5, 4.6 and 4.7 provide each view in greater resolution.

Figure 4.3: Overview of TSCI model

Upon opening the model, a user is presented with options to group patients according to department usage, patient details, injury circumstance, destination upon leaving the hospital or similar patient groups. The model then moves to the first screen, **Data Overview**

The **Data Overview** screen (Figure 4.4) provides brief summaries of patient information, broken up by the selected grouping mechanism. A full representation of all patients is supplied by the "Marginal" group. A user can either draw a direct representation of existing patient records, or engage in "what if" analysis that considers how changes in types of patient may impact the overall status of the health care system. In this case, the model randomly resamples from observed data according to user-specified weights. A user can pull up additional information about one of these groups by clicking on them, taking them to the second screen, **Group Overview**.

The **Group Overview** screen (Figure 4.5) provides an overview of systems information for each group. In this view, the user is presented a detailed summary of systems components for each group, including sociodemographics distribution (age, sex), circumstances of the injury (activity and location when injured), resource usage (hours on mechanical ventilation, Length of Stay), outcomes (DALYs, number of complications), and the number of injuries by body area. The user can also cycle between subpopulations at this level to quickly compare between them.

The third screen, **Group Process** (Figure 4.6), details the care pathways taken by

individual patients within a patient group and represents their care process through a customisable animation that replays the sequence by which each patient visited hospital departments. A patient representation's size, colour and speed can all be customised to show other information within this system, as discussed in Section 4.6.3. The user can click on an individual patient to pull up the final screen, **Patient Overview**.

The **Patient Overview** screen (Figure 4.7) provides a mockup chart presenting information about each patient including a list of most severe injuries (coded by their Abbreviated Injury Scale), and their treatment pathway through the hospital. It also contains a breakdown of how DALYs were calculated for that patient, showing years of life lost and years lived with disability.

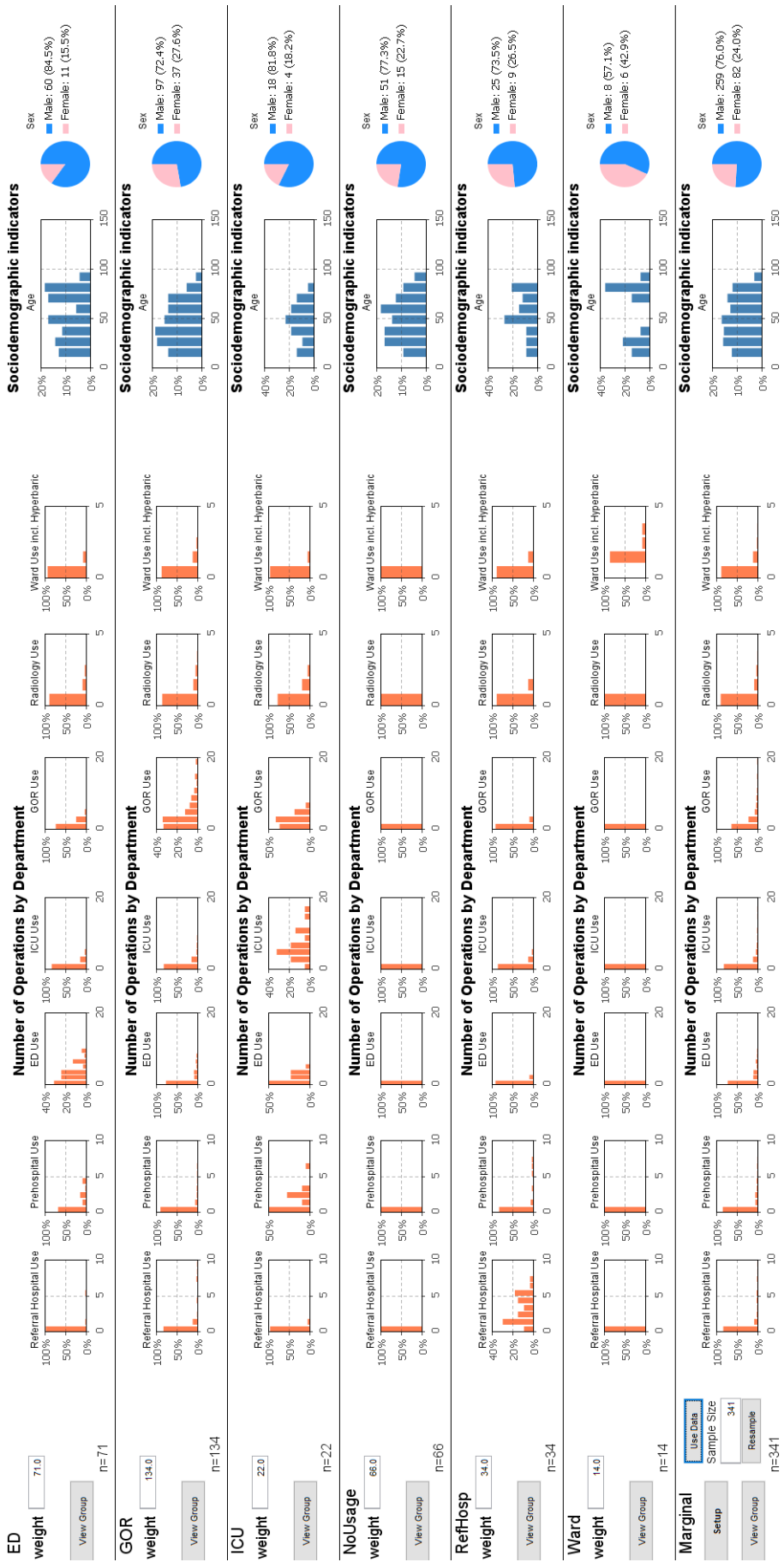


Figure 4.4: Dashboard View of Model

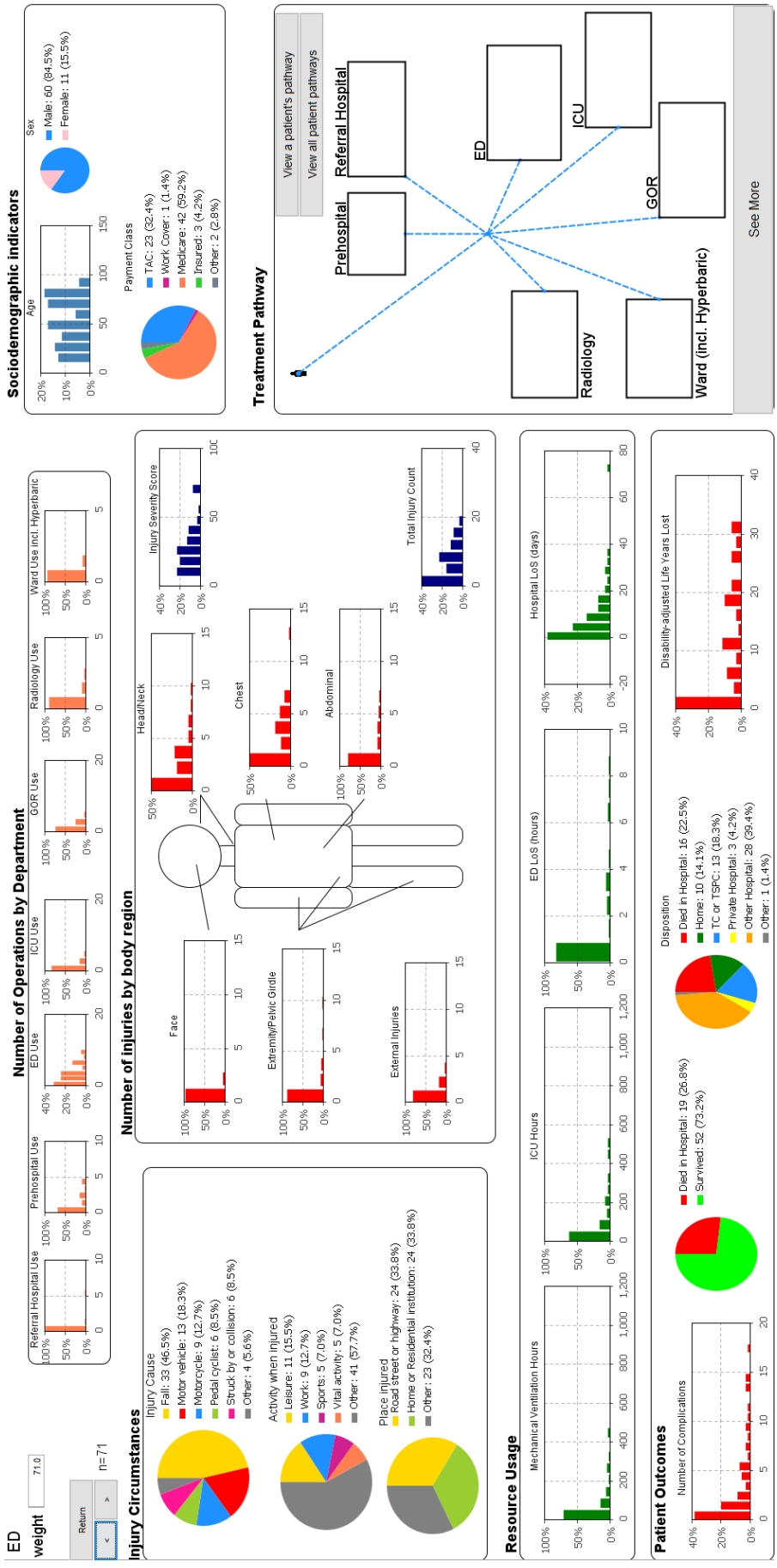
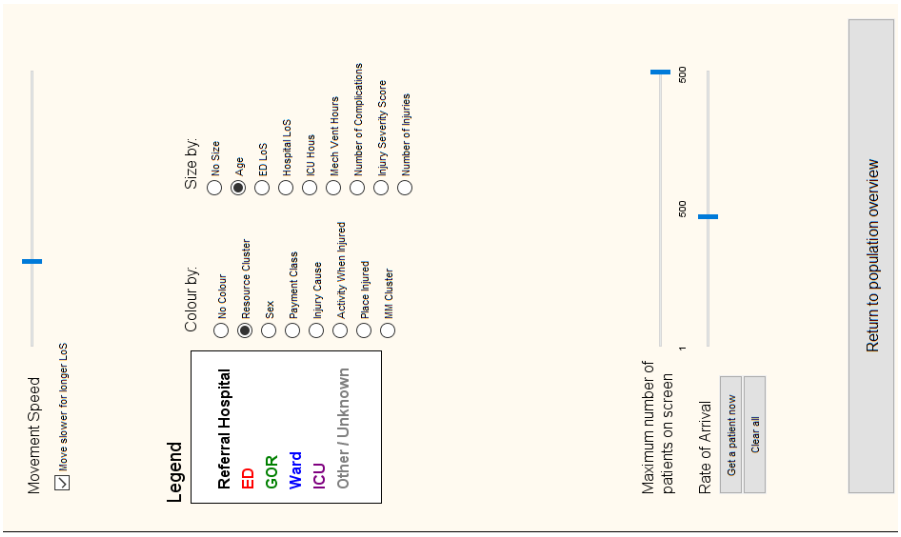


Figure 4.5: Cluster/Subpopulation View of Model



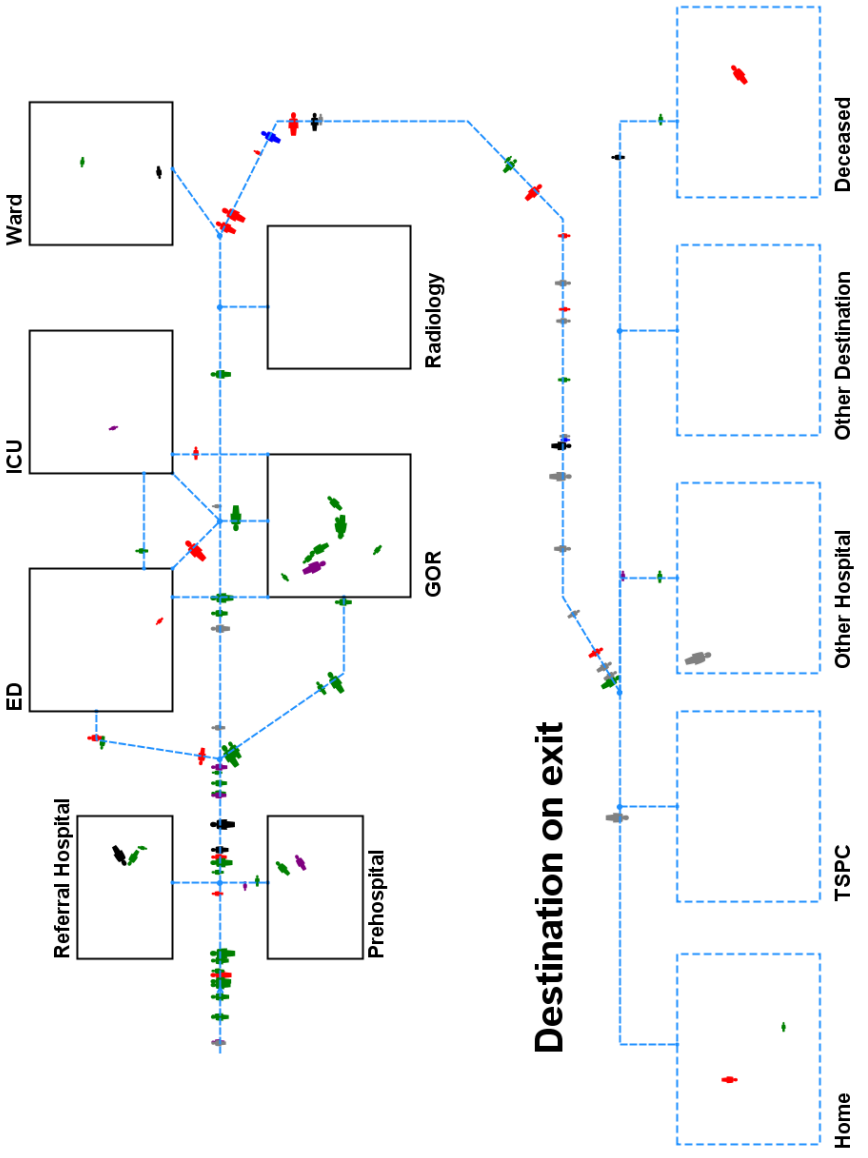


Figure 4.6: Process Animation

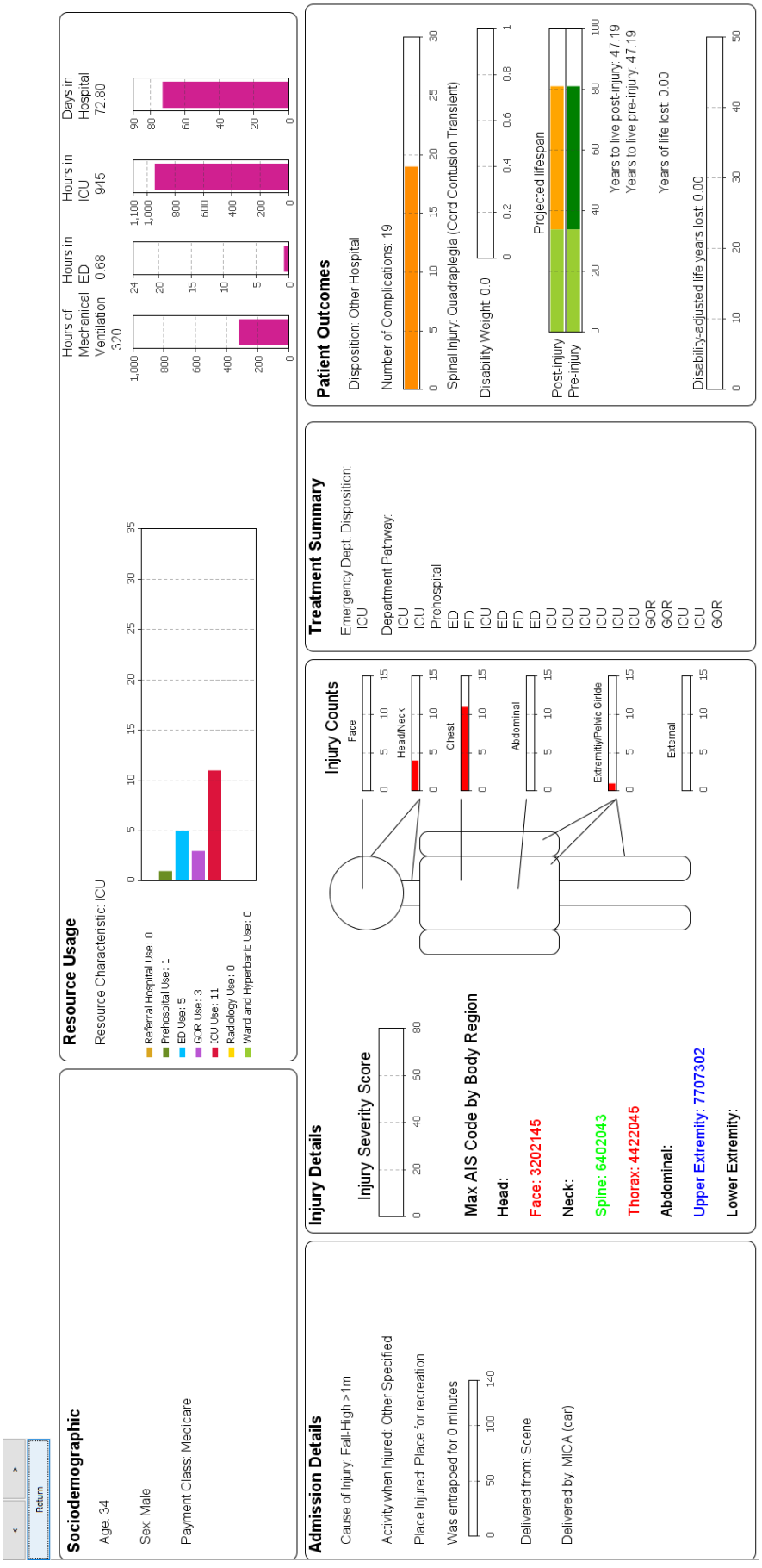


Figure 4.7: Patient Level View

4.7 Validation

This section discusses validation of the *visual systems model* presented in this chapter, and the validation of the *Visual Systems Modelling Framework* which was used to develop the model.

4.7.1 Face Validity

This model underwent two separate rounds of validation though discussion sessions with domain experts, the first consisting of members of ISCRR, and the second with a manager in a major trauma hospital who was not represented in the development of the model. This second validation process was an attempt to extend the model beyond the original purpose and intended model user group.

Upon presenting this model to ISCRR, it immediately lead to debate, with several panellists noting a higher than expected number of patients being discharged to other hospitals. This model reduced the complexity of the acute TSCI health care system to something which was comprehensible, and highlighted previously unknown and unexpected aspects of the system.

In the second discussion, the minimal use of conventional OR/MS tools was seen as a weakness of the model, which was not seen as useful from the manager's perspective. From the manager's perspective, the model would have been more useful had it presented simple summaries of the system, rather than attempting to capture a high degree of detail. The manager's needs from the model would be better described as modelling for *Investigation and Improvement*, or even *Routine Decision Support*.

This suggests that while the model fulfilled its purpose as a *visual systems model* for *Providing Insights for Debate*, and providing additional understanding to researchers who are not involved in the day-to-day running of a hospital, it was less useful for decision support in the context of everyday decision-making. The developed model was suitable for its intended purpose, but had little utility outside of this context.

4.7.2 Validity of Visual Systems Modelling Framework

The validity of the *Visual Systems Modelling Framework* was established by systematically evaluating whether the pre-specified desirable properties (Summarised in Section 4.5) were achieved by the developed model.

The developed model matched all of the criteria set out in the framework with the exception of planned phase-type modelling of Length of Stay (resources being blocked). This is summarised in Table 4.5 by accompanying each entry in the matrix of desirable properties with the *Visualisation Practices* (identified in Section 2.2.4.2) which were used in the application of the *Visual Systems Modelling Framework*.

However, all other components of the developed model met the criteria set out in the desired properties. The *Visual Systems Modelling Framework* was useful in the development of the *visual systems model* described by this chapter.

Table 4.5: Validation of model as provided by systems visualisation framework

	Conventional OR/MS Tools	Visualisation Principles			
		Principle 1: Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Patient Details		Filtering is achievable by health insurance type (**Visualisation Practice 3**)	Patient is able to interactively assign visual components to represent these components (**Visualisation Practices 3, 5**)	Visualisation uses a dashboard format to present information	
Injury Circumstance					
Available Resources					
Injury Details		Model structured to show increasing levels of information as desired (**Visualisation Practice 3**)	User is able to interactively assign visual components to represent these components. (**Visualisation Practices 3, 5**)		Injury details are presented in a way which details injury location and severity
Clinical Pathway	Clustering based on department usage was successful	Patients can be filtered by using this cluster. Clinical pathway and requirements are present at each level of detail, providing more information each time (**Visualisation Practice 3**)	User is able to interactively assign visual components to represent these components (**Visualisation Practice 3,5**)	Process animation replays patient's clinical pathway (**Visualisation Practice 4**)	
Clinical Requirements					These system components are represented in a dashboard format throughout the developed model
Clinical Outcomes	DALYs were calculated	DALYs viewable at group and individual levels	Individual patient screen provides details of how DALYs were calculated.		
Destination upon departure		User can filter by destination upon departure. exit destination is presented at different levels of aggregation through the model (**Visualisation Practice 3**)		Process animation ends with discharge destination (**Visualisation Practice 4**)	
Resources made unavailable	CoxPhT Model of LoS not interpretable	Clusters for LoS not interpretable, grouping based on LoS is not recommended		LoS ties into process animation and controls the speed at which patients move (**Visualisation Practice 4**)	

4.8 Discussion

The case study presented in this chapter demonstrated how the *Visual Systems Modelling Framework* could be applied to improving understanding of TSCI care processes. This application had several unique properties which provide insight on how the *visual systems model* can be used.

This case study demonstrated how the *Visual Systems Modelling Framework* can be used in a process system where the *Modelling Purpose* (Research Question 2) is *Epistemic Representative* in nature, and the model seeks to *Provide Insights for Debate*. The framework was able to accommodate a lack of direction regarding which *system features* included in the model were of primary importance by simply representing all as much information as possible.

It also demonstrated an approach to integrating conventional OR/MS tools with visualisation in a highly customisable way (Research Question 3(a)), with outputs from cluster analysis being used to *filter and zoom* (following the Visual Information Seeking Mantra (Shneiderman, 1996), which was discussed in Section 2.2.4.1), thus using conventional OR/MS tools to navigate the *visual systems model*, and/or control aspects of the visualisation itself, thus using visualisation to interpret the cluster outputs. This can be seen in the process animation in Figure 4.6, which uses the department usage clusters (discussed in Section 4.4.3.2) to control its appearance: Patients in the 'GOR' cluster (coloured green) can be seen entering the operating theatre within the representation of the process.

The integration of visualisation with conventional OR/MS tools by using visualisation to interpret conventional OR/MS tools also demonstrates how visualisation can assist in the validation of these tools (Research Question 3(b)). As discussed above, the fact that the department clusters can be understood in terms of the care pathway taken by each patient provides an additional level of validation to these clusters regarding their interpretability and meaning within the system.

While the department clusters were interpretable in terms of the TSCI care system, the clusters resulting from applying Marshall and McClean (2004) clustering to Length of Stay (discussed in Section 4.4.3.1) could not be interpreted in terms of the underlying Coxian Phase-Type Model. This presents a weakness in the developed model, which was noted in

the validation of this application of the *Visual Systems Modelling Framework* summarised in Table 4.5. The case study provided in this chapter demonstrates an example where Marshall and McClean (2004) clustering is not interpretable, thus illustrating a practical application of the rules developed in Section 3.3.

There were two identifiable weaknesses in the implementation of the *visual systems model* described in this chapter.

Firstly, we used Anylogic 7, which is marketed and designed as a tool for developing simulation models using a mix of agent-based, discrete-event and system dynamics modelling techniques. While this software allowed for rapid development of the *visual systems model* with a minimal amount of programming, it is not designed to be used for the dashboard approach to visualisation used in this application. This placed practical limitations on the particular visualisation approaches used, such as the use of pie charts as shown in Figure 4.5, which may not be the most effective way of representing information (Cleveland and McGill, 1984). Additionally, the use of Anylogic, a proprietary and non-ubiquitous modelling software, impeded the ability for this *visual systems model* to be shared or easily adapted for future use, meaning that it was only useful for improving understanding at the time of model development, for ISCRR.

Secondly, while the *User-Driven* approach to integrating visualisation with conventional OR/MS tools lead to significant flexibility in the developed *visual systems model*, this lack of focus on particular systems features increased both the time required for model development and the eventual complexity of the final model, making it more complicated to navigate and understand. While the decision to use a *User-Driven* approach was justifiable in this case due to both the uncertainty in TSCI care processes and a lack of clarity regarding which system components were of primary interest, the *User-Driven* approach to integrating conventional OR/MS tools with visualisation is likely to be inappropriate in applications with a clearer focus.

4.9 Conclusion

This chapter presented an application of the *Visual Systems Modelling Framework* to understand care processes in Traumatic Spinal Cord Injury. The case study demonstrated

how *visual systems modelling* can be used as an *Epistemic Representative* model for *Providing Insights for Debate*, thus addressing Research Question 2. It also demonstrated how visualisation can be integrated with conventional OR/MS tools in a *User-driven* fashion, and how this can be used to assist validation of conventional OR/MS tools. Additionally, the failure of Marshall and McClean (2004) clustering to produce interpretable clusters demonstrates the need for validation rules for this method. As a result, this case study also addresses Research Question 3 by demonstrating how a combination of visualisation and analytical methods can be used to validate conventional OR/MS tools.

Chapter 5

The AVERT Atlas: A tool for understanding multiscale clinical trial data in stroke rehabilitation

5.1 Introduction

This chapter discusses the second case study contained in this thesis. Section 5.2 summarises issues in the neurorehabilitative care of stroke, and Section 5.3 demonstrates how this care can be considered a process system. Section 5.4 describes how the *Visual Systems Modelling Framework* (developed in Section 2.3) was used to address the challenges outlined in Section 5.2, with Section 5.4.4 providing a matrix of *Desirable Properties* for the visual systems model resulting from the framework's use. Section 5.5 describes the final *visual systems model*, with Section 5.6 describing validation of both the developed model and the *Visual Systems Modelling Framework*.

5.2 Clinical Context

The treatment of stroke involves a continuum of health care processes, ranging from public health and preventative measures (aimed at minimising the incidence of stroke), through to the acute care of stroke (primarily concerned with minimising the time taken to diagnose and treat stroke, given its time-sensitive nature) and eventually to stroke

rehabilitation (concerned with maximising patient recovery post-stroke). While stroke has been of interest to OR/MS experts for some time, published applications in the area have concerned themselves primarily with the acute stage of stroke treatment. The OR/MS community has paid relatively little attention to areas of stroke care such as rehabilitation (Churilov and Donnan, 2012).

Historically, clinical opinion in stroke rehabilitation has been that neurorehabilitation should begin soon after stroke, though there has been inconsistency around recommendations regarding the exact timing of this treatment (Bernhardt, Indredavik, and Langhorne, 2013). The recently concluded A Very Early Rehabilitation Trial (AVERT) clinical trial (Bernhardt et al., 2015) sought to provide strong clinical evidence to support this hypothesis, but instead found that high-intensity, early mobilisation may be harmful to stroke patients (Bernhardt et al., 2015). This unexpected result has resulted in deliberation within the stroke community about why the experimental treatment studied in AVERT was harmful (Luft and Kesselring, 2016) Regardless of the reasons behind the result of AVERT, further investigation and a more detailed analysis of the trial data are required before clinical recommendations can be made resulting from this new evidence (Bernhardt et al., 2015).

Bernhardt et al. (2016b) started this process of "begin[ning] to unpack" the relationship between physiotherapy dose and clinical outcomes by examining the relationship between average physiotherapy received by a patient (in terms of total minutes and total physiotherapy sessions) and patient outcomes, suggesting that short, more frequent physiotherapy sessions may be beneficial to a patient's recovery. However, these results were based on averages, and ignored a large degree of complexity in the system. There remains a "critical need" to identify appropriate physiotherapy regimens for stroke survivors, particularly with respect to the duration and frequency of physiotherapy, intensity of physiotherapy activity, and the differences between subpopulations of patients (Bayley et al., 2017, p. 12).

Identifying appropriate physiotherapy regimens is a significant challenge due to the complexity of stroke rehabilitation. Several prognostic factors, such as a patient's age and their stroke severity, have a significant impact on a patient's outcome post-stroke. In addition to subpopulation effects resulting from these factors, the nature of stroke

rehabilitation is extremely multifaceted and dynamic in nature. A dose of physiotherapy consists of not only an intensity in treatment, but also both a duration (number of minutes) of treatment and frequency of physiotherapy (number of sessions). This dose can change over the duration of a patient's rehabilitative stay, introducing an additional temporal aspect to a given physiotherapy regimen. Complicating matters further, a patient's health may change across time, either in response to treatment received or due to some unforeseen adverse event which leads to a rapid decline in a patient's health (e.g. a serious fall resulting in further injury and disability, pneumonia, or any other event which leads to a sudden worsening in health).

This leads to a strong potential for reverse causality within the system, as a patient's treatment is limited by their ability to tolerate that treatment (Jauch et al., 2013). It may be unclear if a patient had poor health as a result of their physiotherapy dose, or if they received that dose because they were unwell. While such potential presents a challenge to the use of analytical methods within the OR/MS toolbox, it also presents an opportunity where visualisation can be leveraged to reduce the complexity of the system and allow clinicians to use their domain knowledge to identify patterns in physiotherapy which may lead to better outcomes for stroke survivors.

5.3 Stroke Rehabilitation as a Process System

Stroke rehabilitation meets all the criteria required for it to be considered a process system according to the definition adopted in Section 1.1 of this thesis. It can be considered a process under the definition given by Daellenbach (1994, p. 5):

Inputs: The primary input into stroke rehabilitation is stroke survivors, each of whom has specific factors influencing their health (e.g. age, stroke severity, pre-existing health conditions)

Work Activities: Patients who enter stroke rehabilitation undergo physiotherapy, resulting in a change in their health state over time. The therapy these patients receive may be influenced by their health state at that time.

Outputs: Patients are eventually discharged from stroke rehabilitation, with improved long-term outcomes being the primary output from the system.

Likewise, it meets all the criteria to be considered a system under Daellenbach (1994, p. 27):

1. A system is an organised assembly of components. 'Organised' means that there exist special relationships between these components. Stroke rehabilitation is an organised system which seeks to use therapy delivered by neurorehabilitative physiotherapists to improve patient wellbeing. Physiotherapists and patients have a special relationship as a result of this interaction.

2. The system does something, i.e., it exhibits a type of behaviour unique to the system. Stroke rehabilitation seeks to improve long-term outcomes for stroke survivors. The behaviour of stroke patients responding to formal treatment given by physiotherapists is unique to this system.

3. Each component contributes to the behaviour of the system and is affected by being in the system. No component has an independent effect on the system. The behaviour of the system is changed if any component is removed or leaves. The major components of stroke rehabilitation are patients and physiotherapists, and the interaction between them drives the system behaviour. Removing one of them would fundamentally change the nature of the system.

4. Groups of components within the system may themselves have properties 1, 2, and 3. i.e., they may form subsystems. A patient can be considered to be a subsystem, with their health driven by complex biological and neurological forces.

5. The system has an outside - an environment - which provides inputs to the system and receives outputs from the system. Stroke rehabilitation's environment consists of the rest of the health care system and broader society. Stroke rehabilitation receives patients (inputs) from hospital and discharges (outputs) them to home, a nursing facility or elsewhere once their rehabilitation is complete.

6. The system has been identified by someone as of special interest. Stroke is a debilitating condition leading to death and long-term disability worldwide. Improving patient recovery is therefore important to improve the quality of life among stroke survivors.

As stroke rehabilitation can be understood as a process system, challenges within it can be addressed using systems modelling tools. The *Visual Systems Modelling Framework* can therefore be applied to stroke rehabilitation.

5.4 Application of Visual Systems Modelling Framework

This section applies the systems visualisation framework to the stroke rehabilitation process system.

The Conceptual Model and Model Purpose presented in this section were developed with clinical researchers at The Florey Institute of Neuroscience and Mental Health. Model development took place in an iterative process, with the model being modified and improved in response to feedback.

5.4.1 Conceptual Model

As discussed in section 5.3, the neurorehabilitative care of stroke survivors can be understood as a process system. As it meets the definition of a process, it can can be considered in terms of Inputs, Work Activities and Outputs. The stroke rehabilitation system is primarily concerned with the relationship between *Patients* and the *Physiotherapy* they receive, with systems behaviours such as dose-response relationships driven by the interaction between these two components. This two-component view of the system, combined with the perspective of inputs, work activities, and outputs provided by the process interpretation of the model, forms the basis of the conceptual framework for this system, summarised in Table 5.1.

Table 5.1: Summary of Conceptual Model

	Patient	Care
Input	Patient Baseline information	Care Setting
Work Activity	Patient health progression	Physiotherapy regimen
	Dose-Response Relationship	
Output	Patient Outcomes	

This link results in the following *systems features*:

Patient Baseline Information A patient's baseline information (such as age, sex, and pre-existing health conditions) and the details of their stroke (severity and type of stroke) play a significant role in a patient's clinical outcomes.

Care Setting The place in which a patient receives care may impact on either the quality of care provided, or access to care, which would have flow-on effects to the rest of the system.

Patient Health Progression A patient's health may change over time in response to their treatment (work activity performed on them). This is summarised in this system by scoring a patient's daily *functional ability* on an ordinal scale between Level 1 (very poor) and Level 4 (very good). A patient may also experience *adverse events*, which impact on their health.

Physiotherapy Regimen A patient's physiotherapy regimen consists of a sequence of daily physiotherapy treatments, where each day consists of a total number of *minutes* spent in physiotherapy, spread over a number of *sessions*. Not only does the number of minutes and sessions vary across a sequence of daily treatments, but a patient's length of stay (and therefore this *sequence length*) is also variable.

Dose-Response Relationship The systems behaviours driven by the relationship between patient health state and physiotherapy regimen are complex. While patient health can change in response to therapy, the therapy a patient receives may change as a result of

what activity a patient can tolerate on a given day. This interaction must be understood in addition to each individual system component.

Patient Outcomes The ultimate aim of stroke rehabilitation is to improve the long-term health of stroke survivors. The primary clinical measure used in this system is the modified Rankin Scale (mRS), a 7-point clinical measuring a patient's functional independence post stroke (Table 5.2). Additionally, the ability to walk post-stroke is a clear functional measure of the long-term impact that stroke has on a patient's life. In addition to its clinical importance, walking ability is considered an important milestone by stroke survivors (Michael, Allen, and Macko, 2005). Understanding the role of physiotherapy in improving both of these features is therefore important.

Table 5.2: Description of mRS categories (Banks and Marotta, 2007)

mRS	Description
0	No symptoms at all
1	No significant disability; despite symptoms, able to carry out all usual duties and activities
2	Slight disability; unable to perform all previous activities but able to look after own affairs without assistance
3	Moderate disability; requiring some help but able to walk without assistance
4	Moreately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Death

5.4.2 Model Purpose

Unlike the modelling purpose discussed in Section 4.4.2, in this application there is an unambiguous goal (investigate and identify patterns in dose-response relationships to

inform better stroke rehabilitative care). This model therefore has a different purpose than the one developed in Chapter 4. The focus of this model is on *Investigating* stroke care. As Pidd's (2010) taxonomy is a spectrum of model use, this could either be described as a model for *Investigation* but not *Improvement*, or described as falling between *Providing Insights for Debate* and *Investigation & Improvement*. This thesis describes this purpose as having features of both *Providing Insights for Debate* and *Investigation & Improvement*. As this model seeks to develop new knowledge by representing an objective reality, it is *Epistemic Representative* in nature.

5.4.3 Conventional OR/MS Tools

The conventional OR/MS tools used in this application are clustering techniques for identifying common patterns in treatment and health progression within the group. These are used to reduce the perceived complexity of the system, and assist users in navigating the visual components of the model.

5.4.3.1 Patient health progression

A patient's health state can change from day to day. In this system, these changes were tracked using a 4-point ordinal scale, with 1 indicating poor health and 4 indicating good health. Each patient's health progression can be described by a sequence of these daily health states, which provides an indication of their recovery trajectory. The length of this sequence is inherently tied to length of stay, as patient observations cease after discharge or death.

This process was modelled in R (R Core Team, 2017) using agglomerative hierarchical clustering with complete linkage, with the input dissimilarity matrix calculated using the method outlined in Section 3.2.

Parameter p is fixed at 2 to highlight the link between this measure and Cohen's Kappa with Quadratic Weighting, a statistic that is well-understood by clinicians. As it was expected that clusters based on health progression would be correlated with long-term health, this relationship was exploited to select Parameter r. r was chosen to maximise the relationship between resultant clusters (prespecified for 3 clusters) and mRS at 3 months, measured by the test statistic for Pearson's Chi-squared test when clusters and

mRS were crosstabulated.

5.4.3.2 Physiotherapy regimen

A patient receives physiotherapy over time in the form of a total number of *minutes* of physiotherapy each day, and total number of *sessions* each day. To identify patterns in this over time, hierarchical clustering is performed on both the cumulative number of minutes and cumulative number of sessions.

5.4.3.3 Dose-Response Relationship

The relationship between dose and response is captured by using the method outlined in Section 3.2.3, combining baseline patient information (age and stroke severity), physiotherapy (as described in Section 5.4.3.2) and health progression (as described in Section 5.4.3.1). The relative weights were chosen to maximise the relationship between this measure and mRS at 3 months.

5.4.3.4 Patient Outcomes

A patient regaining the ability to walk is an important milestone. To assist understanding of this recovery process, the EMPhT algorithm (Asmussen, Nerman, and Olsson, 1996) will be applied to fit Coxian Phase-Type distributions to the time taken to regain walking ability, sequentially increasing the number of phases in order to optimise Bayesian Information Criterion (BIC). The fitted distribution will then be checked against the validity rules developed in Section 3.3.3 to confirm that the resultant clusters are interpretable in terms of the modelled recovery 0process.

5.4.4 Model Design

Due to the focus of the model on investigating dose-response relationships, system components related to dose and response are emphasised in the developed model. Other systems components are of secondary importance. As such, systems components other than physiotherapy dose, patient health progression and final patient outcomes, while still included in the model, can be relegated to filtering data and allowing subgroup analysis to occur.

To assist subgroup analysis, an overview of the properties of a selected group of patients should be displayed, including summaries of patient baselines, physiotherapy received, health progression and dose-response relationships. Full information about *systems features* of primary importance should also be presented on a patient-by-patient basis. *Static visual cues* such as colour should be used to represent these features.

Table 5.3 summarises these desirable properties for the model and provides criteria which will be used in validating the final model.

Table 5.3: Desirable properties of model arising from this framework

Conventional OR/MS Tools	Visualisation Principles			
	Principle 1: Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Patient Baseline Information	Dose-response clusters			
	Filter based on all recorded information. Provide overview of group and detailed information			
Care Setting				
Patient Health Progression	Response clusters	Show details of patient's health status	Show changes in dose and health over time in ATLAS	Show visual summary of each individual patient in manner that is simple to navigate
Physiotherapy Regimen	Dose Clusters	Show details of physiotherapy regimen		
Dose-Response Relationship	Dose-Response clusters			
Patient Outcomes	Walking Time Clusters	Include mRS in visualisation		

5.5 Developed Model

5.5.1 Data

The data from the AVERT clinical trial was used in the development of this model, consisting of 2104 patients with different physiotherapy regimens, each summarised at a daily level to include their health state (measured on an ordinal scale between 1 and 4), the number of sessions and total minutes of physiotherapy received on each day and the number of adverse events on each day.

5.5.2 OR/MS Tools

This section describes the results of the application of conventional OR/MS tools as described in Section 5.4.3. In each case, the use of these tools was successful, and the results were included in the final *visual systems model*.

5.5.2.1 Patient Health Progression

Patterns in patient health progression were identified using the method described in Section 5.4.3.1. A ratio of $r = 2.205$ maximised the relationship between these clusters and mRS (Figures 5.1 and 5.2). Three clusters were produced, labelled *Fast Recovery* (n=1220), *Slow Recovery* (n=305) and *Did Not Recover* (n=415).

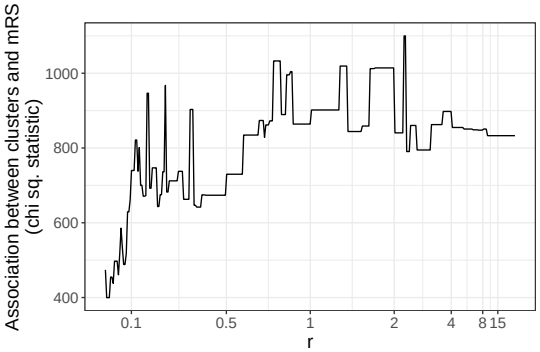


Figure 5.1: Strength of relationship between clusters and mRS

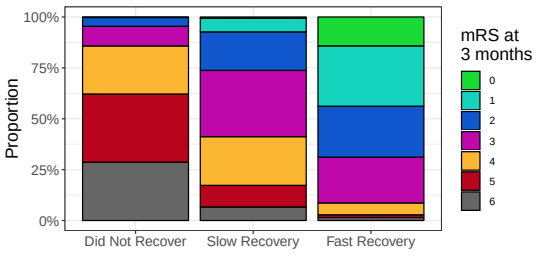


Figure 5.2: mRS by cluster

The *Fast Recovery* group predominantly consisted of patients who started with relatively positive functional levels, who were quickly discharged (median LoS of 5 days). There were relatively few adverse events that occurred to patients in this cluster, mostly

occurring at a steady rate in the first 3 days of their stay.

The *Slow Recovery* group consisted of patients who had poorer functional levels at the start, who stayed for longer than the Fast Recovery group (median LoS of 10 days). While there were a few deaths within the 14-day observation period, there are signs of recovery in this group, with the bulk of observations of Level 1 disappearing over time, replaced by Level 2 observations. Likewise, Level 3 and 4 observations start to appear later into the observation period. Like the *Fast Recovery* group, there are relatively few adverse events, occuring at a steady rate over the first 3 days before slowly tapering off.

The *Did Not Recover* group, by comparison, consists almost exclusively of patients with poor functional ability who either stay past the 14-day observation period or die within it. Approximately 75% of all observed adverse events occur to patients within this group, with a rapid increase in the first 3 days before steadily climbing through the rest of the observation period.

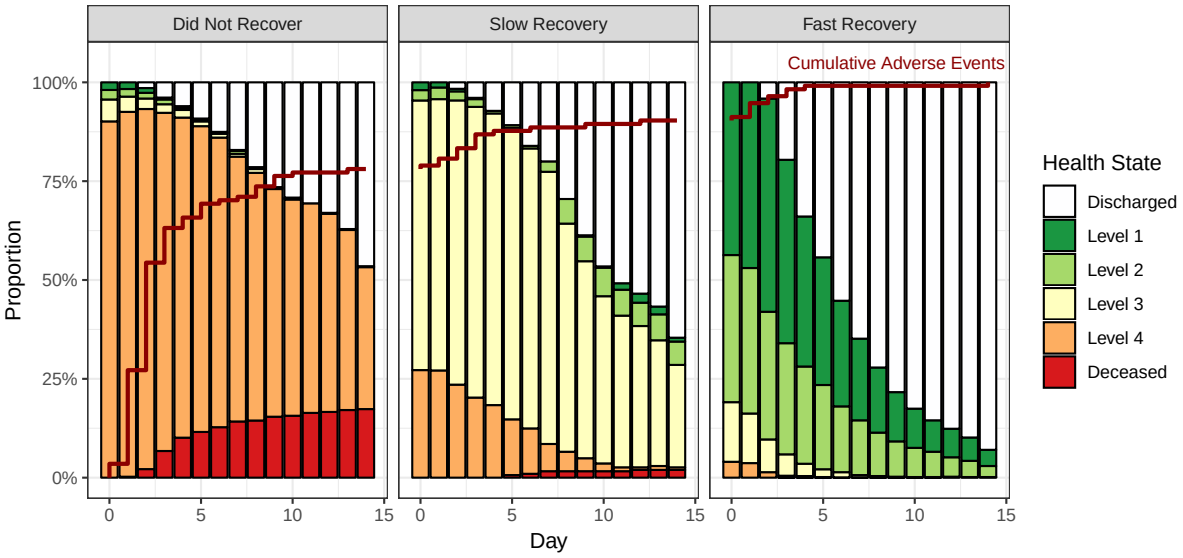


Figure 5.3: Distribution of health state across time, and cumulative adverse events, by cluster

The clusters described here identified several patterns in health patient recovery which can be incorporated into the development of the *visual systems model*.

5.5.2.2 Patterns in Physiotherapy Dose

Patterns in physiotherapy received by patients were identified using hierarchical clustering as described in Section 5.4.3.2. This resulted in three dose profiles based on the frequency

of physiotherapy (number of sessions) (Figure 5.4). These were labelled *Few* (n=1778), *Moderate* (n=307) and *Many* (n=19) sessions.

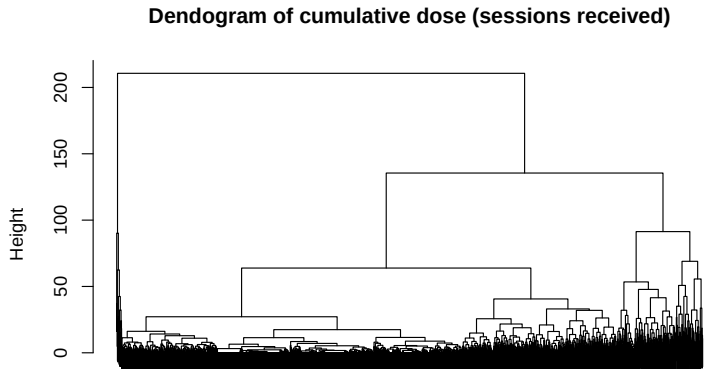


Figure 5.4: Dendrogram of dose frequency

Patients who received *Few* sessions averaged less than 2 sessions of physiotherapy a day, with some patients receiving almost no physiotherapy sessions throughout their entire stay. Where patients did receive more frequent physiotherapy at the start of their treatment, it quickly tapered off with little additional treatment within 3-7 days. Patients who received *Moderate* sessions of physiotherapy averaged 2-3 sessions of physiotherapy a day, with all patients receiving at least 12 sessions of physiotherapy throughout their stay. While patient physiotherapy did taper off over the course of a patient's stay, this occurred later in a patient's rehabilitative stay. Patients who received *Many* sessions of physiotherapy averaged approximately 5 sessions of physiotherapy a day,

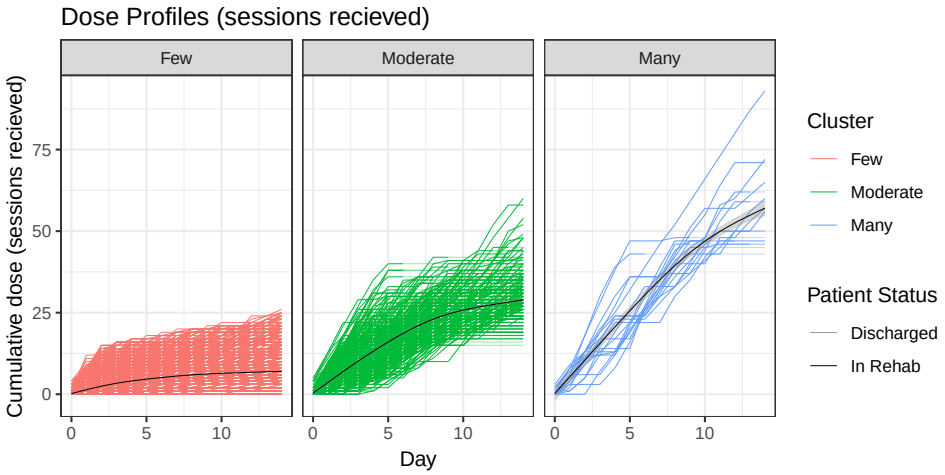


Figure 5.5: Dose profile (frequency) by Cluster. Black line indicates average dose accumulation

Clustering of total minutes resulted in three clusters (Figure 5.6), which were labelled *Short* (n=1826), *Medium* (n=246), and *Long* (n=32) duration. The clustering process

was repeated on the Short duration group, resulting in three sub-clusters (Figure 5.7), which were labelled *Short (Do not Touch)* (n=1268), *Short (Sharp Dose)* (n=191), and *Short (Gradual Dose)* (n=367).

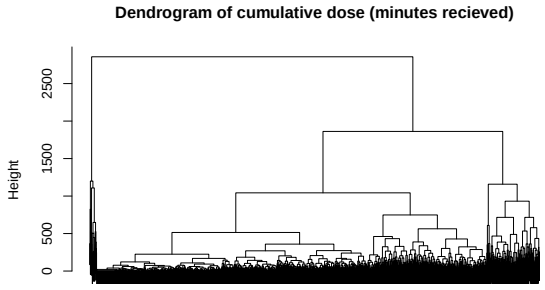


Figure 5.6: Dendrogram of dose duration

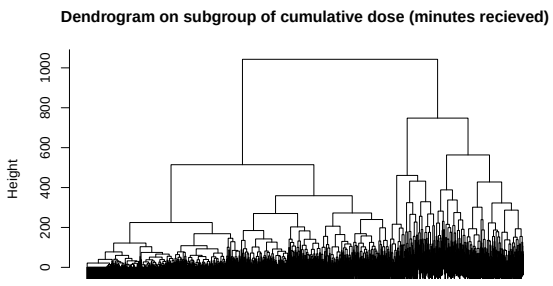


Figure 5.7: Dendrogram of dose duration

Patients in the *Short (Do not Touch)* group recieved almost no physiotherapy, averaging less than an hour of physiotherapy over 14 days. Where physiotherapy was received, it occurred gradually for the first 5 days before tapering off. Patients in the *Short (Sharp Dose)* group received physiotherapy at a rate comparable to the *Medium* Dose group for 5 days before having therapy taper off, reaching an accumulated dose of approximately 250 minutes over 14 days. Patients within the *Short (Gradual Dose)* group received similar total physiotherapy to those in the *Short (Sharp Dose)* group, though this was spread evenly over 14 days rather than concentrated in the first 5. Patients within the *Medium* group accumulated minutes of physiotherapy at a significantly higher rate than in the *Short* subgroups, with comparatively little tapering off of received dose. Likewise, patients with *Long* sessions continuously received physiotherapy, accumulating an average of 800 minutes over 14 days.

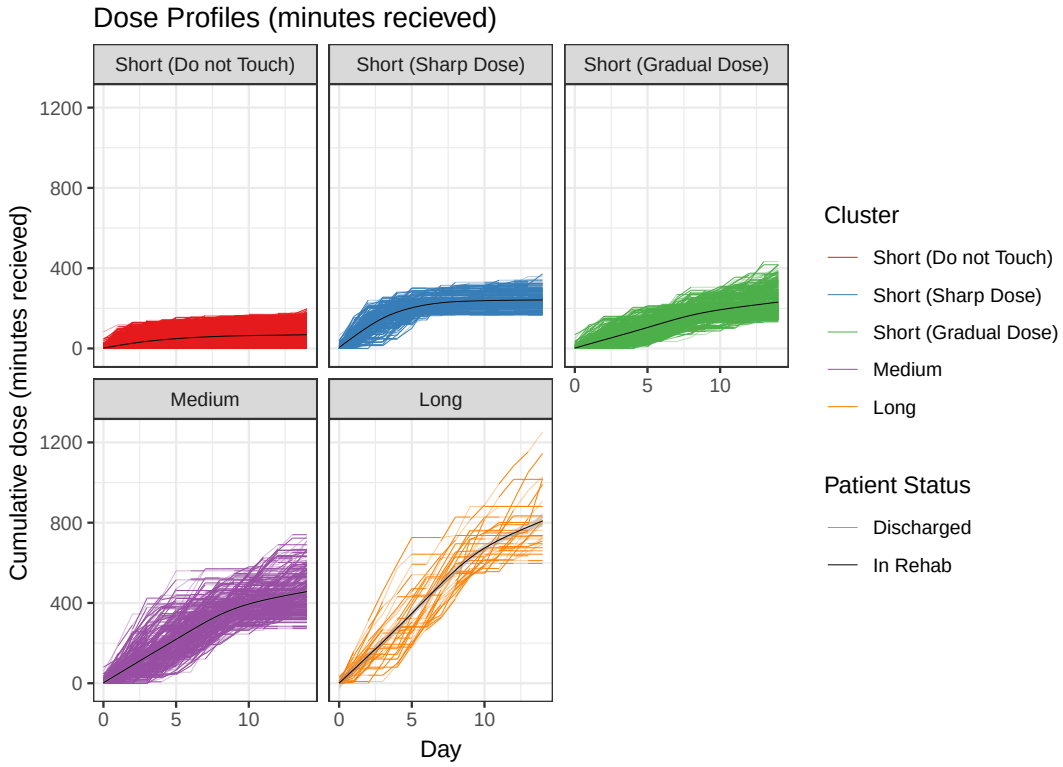


Figure 5.8: Dose profile (duration) by Cluster. Black line indicates average dose accumulation

The clusters developed in this section identify patterns in physiotherapy regimens received by patients, simplifying this part of the system being modelled. These clusters can be used in the development of the final *visual systems model*.

5.5.2.3 Patterns across multiple systems features

Patterns across multiple systems features were identified as outlined in Section 5.4.3.3. Throughout this section, the resulting clusters are labelled according to the following notation:

$$(Age/NIHSS/Level, Direction)$$

Where Age is given as Young (Y), Middle (M) or Old (O), NIHSS is given as Mild (M), Moderate (Mod) or Severe (S), Level is the smallest range of consecutive levels of functional ability which make up at least 75% of all observations on Day 0 in the cluster, and Direction is the overall trajectory of the cluster, either Recovering ($+$) or Declining ($-$). Distinctions between categories for Age and NIHSS are relative to other clusters

rather than based on predefined values.

By providing equal weights to these three distance matrices, 6 clusters are identified (Table 5.4)

Table 5.4: Count of patients in each cluster

$(Y/M/3-4,+)$	$(M/M/3-4,+)$	$(O/M/2-4,+)$
506	123	593
$(Y/Mod/1-2,+)$	$(M/S/1-2,-)$	$(O/S/1-2,-)$
42	232	444

The $(Y/Mod/1-2,+)$ group, could be considered to be one of the most clinically interesting patterns identified here, as this group corresponds to patients who had poor early health but recovered. This suggests that these patients were the ones who responded to physiotherapy in a positive way. However, the cluster size is extremely small by comparison to the other clusters, so extreme caution must be used in interpreting this group in this way.

Almost all adverse events occurred in the $(M/S/1-2,-)$ and $(O/S/1-2,-)$ groups, corresponding to patients with severe strokes (Figure 5.9). $(O/S/1-2,-)$ received minimal physiotherapy, potentially because this patient cohort were too ill for treatment. (Figure 5.10).

The clinically interesting $(Y/Mod/1-2,+)$ group discussed above is difficult to distinguish from the $(Y/M/3-4,+)$ group in terms of baseline patient characteristics, with both cluster's baselines being situated in a similar area. (Figure 5.11). Unfortunately, this means that it is difficult to provide a simple story based on a particular "type" of patient that will respond to treatment. However, these results do suggest that there is a subset of patients who respond positively to treatment, or a specific type of physiotherapy regimen, may be beneficial to stroke survivors.

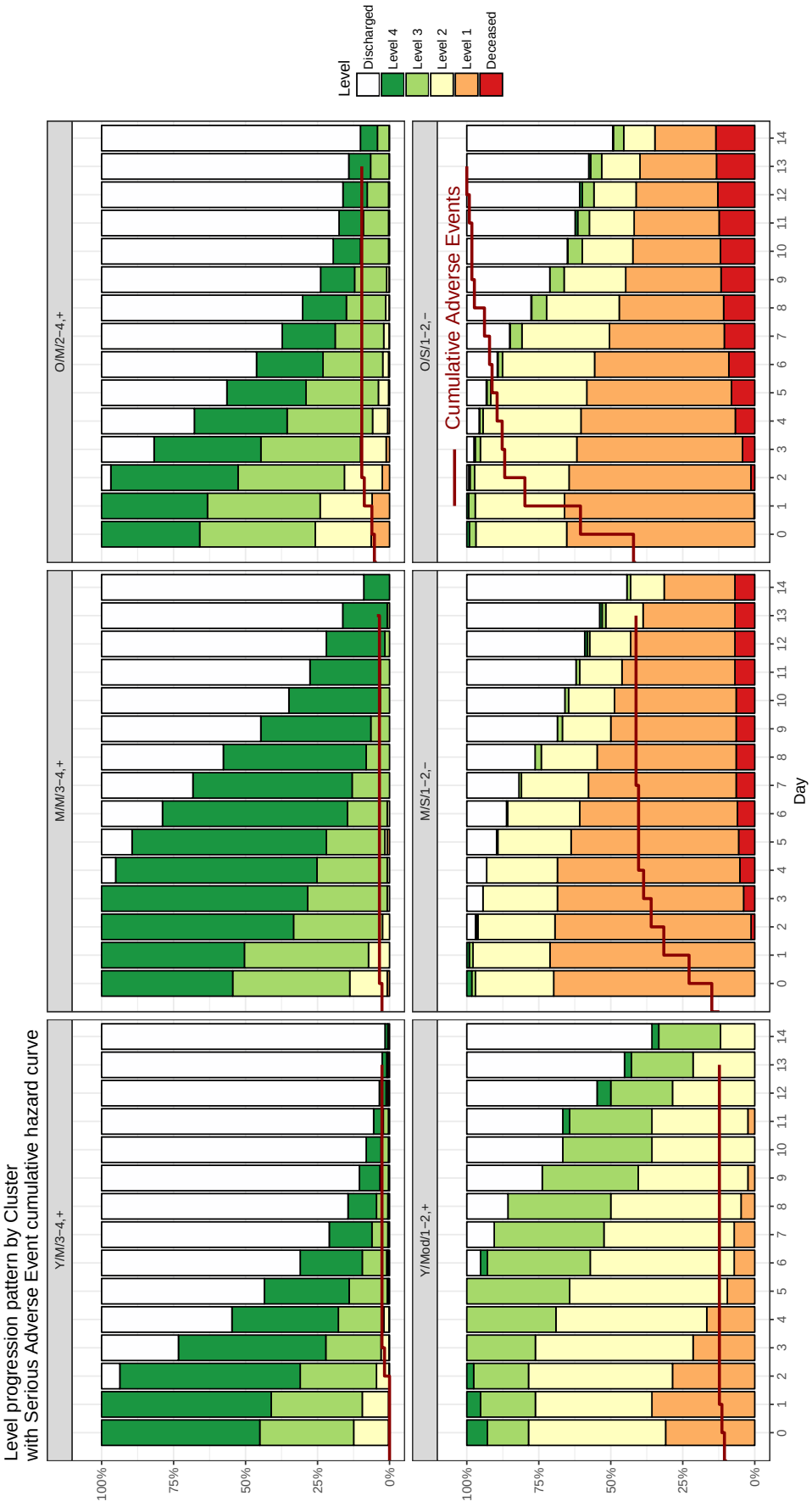


Figure 5.9: Level progression and cumulative adverse events by Grand Cluster

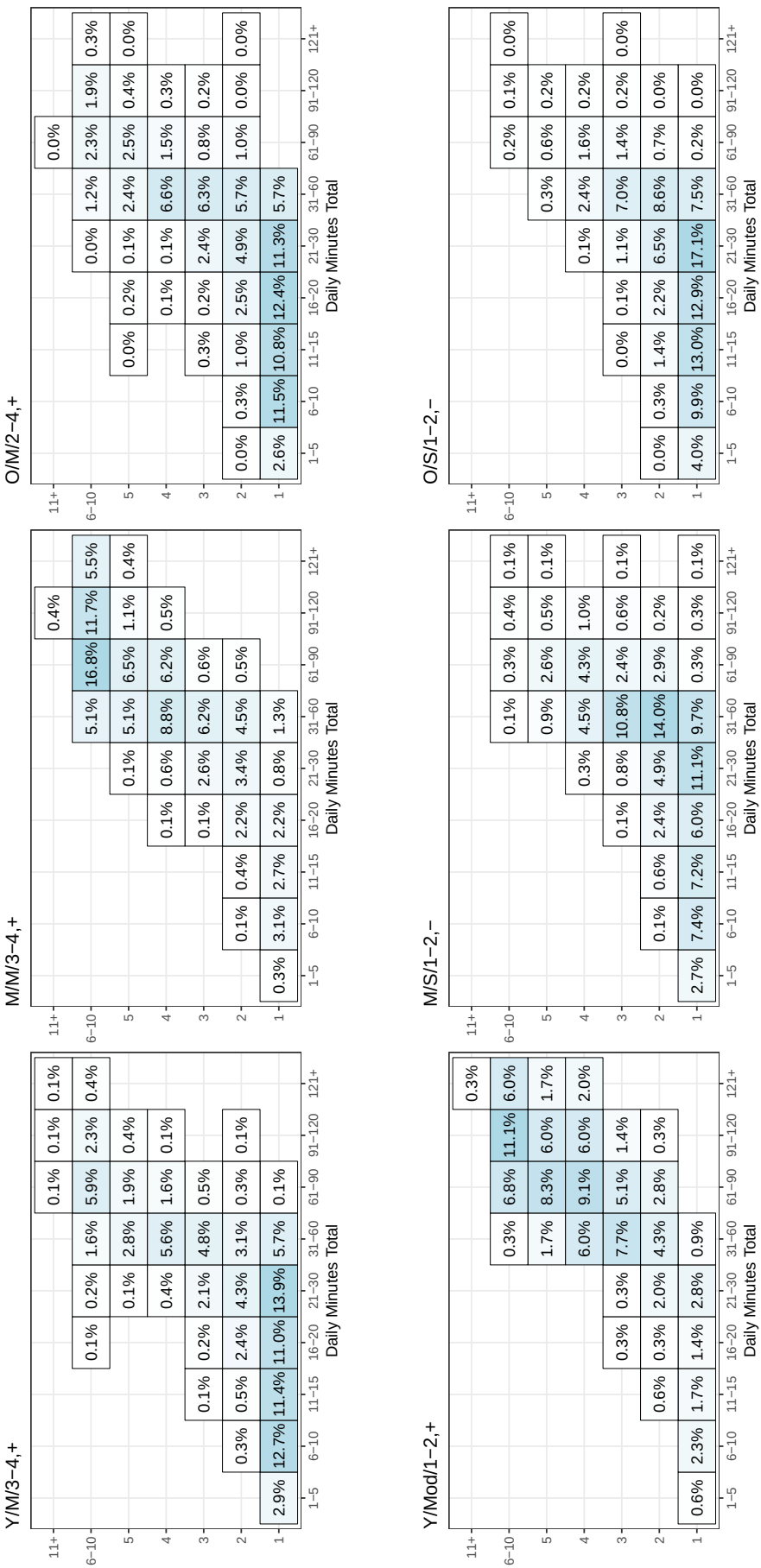


Figure 5.10: Daily Dose Distribution by Grand Cluster

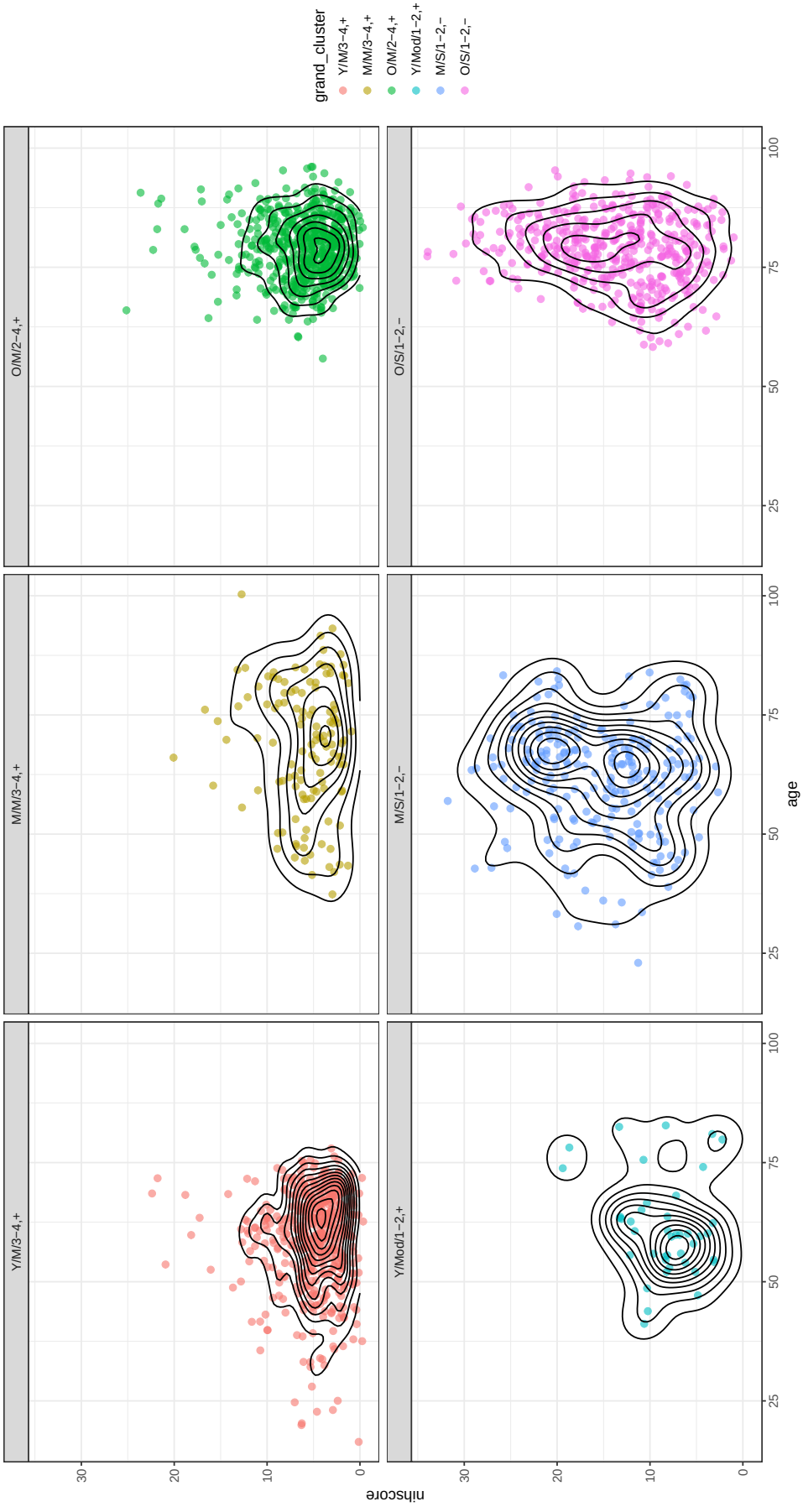


Figure 5.11: Baseline age and NIHSS by cluster

5.5.2.4 Time to ability to walk

The time to recover walking ability was modelled using Coxian Phase-Type distributions as set out in Section 5.4.3.4. Model selection using BIC led to a 3-phase system being chosen with parameters given in Table 5.5.

Table 5.5: Fitted CoxPhT Models for days to walk

			Phase number i				
Number of phases	BIC		1	2	3	4	5
2	14027.99	μ_i	0.123731	0.001511			
		λ_i	0.065435				
3	**13648.89**	μ_i	0.162576	0.012859	0.000330		
		λ_i	0.129564	0.014641			
4	13660.90	μ_i	0.163024	0.013572	8.876172×10^{-04}	4.404296×10^{-73}	
		λ_i	0.131510	0.016983	0.003876		
5	13671.43	μ_i	0.159938	3.019945×10^{-13}	0.015352	0.001141	$6.396853 \times 10^{-167}$
		λ_i	0.110413	0.087452	0.025268	0.004646	

The validation rules developed in section 3.3 were applied to the selected 3-phase CoxPhT model. The CART model was applied by identifying the appropriate nodes in the trees supplied in Appendix B.1, while the Regression model was applied by using the formulas supplied in Appendix B.2, with a positive value required for the model to be considered likely to result in clusters which correspond to the underlying process being modelled.

According to the validation rules developed in Section 3.3, Marshall and McClean (2004) clustering leads to clusters which are likely to correspond to the underlying markovian process being modelled, with a level of agreement according to quadratically-weighted Cohen's Kappa of $\kappa > 80\%$. Therefore, these clusters can be interpreted in terms of the underlying markovian process. Table 5.6 provides a summary these results.

Each phase in this system can be thought of as corresponding to patients who had fairly immediate recovery of walking ability post-stroke, patients who did not have immediate recovery but would eventually recover the ability, or patients who are unlikely to ever recover the ability to walk (represented by the very small value of μ_3, indicating that a patient in this phase will practically never recover ability to walk). These phases

correspond to the generated clusters ($\pi_1 = 0.5565$,$\pi_2 = 0.2074$,$\pi_3 = 0.2361$), with the fitted model drawing cutpoints between these three health pathways at recovery within 9 days and 120 days (4 months). Figure 5.12 shows the distribution of time to regain walking ability, the fitted CoxPhT distribution and the cluster boundaries generated from the CoxPhT model.

Table 5.6: Results of Validation of CoxPhT Model. Ensemble of models suggests that the agreement between clusters and the underlying system is strong ($\kappa > 0.8$)

	CART		Regression	
κ value	Pass?	Node	Pass?	Value
70	**yes**	2 (94.6%)	**yes**	2.018502
75	no	1 (4.4%)	**yes**	0.534062
80	**yes**	2 (84.8%)	**yes**	1.499447
90	no	1 (0.3%)	no	-0.696913

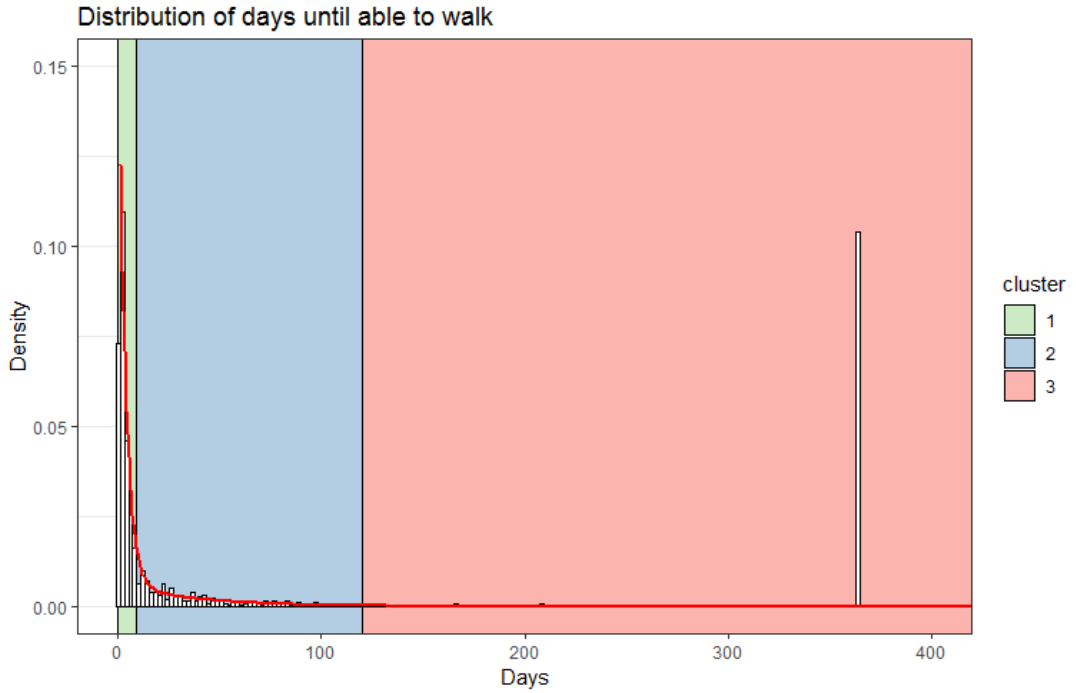


Figure 5.12: Histogram showing time to walking ability with fitted CoxPhT distribution and exit phase clusters. The spike at 365 days corresponds to censored data.

5.5.3 Visual Components of Model

In this application, the purpose of the model is to investigate systems features related to dose-response relationships. As such, systems components which are not directly related to this are de-emphasised, and primarily serve as a means for zooming and filtering in on patient subgroups.

Information that is considered of primary importance, such as physiotherapy dose, day-to-day health progression, clinical outcome and timing of adverse events, is presented in a series of tiles, each representing a patient. Figure 5.13 annotates each component of a typical patient tile.

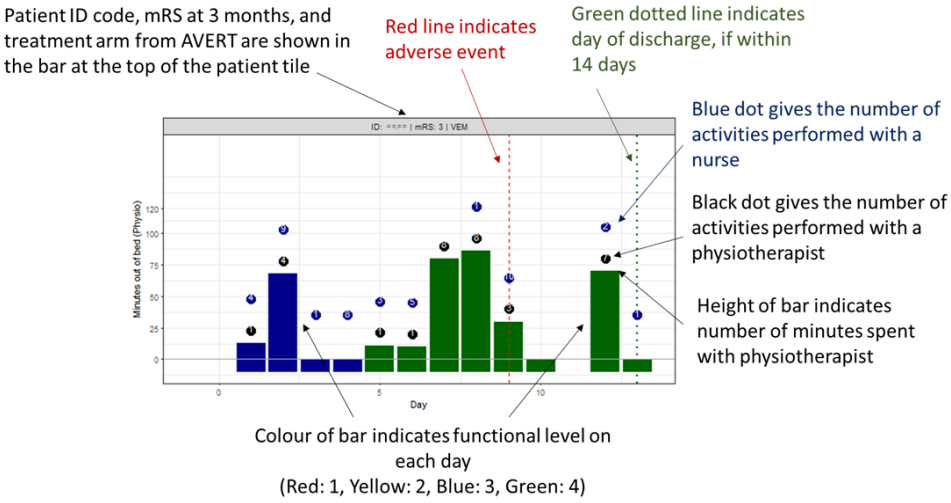


Figure 5.13: Annotated tile from AVERT Atlas visualisation

These tiles are presented next to each other, and can be arranged by total dose received or health progression.

5.5.4 Visual Systems Model

The *visual systems model* developed in this chapter was built in R (R Core Team, 2017), using the *shiny* (Chang et al., 2018) and *ggplot2* (Wickham, 2016) packages. It provides a means for investigators to understand the complex data collected during AVERT, identify patterns in the data, and generate new hypotheses regarding the relationship between clinical outcomes and physiotherapy regimens post-stroke. This model was dubbed the *AVERT Atlas*.

The AVERT Atlas consists of three tabs. The first of these is the Controls Tab (Figure 5.14), which contains all controls used in the systems visualisation. Users can use this section to select subsets of patients, as well as control details of the visualisation such as how many patient tiles should be displayed at once and how these tiles should be arranged. Outputs from analytical modelling outlined in Section 5.4.3 are used in this tab, providing additional options for selecting patient subgroups. Alternatively, if a user is interested in a specific set of patients, they can provide patient ID codes to display just the patients manually specified.

The second tab is the Overview Tab (Figure 5.15). This tab provides a dashboard-style visual summary of the selected patients (discussed in Section 2.2.2). The average physiotherapy dose, and how it relates to mRS is displayed prominently at the top of this screen, as investigating and improving dose-response relationships is the primary objective of this model. The distribution of average daily activity (average number of nursing sessions, average number of physio sessions, average total daily minutes with physiotherapist) is shown immediately below this, followed by the distribution of primary covariates (age and nihss). The selected patients distribution of functional levels across days is also shown to provide an aggregate overview of patient health progression among the selected patients. The distribution of patient outcomes, such as mRS and time to ability to walk, is displayed at the bottom of this tab.

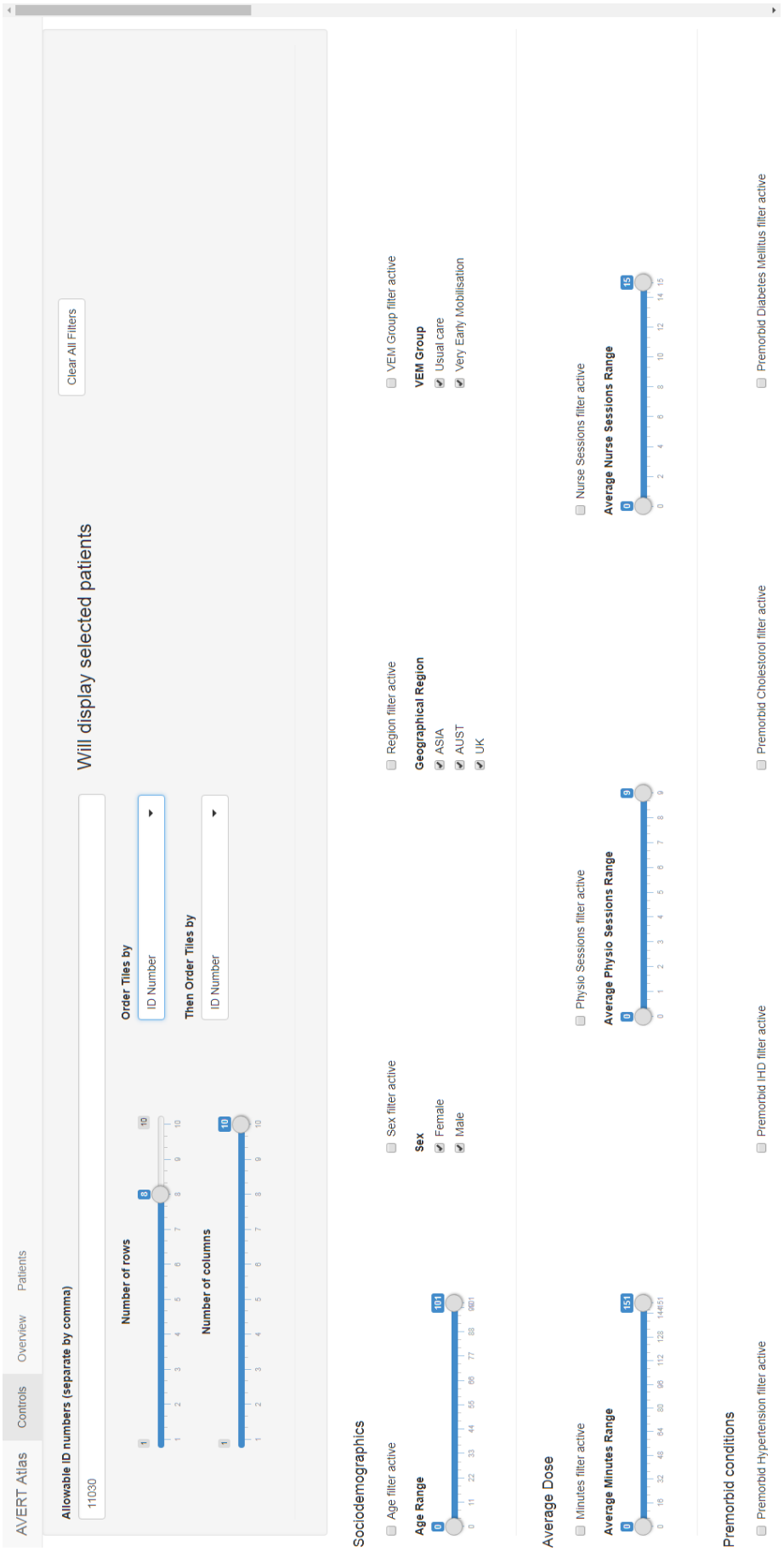


Figure 5.14: Screenshot of Controls tab for AVERT Atlas

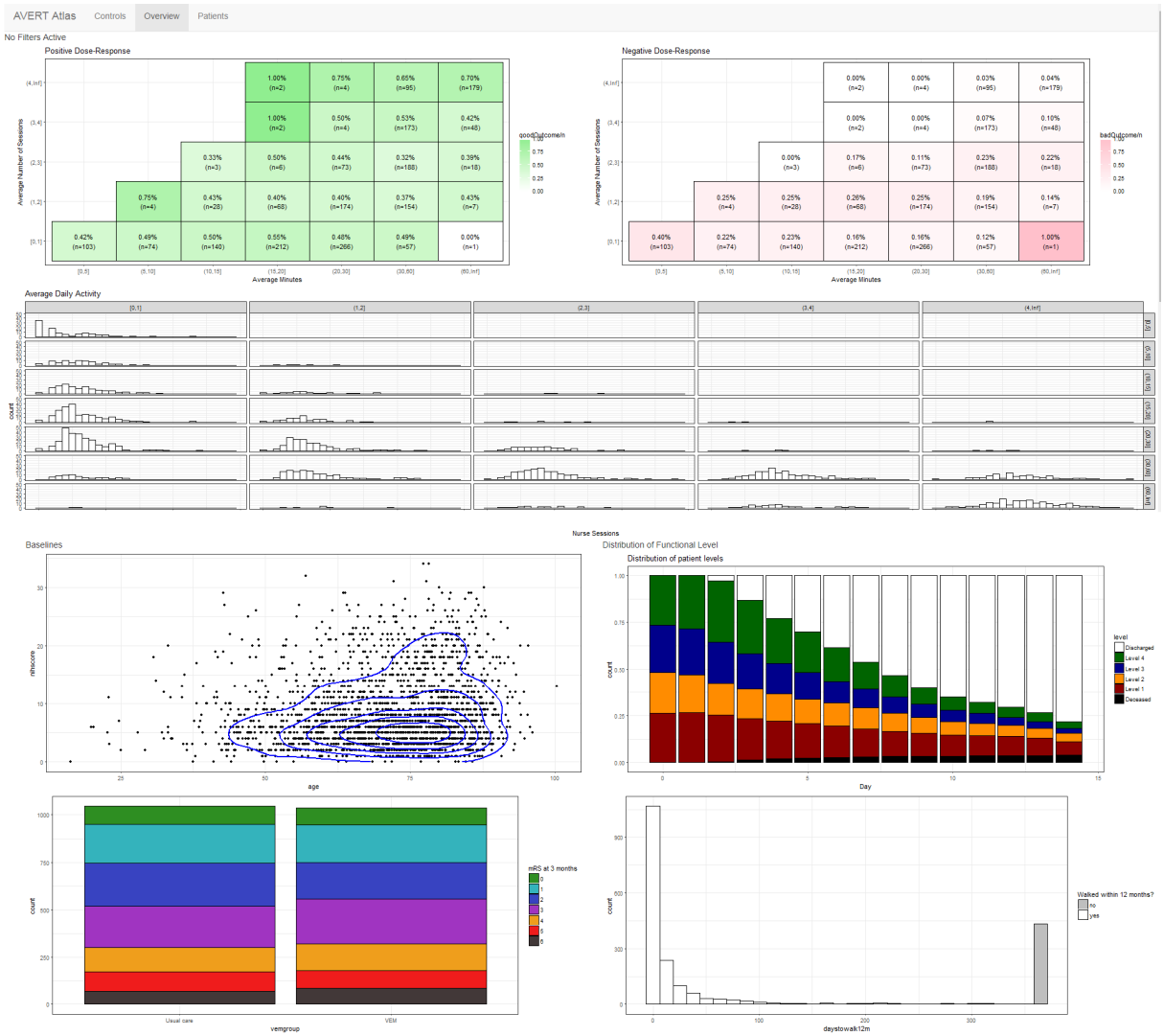


Figure 5.15: Screenshot of Overview tab for AVERT Atlas

The final tab in the AVERT Atlas is the Patient Tab (Figure 5.16). This tab displays the patient tiles discussed in Section 5.5.3, using whatever settings were chosen in the Controls tab. The user can scroll through these patient tiles using the controls at the top.

Figure 5.16: Screenshot of Patient tab for AVERT Atlas

5.6 Validation

5.6.1 Face Validity

This model was validated through continuous discussions with domain experts at the Florey Institute of Neuroscience and Mental Health. The ATLAS has since been made available to researchers within the AVERT research group, and was used to identify promising physiotherapy regimens to prospectively evaluate in the AVERT-DOSE trial (discussed in Chapter 7). The Atlas has been continually upgraded in response to feedback from researchers within the institute.

5.6.2 Framework Validity

The relevance of this framework in this case study was evaluated by confirming that the developed model matches with the matrix of *desirable properties* developed in Section 5.4.4. Where the visualisation practices discussed in Section 2.2.4.2 were used, this has been marked in Table 5.7.

Table 5.7: Desirable properties of model arising from this framework

	Conventional OR/MS Tools	Visualisation Principles			
		Principle 1: Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Patient Baseline Information	Clustering Successful	Overview of dataset is provided prior to full detail. User is able to filter the data based on all system information (**Practice 3**)			
Care Setting					
Patient Health Progression	Clustering Successful		Changes in health state are shown in the context of recieved dose using colour (**Practice 5**)	All dose-response shifts are shown over time	Differences in dose-response can be identified visually
Physiotherapy Regimen	Clustering Successful		Changes in dose are shown in the context of changing health states using height (**Practice 5**)		
Dose-Response Relationship	Clustering Successful				
Patient Outcomes	Clustering Successful		mRS shown in context of dose and changing health state		

5.7 Discussion

The case study presented in this chapter demonstrated how the *Visual Systems Modelling Framework* could be applied to identify patterns in stroke physiotherapy. This application had several unique properties which provide insight on how the *visual systems model* can be used:

This case study demonstrated how the *Visual Systems Modelling Framework* can be used in a process system where the *Modelling Purpose* (Research Question 2) is *Epistemic Representative* in nature, and the model seeks to *Investigate and Improve* the system. As there was a clear idea of what *systems features* were of primary importance, the *visual systems model* was able to be relatively focused on solely on displaying and identifying patterns in dose and response. This minimised extraneous and potentially distracting information, albeit at the cost of losing contextual information.

It also demonstrated an approach to integrating conventional OR/MS tools with visualisation by using the clusters developed in section 5.5.2 to navigate the *visual systems model*. As such, it can be considered an example of *analytically-driven visualisation*. This maintained the tight focus on the *systems features* under investigation at the expense of reducing the ability to interact with the applied OR/MS tools. This led to a reduced ability for the *visual systems model* to be interrogated. Under this approach, by the time the conventional OR/MS tools are integrated into the *visual systems model*, they have to be trusted. While the patterns identified by the applied OR/MS tools appeared meaningful, if other techniques were used this may not have been the case.

The trust in conventional OR/MS tools required by an *analytically-driven visualisation* approach to *visual systems modelling* suggests a need for extensive validation prior to the development of the final *visual systems model*. In this case study, the clusters regarding time to regain walking ability (discussed in Section 5.4.3.4) were interpretable in terms of the underlying Coxian Phase-Type Model. The case study provided in this chapter demonstrates an example where Marshall and McClean (2004) clustering is interpretable. This demonstrates that clusters identified in this way can be successfully applied.

One strength of the implementation of the *visual systems model* discussed in this chapter is that it was developed in the free software R. This means that it can be shared and updated relatively easily as new features are requested or required, as happened in

this case study (discussed in Section 5.6.1). However, this introduced its own technical limitations. The Atlas was built using the *ggplot2* package, which encourages at most one variable to be assigned to one visual aspect (e.g. x, y, colour, etc) of the visualisation. As the Avert ATLAS sought to include additional information into the visualisation, it rapidly ran out of unassigned visual aspects, reducing the ability of this *visual systems model* to incorporate additional features which increased the amount of visualised *system features*. This was not foreseen at the time of model development, and by the time this issue with scalability became a problem it would have required the model to be rebuilt from scratch. Using a different programming language or library for visualisation from the beginning may have allowed for greater flexibility in feature addition.

5.8 Conclusion

This chapter presented an application of the *Visual Systems Modelling Framework* to identify patterns in physiotherapy regimen and patient health in Stroke Rehabilitation. The case study demonstrated how *visual systems modelling* can be used as an *Epistemic Representative* model that can be considered to be between *Providing Insights for Debate* and *Investigation and Improvement*, thus addressing Research Question 2. It also demonstrated how visualisation can be integrated with conventional OR/MS tools in an *analytically driven* fashion, and demonstrated that this approach to may require additional trust in the OR/MS tools applied, thereby increasing the importance of validation (addressing Research Question 3).

Chapter 6

Predictive Models for the AVERT Dataset

6.1 Introduction

As discussed in Chapter 5, the previously developed AVERT Atlas allows for exploration of data collected in the AVERT trial, but it cannot be used to make predictions about the health outcomes for a hypothetical patient. This inhibits its ability as a tool for *Investigation and Improvement*, instead placing it between this point on Pidd's (2010) spectrum and *Providing Insights for Debate*.

This chapter applies the *Visual Systems Modelling Framework* to the same process system discussed in Chapter 5, except in this case study we further narrow the focus of the model to examining dose-response outcomes with the aim of developing a predictive model. As such, in this case study discussions of both clinical context and viewing this context as a systems process have been omitted, as these were discussed in Sections 5.2 and 5.3 respectively.

6.2 Application of Visual Systems Modelling Framework

While this application focuses on the same clinical context as Chapter 5, differences in focus lead to a a different conceptual model which focuses on a sub-system of the

process system described in Chapter 5. This results in a different model arising from the application of the *Visual Systems Modelling Framework*. This section presents a second application of the *Visual Systems Modelling Framework* applied to investigate the effects of physiotherapy on stroke survivors.

6.2.1 Conceptual Model

As discussed in Section 5.3, the neurorehabilitative care of stroke survivors can be understood as a process system, meaning that aspects of the system can be considered in terms of Inputs, Work Components, and Outputs. This remains the same in this application of the *Visual Systems Modelling Framework*.

This application focuses on a sub-system within this context where the differentiation between *patient* and *physiotherapy* components of this system has been removed. Features such as care setting, adverse events, comorbidities and patient information outside of age and stroke severity (both well-understood and important prognostic factors in stroke) are considered to be external to this sub-system. The only aspect of the larger system which is modelled is the *Dose-Response* relationship, and how this relates to patient outcomes. The conceptualisation of this sub-system has one primary type of component, with the conceptual model summarised in Table 6.1.

Table 6.1: Summary of Conceptual Model

	Dose-Response Features
Inputs	Patient Characteristics
Work Activities	Dose-Response behaviour
Outputs	Clinical Outcomes

The three *systems features* arising from this conceptual model are as follows:

Patient Characteristics A patient's characteristics will impact what their clinical outcomes are likely to be. This includes a patient's age, stroke severity, and type of stroke.

Dose-Response Dose-Response includes both the physiotherapy received by patients and the day-to-day health state. The dose of physiotherapy received by patients in this system is the primary system component that can be controlled by clinicians, and is therefore the focus of this model.

Clinical Outcomes Final clinical outcomes within this system are measured in terms of a patient's score on the modified Rankin Scale (mRS) measured at 3 months, and their ability to walk within 12 months of treatment.

6.2.2 Model Purpose

The OR/MS application presented in this chapter seeks to identify new rehabilitation strategies that could lead to better clinical outcomes for patients. This is to be achieved by building a predictive model which can predict likely patient outcomes based on the baseline characteristics and physiotherapy dose that a hypothetical patient receives across their rehabilitative stay. Modelling in this project is for *Investigation and Improvement* under Pidd's (2010) taxonomy, but with less *Human Interaction* than the model purpose discussed in Section 5.4.2. The emphasis in this model is placed on *Improvement*, rather than *Investigation*. Under Bayer et al.'s (2014) taxonomy, this application is *Epistemic Representative* in nature, as it seeks to model reality to generate new information about promising physiotherapy regimens.

6.2.3 Conventional OR/MS Tools

Patient outcomes will be predicted in this application using the *kknn* R package (Schliep and Hechenbichler, 2016), which implements a weighted variant of the k-nearest neighbours algorithm proposed by Samworth (2012). Under this method, predictions are made by comparing a new set of predictive values to existing data, and making predictions based on similar cases in the data that have been observed before. The relative weight placed on each existing record varies based on how similar it is to the features of the hypothetical patient whose outcomes are being predicted. The number of records used to make predictions in this manner will be chosen to minimise prediction errors, calculated by leave-one-out cross validation.

Similarity between records will be matched based on age, stroke type, stroke severity, and cumulative minutes and sessions following the same standardisation process described in Section 5.4.3.2.

6.2.4 Model Design

Due to the focus in this model on the relationship between dose and final outcomes, these system components are emphasised in the developed model in a similar fashion to the approach taken in Chapter 5. Systems components other than physiotherapy dose and final patient outcomes will be included to provide context and transparency to the predictions made, but are de-emphasised. Predictions made by the model should be completely transparent, with the user able to see which observations were used to make each prediction, and able to pull up full information about those patients. These properties are summarised in Table 6.2.

Table 6.2: Desirable properties of model arising from this framework

Conventional OR/MS Tools		Visualisation Principles			
		Principle 1: Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Patient Baseline Characteristics	Weighted k-nearest neighbours to predict patient outcomes based on baselines and dose		Show information about records used to make predictions		Show detailed breakdown of predictions and reasoning in a way that allows the user to visually navigate the system
Dose-Response Behaviour		Allow user to pull up greater detail on the records used to generate predictions			
Clinical Outcomes					

6.3 Developed Model

6.3.1 Data

The data used to develop the model was the same as the dataset described in Section 5.5.1. This dataset contains 1005 cases where modified Rankin Scale was between 0 and 2, and 1658 cases where where the patient was able to walk within 12 months. In this case, only systems features of primary importance are included in the model, such as physiotherapy dose, baseline patient information and patient outcomes recorded in the dataset.

6.3.2 Conventional OR/MS Tools

The relationship between patient baselines, physiotherapy regimen and patient outcomes was successfully modelled using the approach described in Section 6.2.3. In this model, modified Rankin Scale at 3 months is predicted using the 53 closest neighbours (Figure 6.1), while walking ability at 12 months is predicted using the 28 closest neighbours (Figure 6.1).

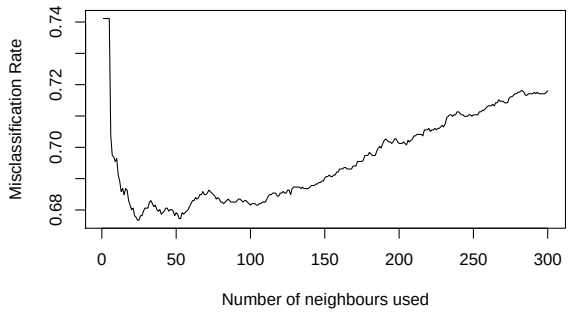


Figure 6.1: Misclassification rate of weighted k-nearest neighbours (predicting mRS at 3 months)

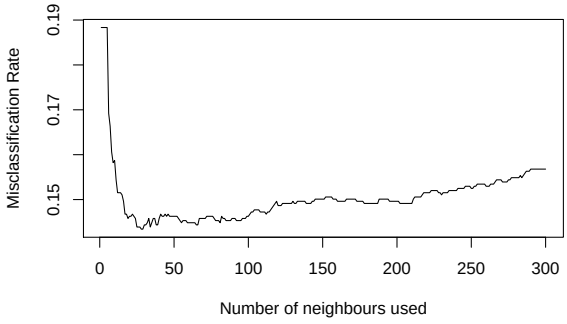


Figure 6.2: Misclassification rate of weighted k nearest neighbours (predicting walking ability at 12 months)

Further validation of this OR/MS tool was performed by 10-fold cross validation, examining the binary predictive quality indicators sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). mRS was dichotomised at 0-2 vs 3-6 (a common practice in stroke research (Weisscher et al., 2008)) to allow these values to

be calculated. Table 6.3 contains these values:

Table 6.3: Quality of dichotomised *kknn* predictions

	PPV	NPV	Sensitivity	Specificity
mRS 0-2 at 3 months	0.6963	0.715	0.6935	0.7177
Can walk at 12 months	0.8638	0.7008	0.9524	0.4263

With the exception of Specificity for walking ability at 12 months, these values are at a minimum of approximately 0.7, which is of reasonable accuracy. As the primary outcome in this system is modified Rankin at 3 months, a reduced ability to reliably distinguish a patient who cannot walk at 12 months post-stroke is not a critical flaw. This predictive tool was deemed acceptable for use in the developed *Visual Systems Model*.

6.3.3 Visual Components of Model

While the focus of this model is on the relationship between patients, physiotherapy regimens and clinical outcomes, in this application of the *Visual Systems Modelling Framework* most *Systems Features* were included in the predictive OR/MS model described in Section 6.3.2. The only *feature* which is not included as either an input or output of the predictive model is a patient's day-to-day health progression. The outputs from this predictive model can be used to understand these encapsulated *systems features*.

The inputs for the developed predictive model (Patient Baselines such as age, stroke severity and stroke type; Physiotherapy Regimen) are presented using slider controls, as this allows the relationship between different inputs to be visually comprehended. In particular, displaying a matrix of sliders for controlling the duration and frequency of physiotherapy for individual days essentially forms a controllable bar chart, with each slider corresponding to physiotherapy received on consecutive days. Additionally, these inputs are visually summarised using the patient tile approach discussed in Section 5.5.3. This provides visual understanding of model controls and places individual inputs in the context of dose on other days.

Patient Outcomes are output by the predictive model in terms of the probability of receiving different outcomes (e.g. mRS score of 0 vs mRS score of 1). These can be represented using a stacked bar chart to show the relative probability of each outcome.

This has the added advantage of being able to compare multiple predictions side-by-side to examine the differences in outcome resulting from changes in dose or patient type.

The only *systems feature* not captured by the predictive model is day-to-day health progression. As there is the potential for reverse causality within this system (discussed in Section 5.2), it is important that even if patient response is not captured by the predictive model, this *feature* should be included in the final *Visual Systems Model*. As k-nearest neighbours operates based on identifying existing records which are similar to a hypothetical case, additional information from these records can be incorporated into the *Visual Systems Model*. Segmented bar charts are used to show the changes in day-to-day health state in the records which are used to make predictions in a similar manner to the overview tab of the AVERT Atlas, discussed in Section 5.5.4. Likewise, the distribution of patient baseline information such as age and stroke severity is shown for these records using a scatter plot with histograms along the margins. These visual components provide important contextual information for the predictions being made.

6.3.4 Visual Systems Model

The *visual systems model* developed in this chapter was built in R (R Core Team, 2017), using the *kknn* (Schliep and Hechenbichler, 2016), *shiny* (Chang et al., 2018) and *ggplot2* (Wickham, 2016) packages. It provides a means for investigators to predict the results of giving a patient a particular physiotherapy regimen, allowing them to experiment to identify the optimal dosage of physiotherapy. This model was dubbed the *AVERT Dose Explorer*.

The AVERT Dose Explorer consists of one page which can be broken up into three parts. The first of these contains the controls for selecting a hypothetical patient's baseline characteristics and the physiotherapy regimen they receive. Each of these values can be adjusted in real time, with the rest of the model updating based on these changes. This is shown in Figure 6.3. Two hypothetical patients can be examined in this way, allowing the user to examine the effect of different physiotherapy regimens on the same type of patient, or how different types of patient respond to the same physiotherapy regimen,

The model then provides contextual information which was used in the calculation of clinical outcomes, showing the distribution of baseline patient information used by

weighted k-nearest neighbours as well as the day-to-day health progression of these patients. It also connects to the AVERT Atlas (discussed in Chapter 5) and allows the user to examine each individual patient which was used in the prediction. Where two patients are being compared, contextual information is provided for both patients. This is shown in Figure 6.4.

The last part of the model presents a visual summary of the patient (or patients) which are to be predicted, using the same approach as described in Section 5.5.3. Segmented bar charts are then used to show the probabilities of each type of outcome. This is shown in Figure 6.5.

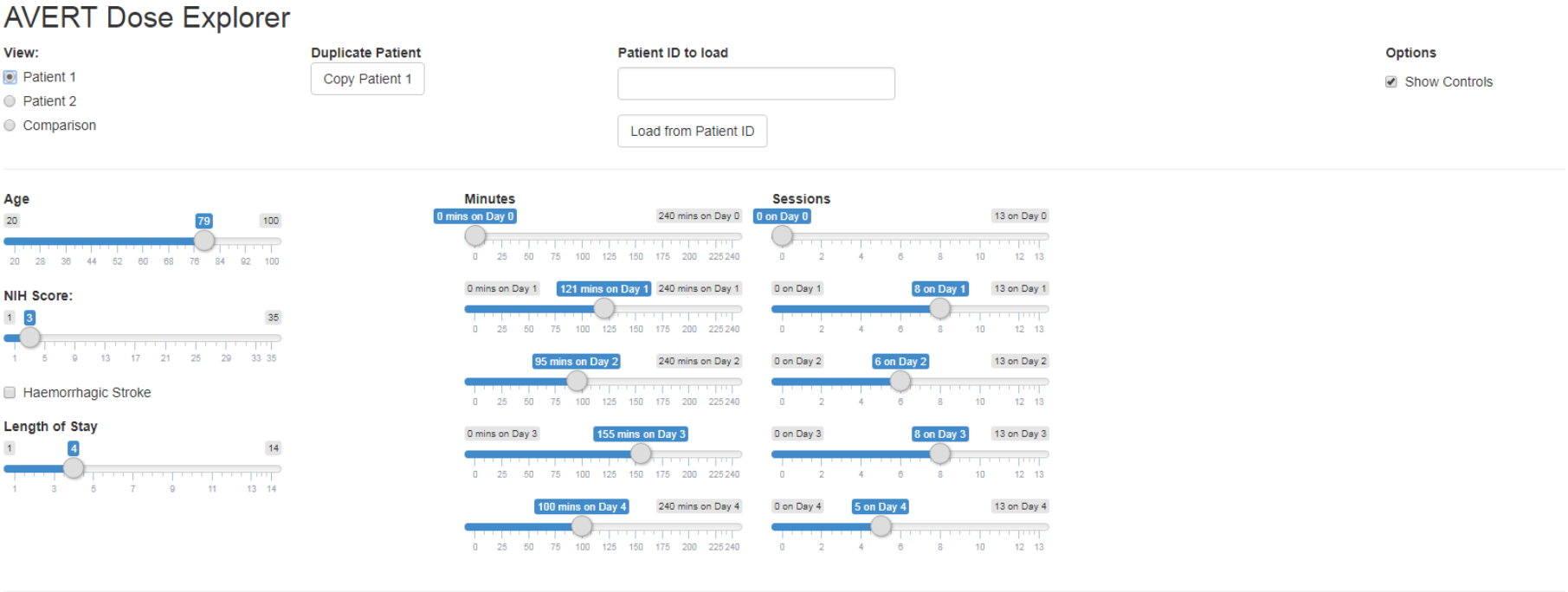


Figure 6.3: Controls for predictive model

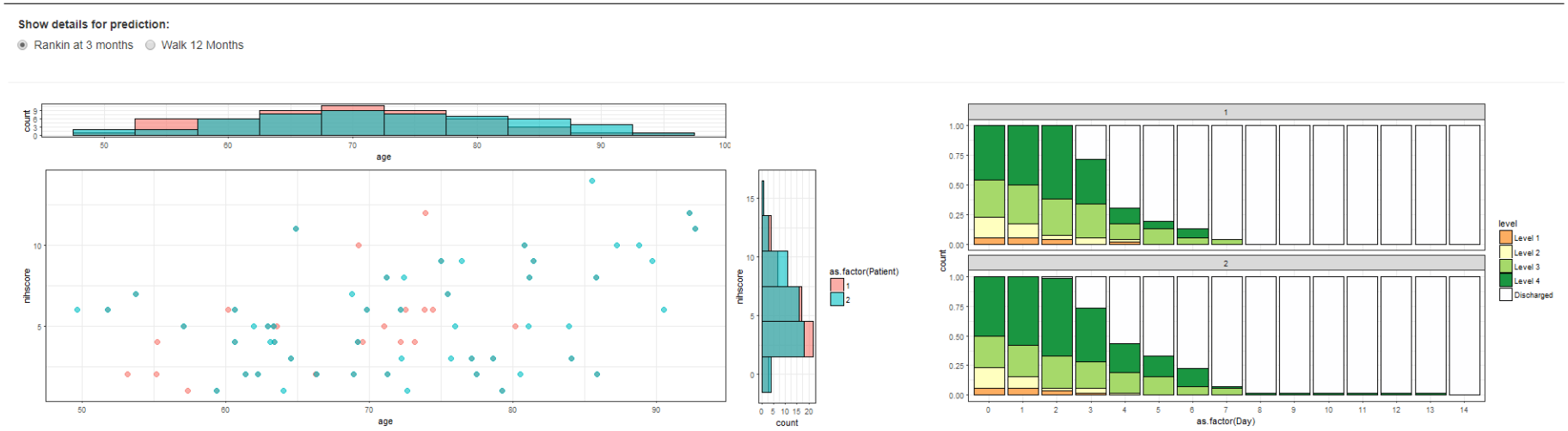


Figure 6.4: Summary of records used to make prediction

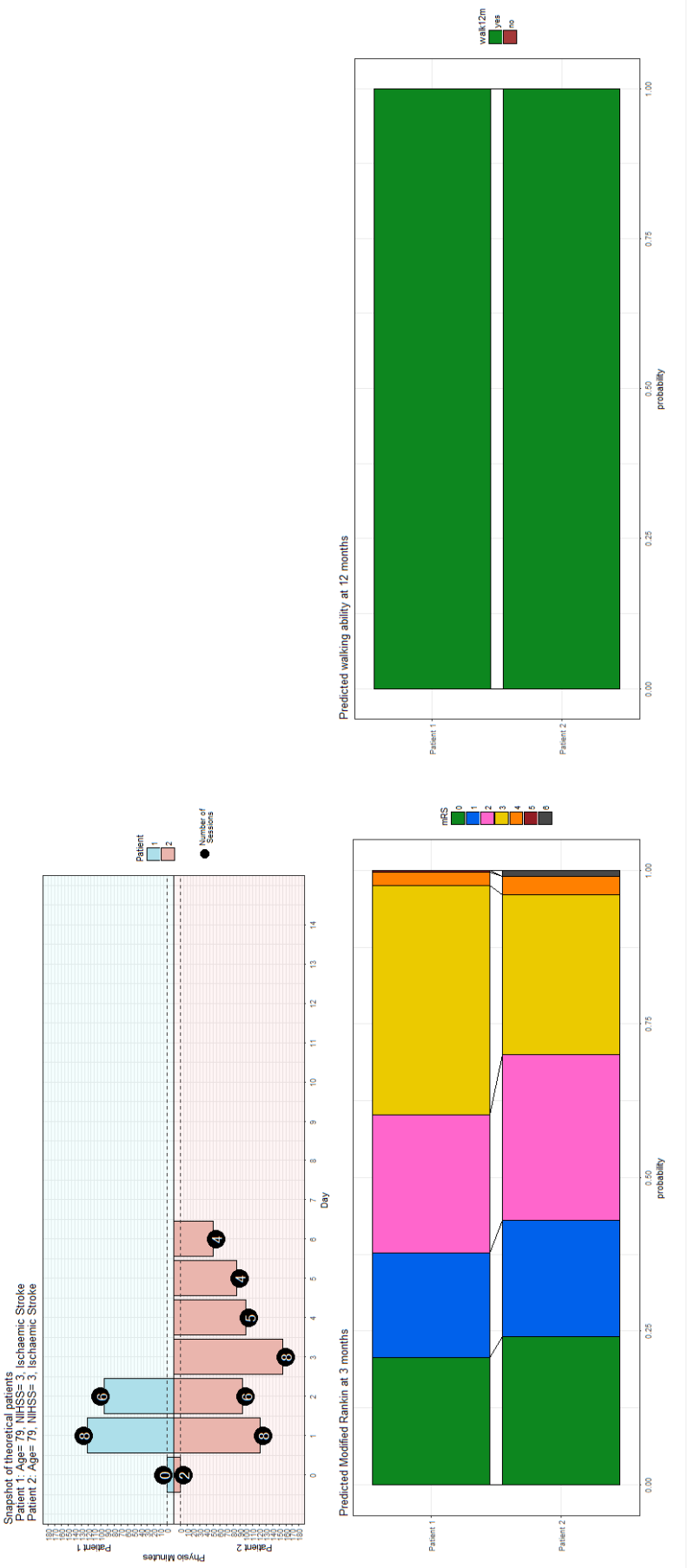


Figure 6.5: Prediction made by weighted k nearest neighbours

6.4 Validation

This section discusses validation of the *visual systems model* presented in this chapter, and of the *Visual Systems Modelling Framework* which was used to develop the model.

6.4.1 Face Validity

This model was validated through discussions with domain experts at the Florey Institute of Neuroscience and Mental Health. The AVERT Dose Explorer addresses deficiencies in AVERT Atlas by allowing model users to predict patient outcomes based on specified therapy doses, thus fulfilling its purpose as a model for *Investigation and Improvement*. For convenience and ease of use, the AVERT Dose Explorer has since been bundled with the AVERT Atlas (discussed in Chapter 5), allowing seamless swapping between these two models.

6.4.2 Framework Validity

The validity of the *Visual Systems Modelling Framework* as applied to this case study was established by systematically evaluating whether the pre-specified desirable properties (summarised in Section 6.2.4) were achieved in the developed model. As all of these properties were met by the developed *visual systems model* (summarised by Table 6.4), the *Visual Systems Modelling Framework* was useful in the development of the model described by this chapter.

Table 6.4: Desirable properties of model arising from this framework

		Visualisation Principles			
Conventional OR/MS Tools		**Principle 1:** Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Patient Baseline Characteristics	Weighted k-nearest neighbours		Show information about records used to make predictions (**Visualisation Practices 3 and 5**)		Show detailed breakdown of predictions and reasoning in a way that allows the user to visually navigate the system
Dose-Response Behaviour		Allow user to pull up greater detail on the records used to generate predictions (**Visualisation Practice 3**)			
Clinical Outcomes					

6.5 Discussion

The case study presented in this chapter demonstrated how the *Visual Systems Modelling Framework* could be applied to predict the likely outcomes of stroke survivors resulting from physiotherapy.

This case study demonstrated how the *Visual Systems Modelling Framework* can be used in a process system where the *Modelling Purpose* (Research Question 2) is *Epistemic Representative* in nature, and the model seeks to *Investigate and Improve*. In comparison to the application discussed in Chapter 5, the further focus on specific *System Features* resulted in a conceptual model simple enough that conventional OR/MS tools were able to capture the majority of the *features* contained within it. The decision to represent most *System Features* through the use of conventional OR/MS tools was accommodated by the *Visual Systems Modelling Framework*, with the outputs of the applied predictive model being visually represented, as opposed to representing these components directly.

By using visualisation to interpret and provide access to the outputs of this conventional OR/MS model (Research Question 3(a)), this application of the *Visual Systems Modelling Framework* illustrates how visualisation can be used to augment conventional OR/MS tools by providing access to model outputs in the context of additional contextual information (in this application, the day-to-day changes in patient health which was not included in the conventional OR/MS tool). This approach to integrating visualisation and conventional OR/MS tools can be considered *visualisation-driven analysis*, as visualisation is primarily used to interact with a conventional OR/MS tool. Where previous OR/MS literature discussed visualisation, it has typically been applied in a similar fashion to that used here (discussed in Section 2.2.3). This chapter therefore demonstrates how this typical approach to the integration of visualisation and conventional OR/MS tools can be accommodated by the *Visual Systems Modelling Framework*.

The *visualisation-driven analysis* approach taken in this application provided transparency for the conventional OR/MS tool contained within the *visual systems model*, assisting in model validation (Research Question 3(b)). The provided transparency improved upon the numerical validation discussed in Section 6.3.2, as not only was the predictive model's average accuracy evaluated, but the logic behind every prediction was made available and interpretable. This means that if the predictive model's internal logic

appears to be inaccurate when compared to the domain knowledge of decision-makers, potentially faulty predicted patient outcomes can be immediately identified as not trustworthy. However, this transparency was possible because k-nearest neighbours provides a list of "similar" cases as part of how it makes its prediction. Had a more abstracted tool (such as linear regression, CART or more sophisticated machine learning approaches) been used instead which did not supply a similar level of simplicity and transparency in how it makes predictions, the additional model validation provided by visualisation may not have been as significant. This result should therefore be understood in the context of the specific conventional OR/MS tool that was used in this application.

A major strength of the implementation of the *visual systems model* discussed in this chapter is that it was developed with the same tools as the AVERT Atlas. Not only did this mean that the *visual systems model* discussed in this chapter can be shared and upgraded with ease, but it also facilitated the use of it in conjunction with the Atlas. The AVERT Dose Explorer can be considered a *visual systems model* which extends the capabilities of the AVERT Atlas. Additionally, reduced the time of model development required, as this model can use the AVERT Atlas to provide patient-level access to the records which are used in a given prediction. This meant that it was sufficient to provide a means for the AVERT Dose Explorer to pass a list of patient records to display to the AVERT Atlas, rather than having to provide this level of systems visualisation itself.

6.6 Conclusion

This chapter presented an application of the *Visual Systems Modelling Framework* to predict patient outcomes based on a given physiotherapy regimen. The case study demonstrated how *visual systems modelling* can be used as an *Epistemic Representative* model for *Investigation and Improvement*, thus addressing Research Question 2. It also demonstrated how visualisation can be integrated with conventional OR/MS tools to provide *visualisation-driven analysis*, thus addressing Research Question 3(a). Additionally, this case study addresses Research Question 3(b) by demonstrating how visualisation can provide additional validation of conventional OR/MS tools beyond that which is offered by analytical validation methods.

Chapter 7

Covariate-Adjusted Response Adaptive Clinical Trial Designs for Stroke Rehabilitation

7.1 Introduction

This chapter discusses the final case study contained within this thesis. Section 7.2 provides an overview of Randomised Controlled Trials and Adaptive Clinical Trial Designs, with Section 7.3 demonstrating how adaptive clinical trial designs can be represented as a process system. Section 7.4 then applies the *Visual Systems Modelling Framework* to this system, before both the model and the use of the framework is validated in Section 7.6. Finally, Section 7.7 discusses the implications arising from failures in validation identified in Section 7.6.

7.2 Randomised Controlled Trials Context

Randomised Controlled Trials (RCTs) are "comparative studies with an intervention group and a control group; the assignment of the subject to a group is determined by the formal procedure of randomization" Friedman, Furberg, and DeMets (2010, p. 69). RCTs are used to draw conclusions about the relative effects that a particular set of treatments have on a broader population of patients, and are considered the "gold standard" in med-

ical research (Concato, Shah, and Horwitz, 2000, p. 1887) as it reduces potential sources of bias in eventual results and accommodates frequentist approaches to statistical inference by allowing researchers to calculate the probability distribution of the differences in patient outcomes, assuming that each treatment effect is equally effective (Friedman, Furberg, and DeMets, 2010). RCTs are therefore widely used to conduct research which incrementally improves the quality of care given to patients across the health care system.

RCTs, like all clinical trials, are "messy", and "constrained by fiscal and human resources, ethical concern for the participants, and the current scientific and political milieu" (Piantadosi, 2005, p. 21). In addition to statistical considerations (e.g. ensuring that patient covariates do not bias trial results, and ensuring that the trial can reliably identify superior treatments), the ethics of randomly assigning patients to experimental treatments are complicated, as some of these patients will receive an inferior treatment (Weinstein, 1974).

These concerns have lead to the development of a family of clinical trials designs known as *adaptive clinical trials*, a variety of procedures which use information gathered during a trial to modify properties of the trial before it has finished. These procedures include a variety of approaches, including conducting a trial in multiple stages, adjusting planned sample sizes to ensure appropriate statistical power, and methods which alter the way in which patients are randomised to experimental arms.

This section discusses two types of adaptive trial design (Multi-Stage trial designs vs Adaptive Allocation Rules), as well as AVERT-DOSE, a new adaptive clinical trial which includes both multi-arm multi-stage and adaptive allocation rules in its design.

7.2.1 Multi-Stage Trial Designs

Multi-stage trial designs are a class of adaptive trial designs where at a prespecified point prior to trial completion an *interim* analysis is performed and a number of decisions about the trial may be made. Such decisions can include rules for stopping a trial early (used in Group Sequential Designs, see Pocock (1977)), and can also include *sample size re-estimation* techniques, which uses currently observed trial data to predict if the trial will achieve sufficient statistical power by the time it completes, increasing sample size if this is not the case (Mehta and Pocock, 2010). This process improves the likelihood of

a trial being successful in identifying new treatments, and has seen adoption in clinical trials investigating the treatment of sleep apnea (Costanzo et al., 2015), hypogycemia (Bergenstal et al., 2013), and stroke (Campbell et al., 2013).

Where there are more than two treatments being compared, another example of clinical trial designs which include interim decisions are *Multi-Arm Multi-Stage (MAMS)* trial designs. MAMS trial designs are considered to be seamless phase II/III clinical trial designs (Kunz et al., 2015), as they combine attributes of a trial intended to test the efficacy of experimental treatments (The role of a phase II trial (Friedman, Furberg, and DeMets, 2010)) and a trial indented to provide strong, confirmatory evidence of effecacy and safety for promising treatments (The role of a Phase III (Friedman, Furberg, and DeMets, 2010)) trial. This occurs through a two-stage process which first explores several possible treatments to identify those which are promising (Phase II), then seek to confirm that those promising treatments are beneficial (Phase III). MAMS trial designs achieve this by first assigning patients to multiple treatment arms during exploration, then performing an interim analysis to select the treatment arm(s) which appears to be the most promising. The trial then continues, comparing only the control and selected arm (Wason and Jaki, 2012). MAMS trial designs allow for multiple potential treatments to be tested at once in a manner which minimises the amount of investment required for each treatment, both financially and in terms of the number of patients given ineffective treatments. This has lead to adoption of these designs in areas such as ovarian cancer (Royston, Parmar, and Qian, 2003), prostate cancer (Sydes et al., 2009), and stroke (Jaki and Wason, 2018).

7.2.2 Adaptive Allocation Rules

In contrast to the interim analysis approach taken by Multi-Stage designs, Adaptive Allocation Rules introduce adaptivity to clinical trials by continually adjusting a trial's properties based on data as it is collected. This includes a variety of techniques which alter the probability of assigning a patient to a given treatment arm based on information such as the current balance of patient covatiates or the observed patient responses to each treatment.

Methods of randomisation based on patient covariates are referred to as *Covariate*

Adjusted (CA) randomisation. As a patient's health is driven by a number of prognostic factors (or covariates) other than their received treatment, it is important that the effect of these on the results of a trial are minimised (Lin, Zhu, and Su, 2015). CA methods seek to ensure that important patient covariates which can impact the effectiveness of a treatment are balanced across treatment arms by dynamically adjusting the probability of being assigned to each experimental arm to favour treatments which have relatively few patients in common with the patient that is being assigned (Shao, Yu, and Zhong, 2010). This encourages covariates to be balanced across treatment arms, reducing the potential for bias resulting from differences among patients. CA randomisation methods have been adopted in areas such as hypertension (Hansson et al., 1998), breast cancer (Romond et al., 2005), glucose control in critically ill patients (Investigators, 2009), and stroke (MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group and others, 2004).

Likewise, methods of randomisation based on observed responses to experimental treatments are referred to as *Response Adaptive (RA)* randomisation. By design, RCTs involve assigning trial participants to different treatments to enable a comparative analysis of those treatments to take place. Allocation of patients to experimental treatments presents ethical challenges, as this results in a number of patients receiving a suboptimal treatment (Weinstein, 1974). RA methods were developed in response to this ethical concern, and seek to maximise the number of patients in a clinical trial which receive the best treatment. This is achieved by dynamically changing the probability of being assigned to each experimental arm to favour treatments which, according to current observations, appear superior (Hu and Rosenberger, 2006). This has the effect of allocating more patients to better treatments, thus addressing this ethical challenge. However, there has been little adoption of them in practice (Thall and Wathen, 2007). Numerous sources (Rosenberger and Lachin, 1993; Hu and Rosenberger, 2006; Friedman, Furberg, and DeMets, 2010; Altman, 1991; Rosenberger, Sverdlov, and Hu, 2012) have at least partially attributed this lack of enthusiasm among clinical researchers to experiences with what they refer to as "the ECMO trial" (Bartlett et al., 1985), a failed clinical trial which faced significant criticism for using unconventional statistical tests and an extremely small sample size, with only one patient being assigned to the control group (Rosenberger, 1999). However, RA trial designs have seen a resurgence in interest in recent years, with the approach

adopted in areas such as the treatment of metastatic sarcoma (Maki et al., 2007) and breast cancer (Rugo et al., 2016), and have been suggested for use in spinal cord injury research (Tator, 2006).

CA and RA approaches to randomisation have been combined to create *Covariate-Adjusted Response-Adaptive* (CARA or RACA) trial designs. These trial designs seek to fulfil both the objectives of RA and CA randomisation by assigning trial participants to experimental arms in a manner which ensures covariate balance across arms whilst also sending patients to treatments that, on current trial trends, are more likely to lead to better patient outcomes (Rosenberger and Sverdlov, 2008). CARA designs are still relatively novel (Rosenberger, Sverdlov, and Hu, 2012), and the design of such trials is an active research area. As such, there are comparatively few examples of their adoption by clinical researchers (Zhao and Durkalski, 2014). Two studies give examples of the use of these methods, both in Stroke. The SHINE trial (Bruno et al., 2014) is an ongoing trial investigating the effect of glucose control on patients with ischaemic stroke, and the AVERT-DOSE trial (Bernhardt et al., 2016a) is a planned trial investigating the effect of physiotherapy post-stroke.

7.2.3 AVERT-DOSE

The A Very Early Rehabilitation Trial – Determining Optimal early rehabilitation after StrokE (AVERT-DOSE) clinical trial (Bernhardt et al., 2016a) is an upcoming prospective clinical trial which combines Multi-Arm Multi-Stage, Covariate Adjustment and Response Adaptation (MAMS-CARA) trial design. This trial seeks to identify beneficial physiotherapy regimens for the treatment of ischaemic stroke from a set of four treatments (three experimental treatments compared to one low-activity control), then confirm the efficacy of the identified regimen. Due to the number of adaptive behaviours within a MAMS-CARA trial design, careful planning is required to ensure the trial behaves as intended.

7.3 MAMS-CARA Trial designs as a Process System

MAMS-CARA clinical trials meet all the criteria to be considered a process under Davenport (1993, p. 5)'s definition:

Inputs The primary inputs in this system are patients who enter the trial (including important covariates likely to influence their clinical outcomes), and the specific rules governing the behaviour of the MAMS-CARA design (e.g. strength of adaptations in randomisation and the timing of interim analysis).

System Components Patients receive therapy and are discharged from the system, and information regarding their treatment is fed into the rules governing the behaviour of the trial as it progresses.

Outputs This system outputs patients with clinical outcomes resulting from their treatment, and generates scientific results (trial outcomes) which can be used to improve patient care.

Likewise, it meets all the criteria to be considered a system under Daellenbach (1994, p. 27):

1. A system is an organised assembly of components. 'Organised' means that there exist special relationships between these components. As a MAMS-CARA trial, AVERT-DOSE has two major components: Trial Participants, and Trial Properties. Patients enter the trial, and are randomised based on rules set out by Trial Behaviour. In turn, the Trial Behaviour changes over time according to observations made about Trial Participants. The relationship between these two components drives the behaviour of the MAMS-CARA design.

2. The system does something, i.e., it exhibits a type of behaviour unique to the system. As an RCT, AVERT-DOSE administers experimental treatments to patients with the intention of evaluating the effects of those treatments in a controlled manner that minimises possible sources of bias. This behaviour is unique to RCTs and has lead to them being the "gold standard" in experiment design.

3. Each component contributes to the behaviour of the system and is affected by being in the system. No component has an independent effect on the system. The behaviour of the system is changed if any component is removed or leaves. Trial Participants are essential to RCTs such as AVERT-DOSE and cannot run without them. Additionally, removing the adaptive behaviours of the trial from the system would turn AVERT-DOSE from a MAMS-CARA trial into a conventional RCT.

4. Groups of components within the system may themselves have properties 1, 2, and 3. i.e., they may form subsystems. A patient's health can be considered to be a subsystem, as discussed in Sections 4.3 and 5.3

5. The system has an outside - an environment - which provides inputs to the system and receives outputs from the system. The environment of AVERT-DOSE consists of both the general population of people who can experience ischaemic stroke and clinical researchers investigating better ways to rehabilitate stroke survivors. Patients enter this system, receive treatment, and leave the system with a certain health state. Upon conclusion of the trial, it also provides new knowledge to clinical researchers on the effects of physiotherapy in stroke rehabilitation.

6. The system has been identified by someone as of special interest. The AVERT clinical trial has left many unanswered questions regarding the appropriate role of physiotherapy in stroke rehabilitation. Answering those questions in AVERT-DOSE will lead to improved outcomes for stroke survivors, meaning that this trial is of interest to neurorehabilitative physiotherapists, clinical researchers and stroke survivors alike. However, the complexity of the chosen MAMS-CARA trial design requires careful planning and communication, and a proper investigation of the expected behaviours of the clinical trial.

7.4 Application of Visual Systems Modelling Framework

This section applies the systems visualisation framework to modelling supporting planning for AVERT-DOSE.

The Conceptual Model and Model Purpose presented in this section were developed with clinical researchers at The Florey Instituite of Neuroscience and Mental Health.

7.4.1 Conceptual Model

As discussed above, MAMS-CARA trials can be understood as a process system, meaning that aspects of the system can be considered in terms of Inputs, Work Activities, and Outputs. In this system, the two main types of system components are Trial Participants and Trial Properties. This system conceptualisation is summarised in Table 7.1

Table 7.1: Summary of Conceptual Model

	Trial Participants	Trial Properties
Inputs	Patient Characteristics	Trial Rules
Work Activities	Patient Treatment	Trial Behaviour
Outputs	Clinical Outcomes	Trial Outcomes

The *systems features* arising from this conceptual model are as follows:

Patient Characteristics Each patient has specific characteristics (covariates or prognostic factors) which will influence their response to treatment. In this system, these are assumed to be stroke severity, age, geographic region and the type of treatment received during the acute phase of stroke care.

Trial Rules Trial rules governs the specific rules designed to control the trial. This includes all parameters governing things such as the sensitivity of adaptive allocation rules and the timing of interim analysis. Changing these rules will change the behaviour of the trial.

Patient Treatment The treatment that an individual patient receives is dependent on the experimental arm that the patient is randomised to in the trial. This is influenced by the rules governing the MAMS-CARA trial design, and the state of the trial at the time of randomisation.

Trial Behaviour As the trial progresses, the probability of new patients being assigned to treatment arms changes in response to current data. This changes the behaviour of the trial over time.

Clinical Outcomes Patients ultimately have some clinical outcome after receiving an experimental treatment. In this system, this outcome is trichotomised to only consider good outcomes (mRS 0-2), poor outcomes (mRS 3-5) and death (mRS 6). The aim of response adaptive randomisation is to maximise the number of patients who receive beneficial treatments, and minimise the number of patients who receive harmful treatments.

Trial Outcomes The primary aim of an RCT is to gather strong evidence to better inform the treatment of patients within the health care system. In a MAMS trial design, trial outcomes are multifaceted, as the trial outcome is a function of not only seeing a significant difference in treatments, but also of which treatment arm was selected at interim analysis.

7.4.2 Model Purpose

The complex nature of the MAMS-CARA trial design, combined with the fact that there are very few examples of this design approach being used in real-world trials, presents two purposes which must both be achieved to support the implementation of the clincial trial design. The models described within this chapter are designed to work in tandem with one another to address these two purposes.

The first of these purposes is to communicate the concepts used in the trial to clinical researchers who are unfamiliar with MAMS-CARA trial designs. It is important that clinicians involved in the trial understand how adaptive properties of the trial interact with one another. This process is *Technical Boundary* in nature, as it intends to transfer existing knowledge from one person to another.

The second of these purposes is to examine the expected behaviour of AVERT-DOSE given a set of assumptions and trial rules, to assist planning of the trial. It is important that the specific trial rules are selected so that the trial behaves in a desired manner. This process is *Technical Representative*, as the effects that different trial rules have on the trial's behaviour is largely understood. This second model is intended to calculate the value of important trial properties, such as statistical power, at different settings.

As this model is intended for repeated, routine use either as a communication aide, examining expected behaviours or both, this model as a combined entity can be considered a tool for *Routine Decision Support*.

7.4.3 Conventional OR/MS Tools

The dual model purpose outlined above can be addressed by modelling this trial with Discrete Event Simulation, a conventional OR/MS tool that has seen widespread application in the modelling health systems (Günal and Pidd, 2010), including modelling of clinical trial designs in oncology (Skolnik et al., 2008). The following mechanisms are used to control adaptive randomisation within this system:

7.4.3.1 Covariate-Adjusted Randomisation Rules

Covariate Adjusted (CA) randomisation balances the spread of important patient covariates (in AVERT-DOSE, this includes Patient Age, Geographic Locations and Acute Treatment) across each arm. CA randomisation in this trial follows the method set out by Pocock and Simon (1975). This approach uses binned categories of each covariate (Age: < 65, $65 - 80$, > 80; Geographic Location: AUS/NZ, Asia, Europe; Acute Treatment: tPA, Endovascular Clot Retrieval (ECR); Both tPA and ECR; neither of tPA or ECRs), and seeks to minimise the amount of imbalance in each covariate bin across experimental arms.

For each covariate i, this method calculates the prospective imbalance $d_{i(k)}$ that would be introduced to the trial in covariate i if a patient was assigned to arm k. This is measured by calculating the standard deviation of the count of patients assigned to each arm across each bin of covariate i, assuming a patient were to be assinged to treatment k.

If then calculates a weighted sum $G_{(k)} = \sum_{i=1}^{M} w_i d_{i(k)}$ of these imbalances across each covariate i, giving the total imbalance if a patient were to be assigned to arm k. Each weight w_i represents the relative importance of each covariate.

The CA randomisation probability is then equal to:

$$p_{CA(k)} = \frac{1}{N-t}\left[1 - \frac{tG_k}{\sum_{\forall j} G_{(j)}}\right] \text{ for } k = 1, \ldots, N \tag{7.1}$$

where t is a constant between 0 and 1. This value controls the sensitivity of CA randomisation component of the trial rules.

7.4.3.2 Response-Adaptive Randomisation Rules

Response Adjusted (RA) randomisation favours the assignment of trial participants to treatments which appear effective. RA randomisation in this trial uses an Urn Model (Wei and Lachin, 1988). Under this model, patients are randomised by randomly sampling balls from an urn (with replacement), with the type of ball representing a given treatment. Upon observing a patient's clinical outcome, if it is a positive outcome (in AVERT-DOSE, mRS between 0 and 2), a number of balls are added to the urn of the that type). If it is a severely negative outcome (in AVERT-DOSE, mRS of 6), a number of balls of that type are removed from the urn. At the start of the trial, all treatment arms begin with an equal number of balls, representing an equal chance of being assigned to each arm (no information about which treatments are superior). The number of initial balls controls the overall sensitivity of response adaptation, while the relative number of balls added or removed upon observing outcomes controls the strength of response adaptation in each direction.

In AVERT-DOSE, RA randomisation is only run on experimental arms until interim analysis, with the probability of randomisation to the control arm fixed at 0.25 and each of the experimental arm RA probabilities rescaled by a factor of 0.75 (the current observed outcomes in the control arm are ignored at this point, meaning RA adaptation only compares experimental treatment to experimental treatment). After interim analysis, the RA probability of control arm assignment varies with the urn model.

7.4.3.3 Covariate-adjusted Response-adaptive randomisation

There are many possible ways to combine CA and RA randomisation. In AVERT-DOSE, this is achieved following a generalised version of the method set out by Ning and Huang (2010), which they term a CARA design. Under their approach, a two-arm CARA design assigns patients to arm A with probability

$$p_{A,RACA} = \frac{p_{A,RA} \cdot p_{A,CA}}{p_{A,RA} \cdot p_{A,CA} + (1 - p_{A,RA})(1 - p_{A,CA})} \tag{7.2}$$

As in a two-arm design, the adaptive probabilities of being assigned to arm B are $p_{B,RA} = 1 - p_{A,RA}$ and $p_{B,CA} = 1 - p_{A,CA}$, this can be rewritten as

$$p_{A,RACA} = \frac{p_{A,RA} \cdot p_{A,CA}}{p_{A,RA} \cdot p_{A,CA} + p_{B,RA} \cdot p_{B,CA}} \tag{7.3}$$

for a number of treatment arms $N > 2$, this can then be generalised to give the final probability $p_{(k)}$ of being assigned to treatment arm k as:

$$p_{(k)} = \frac{p_{CA(k)} \cdot p_{RA(k)}}{\sum_{j=1}^{N} p_{CA(j)} \cdot p_{RA(j)}} \tag{7.4}$$

7.4.4 Model Design

The dual model purpose in this application is handled separately by separating them into two models which are intended to be used together, with these models developed in parallel to complement each other. One of these models, termed the communication model, focuses on communicating trial concepts to clinicians. It places emphasis on intuitive visual representation of the MAMS-CARA trial design, using animation to demonstrate and explore the dynamic behaviour of the trial. The desirable properties arising from the use of the systems visualisation framework in this model are outlined in Table 7.2.

The second model, termed the calculation model, focuses on calculating aggregate information of the trial to explore the expected results and properties of the trial based on a given set of rules. This is achieved by rapidly simulating the trial many ($> 20,000$)

times and calculating aggregate values such as the proportion of times the trial resulted in a significant outcome (statistical power), or the distribution of sample size in each trial arm. This can be repeated over many different settings of trial rules to identify the optimal choice of rules. Additionally, this model can run a small number of simulations with different settings in order to examine the dynamic behaviours of the trial (e.g. adaptive arm assignment probabilities) resulting from changes to assumptions or trial rules. The calculation model does not use visualisation, instead generating detailed logs of the simulation which can then be visualised to understand the results.

The desirable properties arising from the use of the systems visualisation framework in this model are outlined in Table 7.3.

These two models complement each other to aid planning and development of AVERT-DOSE.

Table 7.2: Desirable properties of visual model arising from this framework

	Conventional OR/MS Tools	Visualisation Principles			
		Principle 1: Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Patient Baseline Information	MAMS-CARA methods modelled using Discrete Event Simulation	Model provides detailed view of changing system dynamics, complimenting the calculation model	Use shape/colour in animation to identify patient types		Animation should be simple and require no navigation to see the full model
Trial Rules					
Patient Treatment			Display each individual patient's treatment assignment in animation	Use animation to show how patients are directed to different treatment arms as the trial progresses	
Trial Behaviour			Show breakdown of covariate balance and responses in each arm. Show probability of assignment to each treatment	Animate breakdown of adaptation logic, showing change over time	
Clinical Outcomes			Show individual patient outcomes. Show running tally of observed clinical outcomes in each group	Show clinical outcomes in animation as they are observed	

Table 7.3: Desirable properties of calculation model arising from this framework

		Visualisation Principles			
Conventional OR/MS Tools		**Principle 1:** Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Patient Baseline Information	MAMS-CARA methods modelled using Discrete Event Simulation	Provides access to aggregate-level behaviour as well as trial-level behaviour, complimenting the communication model.	Provide access to model outputs for external visualisation	Provide access to model outputs for external visualisation	Provide access to model outputs for external visualisation
Trial Rules					
Patient Treatment					
Trial Behaviour					
Clinical Outcomes					
Trial Outcomes					

7.5 Developed Model

Unlike the the case studies discussed in Chapters 4, 5 and 6, the model developed in this case study did not rely on data, beyond in the development of assumptions regarding treatment and covariate effects. This section describes the model which was developed using the *Visual Systems Modelling Framework*. Section 7.5.1 describes the application of the conventional OR/MS tools discussed in Section 7.4.3. Section 7.5.2 describes the specific visualisation methods which were used in this case study to represent each systems feature. Finally, Section 7.5.3 describes the fully developed model itself.

7.5.1 Analytical Methods

Both of the models used in this case study used Discrete Event Simulation, though their implementations were very different. In both cases, they used the adaptive trial mechanisms described in Section 7.4.3

The communication model was developed in Anylogic 7 (The Anylogic Company, 2015), taking advantage of its ability to animate simulation models. As this model was intended for communication and was not required to accurately present the system, there was no need for this model to incorporate realistic assumptions. The number of patient covariates was limited to two, and there was no limit placed on the number of patients which could be recruited into the trial.

In contrast, the calculation model was developed in C++ and R (R Core Team, 2017), and was validated through experimentation with the model to confirm that it behaved as expected under different assumptions and settings. This model was designed to incorporate realistic assumptions, and was built to allow a user to supply however many covariates they desired, with a given simulation of the trial concluding upon reaching a prespecified number of patients.

7.5.2 Visual Components of Model

The communication model visualises the system through the use of an animated representation of a discrete event model, visualising the clinical trial as a process where each treatment arm corresponds to a separate work activity. This provides a means for the

trial behaviours to be easily understood.

As discussed in Section 7.4.4, the calculation model simply provides data containing the outputs of the simulation, and leaves it to the user to analyse or visualise these results as they see fit.

The approach taken to visualisation by these two models is summarised in Table 7.4

Table 7.4: Visualisation Components

	Communication Model	Calculation Model
Patient Baseline Information	changing the shape and colour of patients as they move through the system	Provide simulation outputs and visualise using conventional data visualisation methods
Trial Rules		
Patient Treatment	Assigned treatment arm shown in animation	
Trial Behaviour	Shown through animation of trial and graphs showing covariate and outcome balance, as well as response-adaptive probability	
Clinical Outcomes	Shown by a smiley face on each patient entity	
Trial Outcomes		

7.5.3 Visual Systems Model

The *visual systems model* developed for communicating the dynamic behaviour of adaptive clinical trials provided a method to communicate and explain concepts in the trial to clinical researchers who are unfamiliar with the design.

Unlike the *visual systems models* discussed in Chapters 4, 5 and 6, this communication model presents a complete representation of the system in a single frame (Figure 7.1). Patients enter the system from the left and enter a treatment arm based on adaptive randomisation. The colour and shape of these patients represent covariates related to pa-

tient outcomes, which the *covariate-adjustment* component of the randomisation process will attempt to balance between treatment arms. To the right of the frame, the current covariate balance in each treatment arm is displayed with stacked bar charts. These bar charts update automatically in response to new patients being randomised.

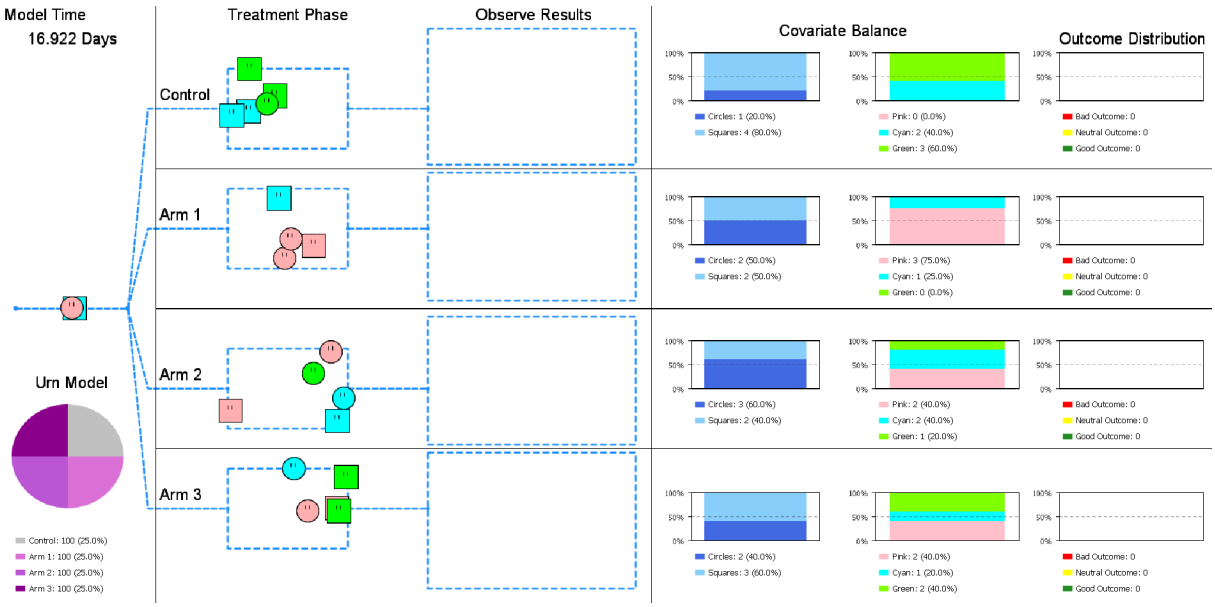


Figure 7.1: Communication Model at Start of Trial

Patients can experience a bad outcome (death) prior to 3 months post-treatment. Such deaths are fed into the adaptive randomisation process as soon as the information becomes available. Figure 7.2 shows the *visual systems model* after a patient has died prior to their 3 month evaluation. This patient has moved from the *Treatment Phase* to *Observe Results*, and their appearance has updated to show a frowning face, indicating a bad outcome. On the far right of the frame, a segmented bar chart has updated to record this negative outcome for this treatment arm.

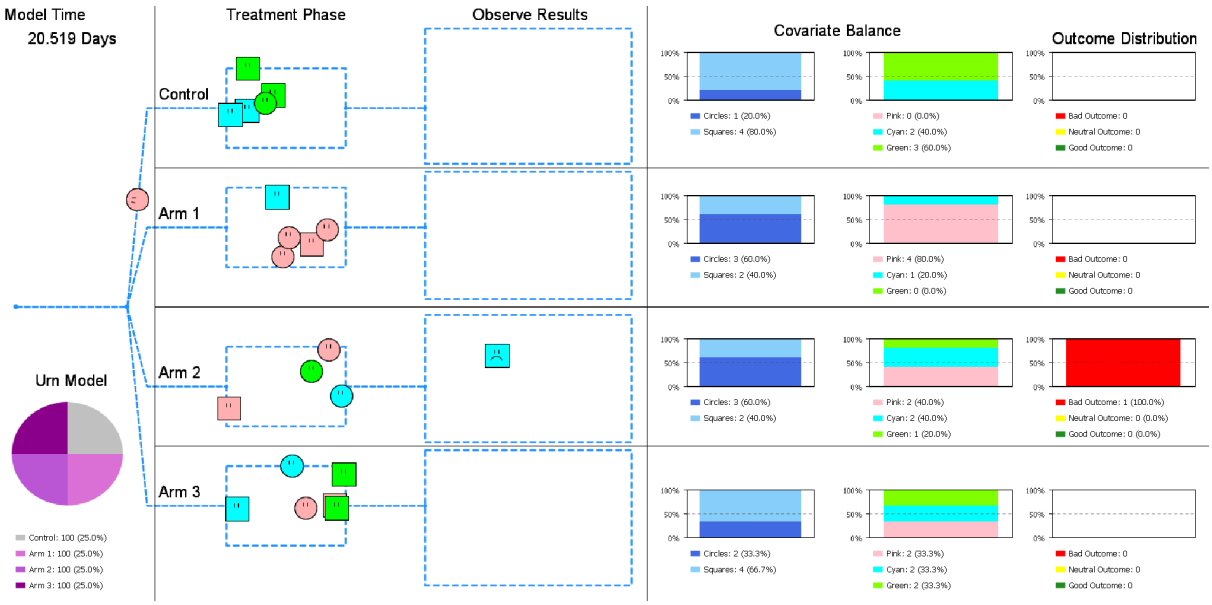


Figure 7.2: Communication Model after first patient outcome

After 3 months have passed, patient outcomes begin to be observed. These patients move to *Observe Results*, with their appearance updating to indicate their outcome (smile for good outcome, neutral for outcome neither good nor bad or frown for a bad outcome). By the time in the trial displayed in Figure 7.3, final patient outcomes have started to be observed. The distribution of outcomes in each arm is shown on the far right, and this information is fed into the *Urn Model*, presented in the bottom left of the frame. This changes over time with the graphs displayed on the right of the frame.

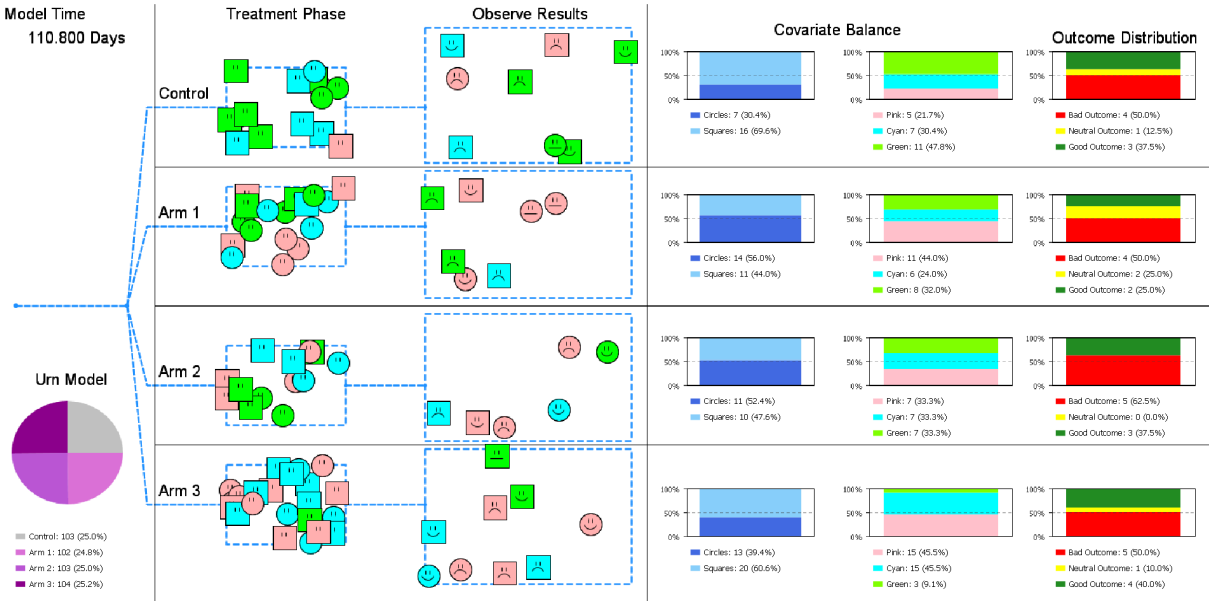


Figure 7.3: Communication Model after 3 month outcomes are observed

As the trial progresses, covariates become increasingly balanced, and the urn model begins to reduce the probability of a patient being assigned to suboptimal treatments (Figure 7.4).

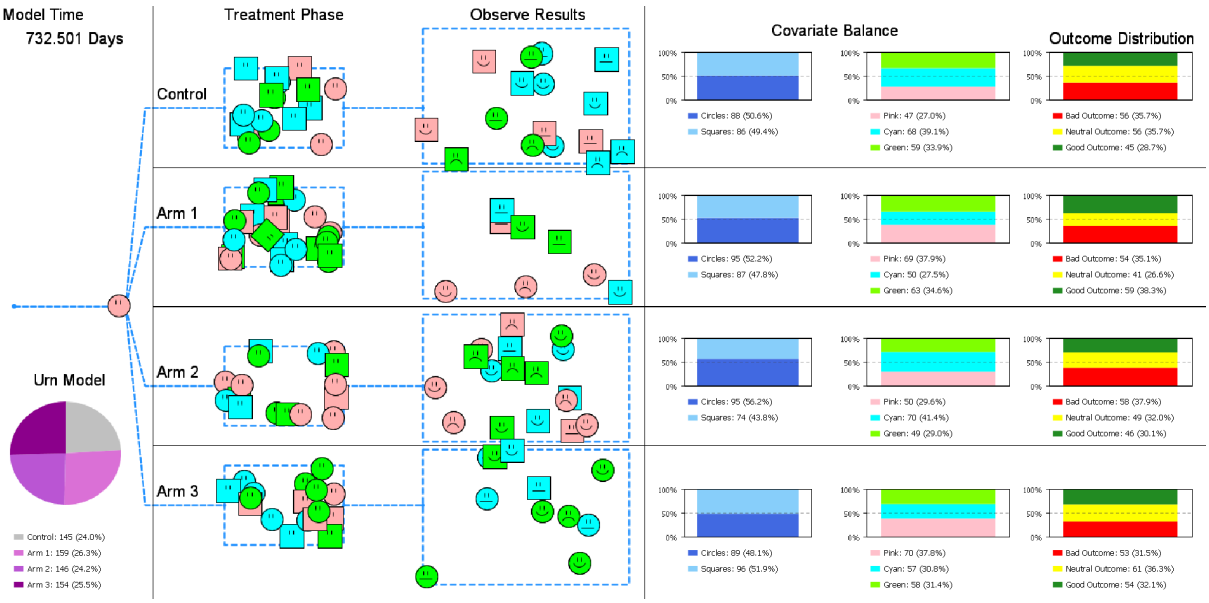


Figure 7.4: Communication Model late in the trial

This *visual systems model* provides an intuitive way for clinical researchers to develop and understanding of the dynamic behaviours of adaptive trial designs. It therefore helps build trust in the unconventional design, which assists the use and acceptance of the *calculation* model.

The *calculation* model provides access to detailed model outputs which were then visualised using the *ggplot2* (Wickham, 2016) in R (R Core Team, 2017) to examine the relationship between trial rules and anticipated results. For example, Figure 7.5 shows results from the calculation model providing trial-level information by illustrating the shift in response-adaptive treatment assignment over time, with each colour representing an arm of the trial. Prior to 90 days, the probability of being assigned to each arm is equal, as there have been no observed trial outcomes. After 90 days, Trial Arm 0 becomes the favoured treatment arm (shown in red), though as the trial progresses the chances of being assigned to this arm become no better than other treatments. At approximately 675 days into the trial, two treatment arms are closed, and the trial continues with Arms 0 and 1

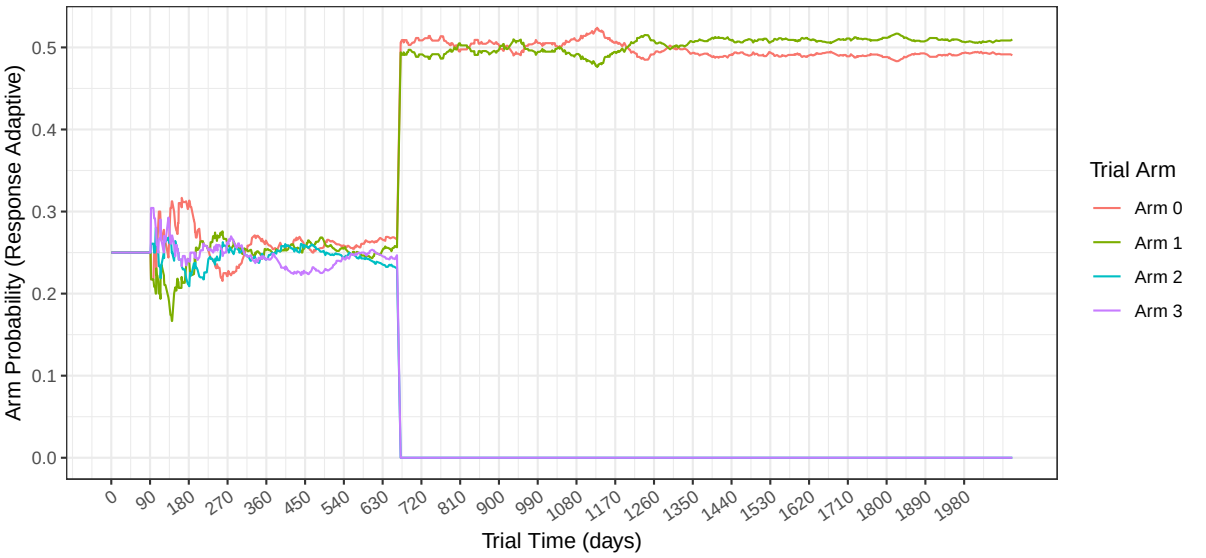


Figure 7.5: Visualisation of dynamic RA probability

This process is repeated to investigate aggregate-level information. For example, Figure 7.6 illustrates how the probability of selecting the best treatment arm changes depending on both the sensitivity of response adaptation and the assumptions made about treatment effects. According to the trial settings and assumptions tested in this demonstration, where one of the four experimental arms is worse than the control arm (shown in green), reducing the strength of response adaptivity improves the probability of selecting the correct treatment arm. This improvement would have to be balanced against the fact that more patients would be assigned to treatment arms that are dropped from the trial, testing many different assumptions about the trial. Such investigation can also be achieved through visualisation of data generated by this model.

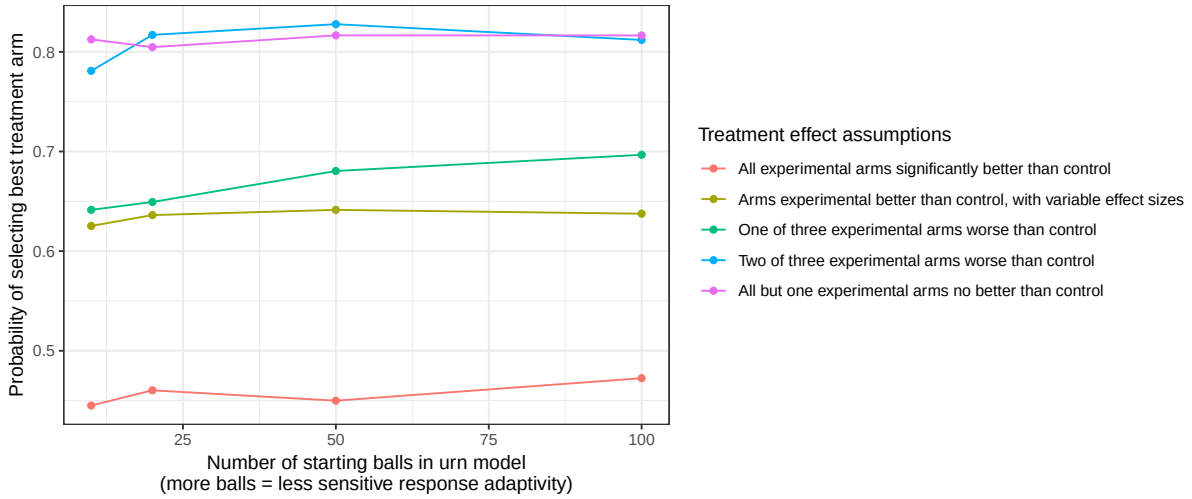


Figure 7.6: Visualisation of the relationship between RA sensitivity and probability of selecting optimal arm, with different assumptions

7.6 Validation

This section discusses the validation of the *visual systems model* presented in this chapter, and the validation of the *Visual Systems Modelling Framework* which was used to develop the model.

7.6.1 Face Validity

The communication model presented in this chapter was validated through practical use, where it was presented to members of the AVERT steering committee (15 members), including a range of clinical and methodological specialists. None had prior experience with MAMS-CARA trial designs. When shown to clinical researchers who did not understand the mechanics of the trial design, it helped to communicate the ideas behind the design to them, and was used throughout planning for AVERT-DOSE as a tool for communication. While the calculation model was validated entirely through computational experiments (face validation was not sought), the use of the communication model improved trust in the calculation model. As such, both models developed in this case study fulfilled their roles. The communication model was able to improve basic understanding of the concepts used within the trial among clinical researchers, which aided the trust in results generated by the calculation model.

7.6.2 Framework Validity

Following the same process used in Chapters 4, 5 and 6, the validity of the *Visual Systems Modelling Framework* to the models developed in this chapter was established by confirming that the developed model matches with the matrix of *desirable properties* developed in Section 7.4.4.

The communication model matched all of the criteria set out in the framework (Table 7.5), suggesting that the use of the *Visual Systems Modelling Framework* was useful in the development of this *visual systems model*.

Visualisation of outputs from the calculation model matched all of the criteria set out in the framework except for *Principle 4* (Visual navigation should be facilitated and made intuitive) (Table 7.5). Instead, navigation though model results was achieved by using conventional data visualisation techniques, with data being filtered and arranged prior to visualisation.

Notably, in both of these models *Visualisation Principle 1* (Users should be able to control what information is shown and level of detail to which it is shown) was achieved by swapping between these models rather than through visual methods. If aggregate or trial-level information was required, this could be attained from the communication model. If patient level information was required, this could be attained from the communication model.

Table 7.5: Desirable properties of visual model arising from this framework

	Conventional OR/MS Tools	Visualisation Principles			
		Principle 1: Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Patient Baseline Information	MAMS-CARA methods modelled using Discrete Event Simulation	Model provided detailed view of changing system behaviours at an individual patient level. This is in contrast to the trial and aggregate level options provided by the calculation model	Patient covariates were represented using shape (square vs circle), and colour(blue vs green vs pink) **(Visualisation Practice 5)**		The full model fitted into a single frame. There was no need for navigation within this model beyond simply looking at different parts of the model.
Trial Rules					
Patient Treatment			Individual patients were visibly sent to different treatment arms, which were represented as separate geographical locations within this model.	Patients persist in the *Observe Results* section of the model for a period of time, giving an indication where most patients are currently being sent **(Visualisation Practice 4)**	
Trial Behaviour			Logic used in CARA randomisation is represented through a series of charts showing current balance and outcomes within the trial	Balance of CARA randomisation factors is animated and changes over time, demonstrating the dynamic nature of trial behaviour **(Visualisation Practice 4)**	
Clinical Outcomes			Clinical outcomes are tallied and shown in the model as they are observed. Individual patient outcomes shown with a "face" on each patient representation **(Visualisation Practice 5)**	Outcome tallies are animated and update overtime **(Visualisation Practice 4)**	

Table 7.6: Desirable properties of calculation model arising from this framework

	Conventional OR/MS Tools	Visualisation Principles			
		Principle 1: Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Patient Baseline Information	MAMS-CARA methods modelled using Discrete Event Simulation	Model outputs provide access to aggregate-level behaviour of model as well as trial-level behaviour. This complements the communication model, which shows patient-level behaviour	In visualisation of aggregate information, colour was used to represent multidimensional data and illustrate the effect of features such as assumptions about treatment effects on the model **(Visualisation Practice 5)**		Visual Navigation not used
Trial Rules					
Patient Treatment					
Trial Behaviour				In visualisation of individual trials, x axis was associated with time to plot dynamic trial behaviour	
Clinical Outcomes					
Trial Outcomes					

7.7 Discussion

The case study in this chapter demonstrated how the *Visual Systems Modelling Framework* can be applied to assist the development of an adaptive clinical trial. This case study demonstrated how the *Visual Systems Modelling Framework* could be applied where the *Modelling Purpose* (Research Question 2) is either *Technical Boundary* or *Technical Representative* in nature, and the model seeks to provide *Routine Decision Support*. This chapter also demonstrated how visualisation could be integrated with conventional OR/MS tools (Research Question 3(a)) by animating the simulation model which was used in the case study or by visualising simulation model outputs.

The approaches to visualisation presented in this chapter are not novel. Visualisation of Discrete-Event Simulation models is a widely-used method of providing interpretability and validation to complex simulation models (as was noted in Section 2.2.3), and the use of data visualisation techniques to interpret data created by simulation is equally well-established. As such, this chapter demonstrates that the *Visual Systems Modelling Framework* can be used for conventional systems modelling applications in addition to less common approaches as discussed in Chapters 4-6.

The use of a parallel modelling approach in this case study raised two implications on the use of the *Visual Systems Modelling Framework*.

First, the design of the communication model impacted the design of both models. By developing a separate model for communication, the need for visualisation in the calculation model was heavily reduced, meaning that it was sufficient to use conventional data visualisation approaches to interpret results from this model. Likewise, with the calculation model to provide detailed and accurate results, the communication model only had to provide understanding, with the overall accuracy of the simulation being irrelevant. This *specialisation* aided model development by minimising the need to consider trade-offs between criteria such as interpretability and speed. Had a single model been developed instead, the requirements for validation and visualisation would have changed, as the model would have been required to fulfil both of the functions of the models developed in this case study. The resulting model would likely have given results different to those discussed in this chapter.

The second implication raised by the use of a parallel modelling approach is that

it presents a philosophical limitation to the results that have been presented regarding the application of the *Visual Systems Modelling Framework*: Given the communication and calculation models were designed and intended to be used together and their developments influenced each other, it could be argued that these two models could be considered an example of *multimethodology*, "i.e. combinations of methods used together" (Munro and Mingers, 2002, p. 374). If these two models are considered component models of a multimethodological modelling approach, it could be argued that the validation of the *Visual Systems Modelling Framework* established in Section 7.6.2 is incomplete, as this validation only considered the two component models individually. However, this argument is dependent on the specific definitions, and interpretation of what is considered a model. Following the definition of a model set out under 1.1 (A model is "an external and explicit representation of part of reality as seen by the people who wish to use that model to understand, to change, to manage and to control that part of reality" (Pidd, 2003, p. 12)), this thesis considers the two models developed in this case study to be separate models, as they relied on different representations of, and assumptions about reality, and were intended for use on a day-to-day basis in separate contexts.

There were two weaknesses in the implementation of the systems models presented in this chapter. First, the systems model for this case study was effectively implemented twice (once for communication and once for calculation), effectively leading to a *duplication of work*. This increased time required for model development and model changes, as development in one model would have to be replicated in the other. Likewise, this duplication would have increased the risk of errors occurring in the model due to repetition in development. In addition to this weakness, like in Chapter 4 the communication model was developed in AnyLogic. While in this case the software was being used for its intended purpose as a simulation platform, it retains the same weaknesses regarding the ability to share or adapt the model. As the communication model was not intended to be an accurate representation of the real world, the ability to edit the model was not necessary, and given the whole model could fit into a single frame, interactivity was not overly important either. A video recording of the model as it ran provided a convenient means to use the model as a communication tool where AnyLogic was not available.

7.8 Conclusion

This chapter presented an application of the *Visual Systems Modelling Framework* to assisting the planning of an adaptive clinical trial. This case study demonstrated how *visual systems modelling* can be used as a *Technical boundary* model for *Routine Decisions Support*, thus addressing Research Question 2. It also identified where the *Visual Systems Modelling Framework* stops being a useful tool for systems modelling, and demonstrated how it can be used to create models which are comparable with conventional OR/MS tools which have a standardised visual component, thus addressing Research Question 3(a).

Chapter 8

Discussion and Conclusion

This chapter summarises the findings and contributions made by the research contained within this thesis, and discusses limitations and future directions. It is structured to answer each of the Research Questions discussed in Section 1.3 separately, summarising the findings of this thesis, discussing the implications of these findings and how they contribute to OR/MS literature, before identifying limitations in the presented results and proposing directions for future research.

8.1 Research Question 1

How is visualisation currently used in quantitative OR/MS?

Chapter 2 addressed this question by providing a systematic literature review of visualisation use within OR/MS literature, categorising the reviewed literature as discussing visualisation concepts, specific visualisation techniques or visualisation in the context of conventional OR/MS tools.

8.1.1 Findings

The literature review contained in Chapter 2 identified a lack of discussion within OR/MS literature on the use of visualisation as a systems modelling tool. Where visualisation was discussed, this literature was synthesised into a series of *Visualisation Principles*, relating to general properties of visualisation which are beneficial, and *Visualisation Practices*, relating to methods which can be used to fulfil the *Visualisation Principles*.

These *Visualisation Principles* are:

1. *Users should be able to control what information is shown and level of detail to which it is shown*
2. *Contextual information should be preserved, and dimensionality and scale should be respected*
3. *Static and dynamic system components should remain distinguishable*
4. *Visual navigation should be facilitated and made intuitive*

These *Visualisation Practices* are:

1. *Build visualisations iteratively*
2. *Decouple "design" and "analysis" steps in visualisation development*
3. *Provide user control for interactivity and customisation*
4. *Take advantage of animation*
5. *Use static visual cues to represent multi-dimensional data*
6. *Automate repetitive tasks*

The results of this review were then used to develop the *Visual Systems Modelling Framework* discussed in this chapter, which addressed the gap identified by the review by proving a method for the use visualisation as a systems modelling tool, as well as a method for addressing the rest of the research questions contained within this thesis. This framework was applied in four different case studies to develop models in systems as varied as health care for traumatic spinal cord injury (Chapter 4), stroke rehabilitation (Chapters 5 and 6), and adaptive clinical trial design (Chapter 7). These four case studies each demonstrate the applicability of the *Visual Systems Modelling Framework* to a variety of systems, and demonstrate the validity of the framework, as well as how the *Visualisation Principles* and *Visualisation Practices* identified within the review can be applied in *Visual Systems Modelling*. The use of these *principles* and *practices* is summarised by Table 8.1

Table 8.1: Summary of which *Visualisation Principles* were applied in addressing the *Visualisation Practices* used in each case study.

	Principle 1: Users should be able to control what information is shown and level of detail to which it is shown.	**Principle 2:** Contextual information should be preserved, and dimensionality and scale should be respected.	**Principle 3:** Static and dynamic system components should remain distinguishable.	**Principle 4:** Visual navigation should be facilitated and made intuitive.
Chapter 4	3	2, 3, 5	4	
Chapter 5	3	5		
Chapter 6	3	3, 5		
Chapter 7 (communication model)		5	4	
Chapter 7 (calculation model)		5		

Notably, none of the identified *Visualisation Practices* were used to achieve the fourth *Visualisation Principle* (Visual navigation should be facilitated and made intuitive). While this *principle* was facilitated within each case study, the applied *practices* did not help to achieve this.

Visualisation Practices 1 (Build visualisations iteratively) and 2 (Decouple "design" and "analysis" steps in visualisation development) were used in the development of the case studies presented in this thesis (each model was updated in response to feedback from domain experts, and the application of the *Visual Systems Modelling Framework* ensured that the model was well-designed prior to model development and resulting analysis), but are not shown in Table 8.1 as they did not directly address any *Visualisation Principle*. This distinction between *Visualisation Practices* 1-2 (development practices) and 3-6 (visualisation techniques) was discussed in Seciton 2.2.4.2.

Of the *practices* relating to visualisation techniques, *Visualisation Practice* 6 (Automate repetitive tasks) was not used in any of the included case studies. Additionally, not all of the *practices* were used with the same frequency throughout this thesis. If the case studies presented within this thesis are representative of *visual systems modelling* tasks, this suggests that not all of the *principles* or *practices* identified by the review are equally as applicable or common in *visual systems modelling*.

8.1.2 Contributions and Implications

The literature review discussed here is the first systematic review of visualisation as it applies to general OR/MS practice, with the only literature review published prior to this research being a literature review of visualisation within OR/MS as it applies to the development of process management systems (Jääskeläinen et al., 2016). As such, it clearly illustrated a gap in OR/MS literature, and presents an opportunity for the OR/MS community to improve upon existing techniques for developing and using models.

Additionally, the *Visual Systems Modelling Framework*, developed in response to this demonstrated gap, provides a novel and generic framework for integrating visualisation into the OR/MS system modelling toolkit. This framework is the first contribution to OR/MS literature which provides a methodological basis for the development of *visual systems models*, and due to its generic nature it is applicable to a wide variety of systems. It therefore has the potential to improve OR/MS methodology across many different areas of application, better enabling systems modellers to aid decision makers.

8.1.3 Limitations and Future Directions

There are two limitations in the findings of the review contained in Chapter 2.

The first limitation is the formulation of the literature search string in this review to focus on literature discussing data in order to exclude "soft" OR/MS methods from the review. This may have also removed relevant papers from the results of the search. A different phrasing in the literature search, or a different approach to excluding "soft" OR/MS methods from the results, may have resulted in different papers being included for review.

Secondly, the selection of papers to include at each step of this review was not cross-checked against the results of selection by a second reader, meaning that some abstracts may have been read, but mistakenly excluded from full-text reading. However, the literature which was included within the review made no reference to other papers discussing visualisation within the context of OR/MS. It therefore seems unlikely that these two limitations significantly impacted the findings of the review.

Additionally, the development of the *Visual Systems Modelling Framework* which responded to this review incorporated the review's synthesised *Visualisation Principles* and

Visualisation Practices. Given the scarcity of literature discussing the use of visualisation in OR/MS, it is likely that these *principles* and *practices* are incomplete.

Likewise, not all *practices* which were identified in the review were used in the case studies contained within this thesis, and not all *principles* were addressed through these *practices* (Table 8.1). While this suggests that the identified *Visualisation Principles* and *Visualisation Practices* are incomplete and not of equal importance in *visual systems modelling* (as discussed in Section 8.1.1), it also meant that this thesis did not examine how all of these *principles* or *practices* could be used in the *Visual Systems Modelling Framework*. As this thesis did not demonstrate the use of *Visualisation Practice* 6 (Automate repetitive tasks) within any of the case studies contained in this thesis, it did not provide any illustrations of how it could be applied within the *Visual Systems Modelling Framework*.

While the *Visual Systems Modelling Framework* was useful in each case study contained within this thesis, the limitations discussed in this section present an opportunity for further refinement of the framework developed by this thesis. Future research in this area should investigate which *principles* and *practices* are most useful in the practical development of *visual systems models*, as well as identify what *principles* or *practices* should be added to the ones synthesised in this thesis. While such research should be informed by published case studies which use and report on visualisation in the context of systems modelling, additional insights can likely be adopted from other research disciplines such as usability engineering, informatics and analytics, which were not discussed in this thesis. An interdisciplinary approach to discussing *visual systems modelling* may therefore assist in the refinement of the *Visual Systems Modelling Framework* presented in this thesis.

8.2 Research Question 2

> *How does model use across Pidd's (2010) and Bayer et al.'s (2014) taxonomies influence how systems visualisation can be used?*

The case studies presented in this thesis (Chapters 4, 5, 6, and 7) addressed this question by applying the *Visual Systems Modelling Framework* developed in response to *Research Question 1* to a number of modelling applications which ranged from generating

new insights and understanding of patient flow in traumatic spinal cord injury care (Chapter 4), identifying patterns in stroke rehabilitation (Chapter 5), predicting outcomes in stroke rehabilitation (Chapter 6), and routine planning for a clinical trial (Chapter 7).

8.2.1 Findings

Each case study presented in this thesis served a different modelling purpose, addressing this research question by providing examples of how the *Visual Systems Modelling Framework* can be applied across multiple modelling purposes.

Chapter 4 developed an *Epistemic Representative* model for *Providing Insights for Debate*. While this model was intended to represent *Reality*, it was intended to include as much systems information as possible without imposing restrictions on what features were of importance, allowing the model to preserve the opinions and beliefs of multiple users with different understandings of the system or different priorities. As such, *communication* was an important aspect of this model, and it can be considered to be close to serving as a *Boundary* model.

Chapter 5 developed an *Epistemic Representative* model for *Improvement*, which had features of both Pidd's (2010) *Providing Insights for Debate* and *Investigation and Improvement*. Like in the model developed in Chapter 4, there is a strong *communication* component within this model, with the model providing multiple approaches to identifying patterns within the system. However, unlike Chapter 4, this chapter imposes restrictions on what features are considered important. As such, it is slightly further away from being a *Boundary* object than the previous model.

Chapter 6 also developed an *Epistemic Representative* model for *Investigation and Improvement*. However, human interaction with the model played a smaller role than it did in the model developed in Chapter 5, as in this case the user of the model provides a limited number of inputs to predict hypothetical patient outcomes. This model does not provide the flexibility in approach that the previous model did, and instead imposes a particular understanding of *reality* on the model. As such, this model is further removed from being considered a *Boundary* object than the previous model.

Chapter 7 developed two models intended to be used in tandem: one *Technical Representative* and one *Technical Boundary* model, which when used together were intended

as a tool for *Routine Decision Support*. The *Technical Representative* model placed even further restriction on the reality used in the model than in Chapter 6. In this case, there was no ambiguity as to the reasons why the system may behave in a particular way, as all behaviours were explicitly programmed based on well-defined assumptions rather than based on empirical data. In this case, systemic behaviours explicitly arose from interactions between the prespecificed behaviours of the system. As such, this lack of ambiguity means that this model explicitly *Represents* a particular, well-defined reality. The *Technical Boundary* model essentially represented the same system as the *Technical Representative* model, though in this case, the emphasis of this model was on communication. No realistic assumptions were built into this model, as its purpose was to communicate the expected properties and behaviours of the trial, and why they occur.

Figure 8.1 summarises the model purposes demonstrated in each case study.

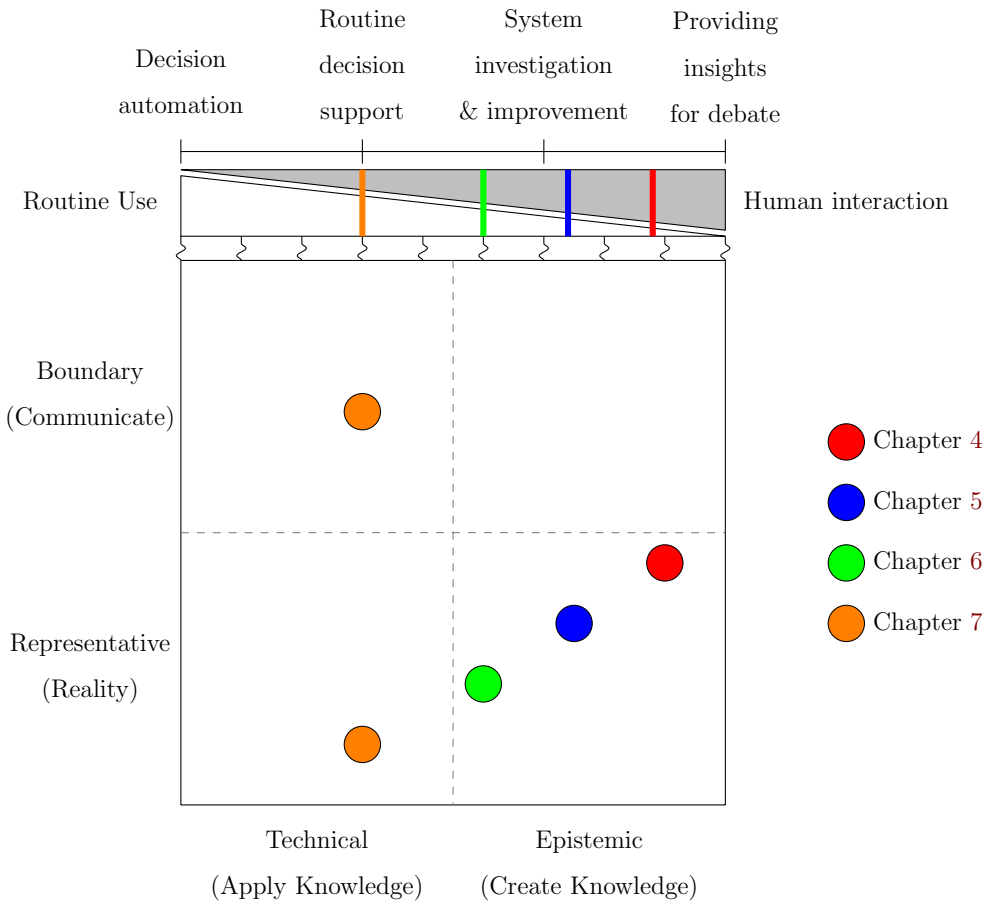


Figure 8.1: Pidd's and Bayer's combined taxonomies of model use (Pidd, 2010, p. 16), (Bayer et al., 2014, p. 128), as used in the four case studies presented in this thesis

Notably, as the case studies placed less focus on *Human Interaction* under Pidd's

(2010) taxonomy, they also became more focused on representing a particular view of *Reality*, placing less focus on *communication*. The exception to this was the *Technical Boundary* model developed in Chapter 7, which was used for communication rather than direct decision support. This suggests that where *visual systems models* are intended to be used for decision support, as these models become focused on *applying* knowledge rather than *generating* it under Bayer et al.'s (2014) taxonomy, or as models become intended more for *Routine Use* under Pidd's (2010), they tend to require increasing levels of focus on a specific way of understanding reality.

The use of visualisation within these chapters varied significantly.

Chapter 4 used a "dashboard" approach to visualisation, attempting to display as much information at once in a comprehensible fashion. This approach provided flexibility in the visualisation techniques used to visualise systems components, as the approach taken to visualisation for one component did not affect the approach taken to visualise another component.

In comparison, Chapter 5 used individual visual summaries to present a matrix of information about changes in health states. As under this approach to visualisation, it was important that individual visual summaries be quick and simple to compare, there was additional restriction placed on the use of visualisation here, as each patient representation had to be simple and uniform.

Chapter 6 used visualisation to provide access to the outputs of a conventional, predictive OR/MS model (weighted k-nearest neighbours). While this also took a "dashboard" approach to visualisation in a similar fashion to that used in Chapter 4, in this chapter visualisation was largely limited to the outputs of the used predictive OR/MS tool. As k-nearest neighbours is a transparent and intuitive technique, this did not place much practical restriction on the use of visualisation, and systems components which were not included in the applied OR/MS tool could be included in the developed model. Had a different conventional OR/MS tool been used, this restriction may have placed significantly greater limits on the use of visualisation in this case study.

Finally, Chapter 7 used an animated Discrete Event Simulation model to illustrate and communicate counterintuitive adaptive trial behaviour to clinical researchers without a background in mathematics. As in Chapter 6, the use of visualisation was restricted by

the choice of conventional OR/MS tool. In this case, however, visualisation was entirely restricted to the outputs provided by the Discrete Event Simulation component of the model.

As these models moved towards the *Decision Automation* end of Pidd's (2010) spectrum, the use of visualisation became increasingly focused and inflexible. This could suggest that the use of visualisation in OR/MS is partially dependent on the model's purpose. Alternatively, it could suggest that as additional importance is placed on applied OR/MS tools (which is likely tied to the model's purpose), visualisation becomes secondary, and relegated to providing access to the of outputs of conventional OR/MS tools. For either explanation of this behaviour, these results suggest that visualisation should be an important consideration from the start of planning the development of a *visual systems model*, with the modelling approach carefully chosen to ensure appropriate visualisation of the system being modelled.

8.2.2 Contributions and Implications

The case studies contained within this thesis demonstrate how visualisation can be integrated into systems modelling for a variety of purposes. As such, these case studies collectively illustrate that visualisation, when applied through the developed *Visual Systems Modelling Framework*, is a flexible tool which can be applied across many different OR/MS challenges. As such, this thesis not only reiterates the existing calls to action within OR/MS literature made by Andreinko et al. (2007), Zhu and Chen (2008) and Jääskeläinen et al. (2016), but also clearly demonstrates how this call to action can be addressed across a variety of modelling purposes. It also calls for greater attention to be paid at the planning stage of model development to the use of visualisation within OR/MS practice in order to effectively use visualisation as a systems modelling tool.

The variety of purpose among the presented case studies also supports the usefulness of the developed *Visual Systems Modelling Framework* as a method for integrating visualisation into the systems modelling toolkit, as it illustrates the flexible nature of the *framework*, and how it can accommodate the needs of many different modelling purposes. This suggests that the application of the developed *Visual Systems Modelling Framework* could be useful as a general method within OR/MS practice.

8.2.3 Limitations and Future Directions

While this thesis demonstrated how visualisation can be used across different modelling purposes, this demonstration was not comprehensive. In particular, Bayer et al.'s (2014) *Boundary* objects were only included in the form of one of the parallel models developed in Chapter 7. Likewise, most of the models presented were *Epistemic* in nature, seeking to generate new knowledge rather than represent existing knowledge. As such, the applicability of visualisation to these systems modelling tasks, or the use of the *Visual Systems Modelling Framework* in these contexts, has not been established. Additionally, while the findings in this thesis regarding how visualisation can be used in different contexts may be an artefact of the specific choices of conventional OR/MS tools applied within each case study. As decisions regarding the selection of conventional OR/MS tools are based on many factors other than the modelling purpose (e.g. what data is available, the audience or users of the model, time and budgetary constraints, the expertise of the modeller), the pattern observed in the relationship between modelling purpose and how visualisation can be applied may have resulted from these other aspects of model development.

These limitations can be addressed through future research, based on both the development of new visualisation methods and published case studies on the application of *visual systems modelling* within OR/MS practice. The *Visual Systems Modelling Framework* developed in this thesis may help in the development of such models.

8.3 Research Question 3(a)

> *How can visualisation as a systems modelling tool be used in conjunction with conventional methods within the OR/MS toolkit to enhance decision support, specifically: How can conventional OR/MS tools (such as k-nearest neighbours or clustering methods which use Coxian Phase-type distributions or novel dissimilarity measures) be integrated into visual systems modelling of clinical and health process systems?*

This question was addressed by the case studies in this thesis, each of which integrated visualisation with conventional OR/MS tools in a different manner.

Chapter 4 applied a *User-Driven* approach to integrating visualisation and conventional OR/MS tools. This approach emphasised customisability, and allowed users to control in real-time how visualisation was used with applied conventional OR/MS tools. A decision-maker could use developed clusters based on department utilisation to assist in navigating the developed *visual systems model* by filtering through subsets of patients, or they could use those clusters to control aspects of the model such as the appearance of the process animation which was included within it.

Chapter 5 employed an *Analytically-driven visualisation* approach to integrating visualisation and conventional OR/MS tools. Conventional OR/MS approaches used in this chapter were used to identify patterns which could then be used to identify aspects of the developed visualisation (in this case through filtering), without imposing restrictions on how the system should be represented.

In contrast to this, Chapter 6 demonstrated a *Visualisation-driven analysis* approach to integrating visualisation and conventional OR/MS tools. Rather than using conventional OR/MS tools as a means of interrogating visualisation of a system, this approach used visualisation to interrogate a conventional OR/MS tool by modelling the majority of systems features with a conventional OR/MS tool (in this case, weighted k-nearest neighbours), then used these outputs as the basis for systems visualisation. The developed *visual systems model* was then used to interpret the outputs of this predictive model, and contextualise these outputs in systems features which were not encapsulated by the predictive model.

Chapter 7 presented a *Parallel Model Development* approach to integrating visualisation with conventional OR/MS tools. In contrast to the other case studies discussed above, this chapter distinguished between visualisation and conventional OR/MS tool use, and developed two models in parallel. This allowed one model to focus entirely on visualising the system, and the other to focus entirely on modelling the system in a numeric, conventional OR/MS fashion.

8.3.1 Findings

These four case studies each illustrate a different method for integrating visualisation with conventional OR/MS tools, each with their own advantages and drawbacks.

The *User Driven* approach to *visual systems modelling* presented in Chapter 4 provided *flexibility* to the model, allowing the model to easily adapt to new questions. While this allowed for minimal prespecification of what aspects of the *visual systems model* were considered important, or how they should relate to one another (thus allowing the model to retain different points of view), it also *increased the time required* to develop the model

The *Analytically-driven visualisation* approach to *visual systems modelling* presented in Chapter 5 provided a *means to navigate a complex system.* This approach to integrating conventional OR/MS techniques with visualisation preserved the full complexity of the system being modelled while providing a means to understand it. This meant that there was minimal simplification involved in the system. However, this approach also made the applied OR/MS techniques *difficult to interpret*, as they played minimal role in the final visualisation.

In contrast to this, the *Visualisation-driven Analysis* approach to *visual systems modelling* presented in Chapter 6 provided a *reduction of system complexity* within the model. By using conventional OR/MS tools to model and simplify the system, this approach to *visual systems modelling* developed a model that was easy to comprehend and had minimal parts which needed to be interpreted. However, this simplification reduced the level of information captured by the model, risking a *loss of detail* that could be an important part of the system under investigation.

The *Parallel Model Development* approach to *visual systems modelling* presented in Chapter 7 enabled *specialisation* in the modelling process, and allowed each of the developed models to become hyper-focused on their individual tasks. The model developed for communication was able to be developed solely for this purpose, with unnecessary assumptions not required to be incldued, while the model developed for calculation was able to focus on speed and calculations. However, this *duplication of work* may have lead to an increase in the time required in model development, as the model was effectively implemented twice. Likewise, significant changes to the model may double the amount of work required in updating the models. Additionally, by developing the model twice, the chance for errors to occur in model development increases. This may further increase time required for model development.

Table 8.2 summarises these properties.

Table 8.2: Summary of integration approach and comparative benefits and drawbacks

	Strengths	Weaknesses
User Driven (Chapter 4)	Flexible	Longer Development Time
Analytically driven visualisation (Chapter 5)	Means to navigate a complex system	Hard to interpret conventional OR/MS tools
Visualisation-driven analysis (Chapter 6)	Simplifies complex system	Sacrifices detail
Parallel Model Development (Chapter 7)	Accommodates specialisation	Duplication of work

8.3.2 Contributions and Implications

This thesis illustrated four different approaches to integrating visualisation with conventional OR/MS tools, and identified the comparative strengths and weaknesses of each of these methods. The identified methods discussed in this thesis represent general approaches to *visual systems modelling*, and contribute to the use of the *Visual Systems Modelling Framework* by identifying how conventional OR/MS tools can be aligned to *Visualisation Principles* (as discussed in Section 2.3.4). This supports the practical use of this *framework* in other OR/MS applications.

8.3.3 Limitations and Future Directions

While the methods for integrating conventional OR/MS tools with visualisation presented in this thesis demonstrate a variety of approaches to *visual systems modelling*, the strengths and weaknesses of each identified method may have resulted from the specific applications of the *Visual Systems Modelling Framework*, not from the methods of integration themselves. Additionally, there are likely other methods of integrating conventional OR/MS tools with visualisation that were not identified or discussed within this

thesis.

This limitation can be addressed with future research on development of *visual systems models*, driven by case studies examining where and how conventional OR/MS techniques have been integrated with visualisation. The linking process discussed in Section 2.3.4 of the *Visual Systems Modelling Framework* may provide a standardised method for examining the method of integration across applications and domains.

8.4 Research Question 3(b)

> *How can visualisation as a systems modelling tool be used in conjunction with conventional methods within the OR/MS toolkit to enhance decision support, specifically: How can visualisation help validate conventional OR/MS tools such as those described in question 3(a)?*

This question was addressed in Chapter 3, as well as in the case studies presented in Chapters 4, 5 and 6. Chapter 3 developed a series of analytical rules for the validation of Marshall and McClean (2004) clustering, which were used in Chapters 4 and 5 in conjunction with visualisation to validate applied conventional OR/MS tools within these chapters. Chapters 4 - 6 address how visualisation can be used to validate conventional OR/MS tools.

8.4.1 Findings

The first three case studies each used visualisation to assist the validation of the conventional OR/MS models which were applied within them.

Chapter 4 used the rules developed in Section 3.3 to validate the use of Marshall and McClean (2004) clustering in modelling length of stay, and found that the developed clusters was not interpretable. Clusters based on departmental usage were validated through the use of the process animation contained within the *visual systems model*, with departmental usage being interpretable in terms of the patient's clinical pathway. In this case, visualisation *contextualised* the results from the application of conventional OR/MS tools, thereby assisting validation. While Disability-Adjusted Live Years (DALYS) were also used in this case study, validation was not applicable to this measure.

Chapter 5 used the rules developed in Section 3.3 to validate the use of Marshall and McClean (2004) clustering in modelling the time taken to regain the ability to walk after surviving a stroke. Clusters based on changes in physiotherapy regimen, health state and dose-response relationships were validated though visualisation developed outside of the *visual systems model* (*external visualisation*). These external visualisations can be found in Figures 5.3, 5.5, 5.8, 5.9, 5.10, and 5.11. As this validation was not included in the final model, it was necessary to trust that these models worked as intended.

Chapter 6 used 10-fold cross-validation to validate the applied k-nearest neighbours model, and used visualisation to make the logic used by the predictive model transparent and understandable. Unlike the case discussed in Chapter 4, visualisation was used to help validation of applied OR/MS tools by *visualising model outputs*, rather than through using visualisation to examine how those outputs can be interpreted in the context of the model. Table 8.3 summarises these approaches.

Table 8.3: Summary of integration approach and validation methods

	Conventional OR/MS tools	Validation method
User Driven (Chapter 4)	Departmant Resource Use Clusters	Contextualisation
	Length of Stay Clusters	Analytical rules
	DALYs	N/A
Analytically driven visualisation (Chapter 5)	Health Progression Clusters	External Visualisation
	Dose Clusters	External Visualisation
	Walking ability clusters	Analytical Rules
Visualisation-driven analysis (Chapter 6)	Weighted k-nearest neighbours	Cross-validation and Visualisation of model outputs

In these cases, visualisation was used alongside conventional analytical approaches to validation. While visualisation does not replace conventional approaches to model validation, these case studies have demonstrated how it can augment validation results.

The Analytically-driven visualisation approach used in Chapter 5 provided no means of validating the conventional OR/MS tools applied within the developed *visual systems*

model. As a result of this, the results of these tools had to be trusted in order to use them. This is in contrast to the case studies provided in Chapter 4 and 6, where conventional OR/MS tools were far easier to interptet, and therefore validate and trust. This suggests that for conventional OR/MS tools to be reliably used as a part of *visual systems modelling*, they either have to be trusted, or the *visual systems model* needs to provide transparency to the conventional OR/MS tools. As models are approximations of the real world, and therefore imperfect, in practical terms this implies that, when developing *visual systems models*, visualisation should be used wherever possible to improve access, transparency and validity to applied conventional OR/MS tools

8.4.2 Contributions and Implications

This thesis demonstrated how visualisation can be used to augment the conventional validation of conventional OR/MS tools, and illustrated that the ability to provide such validation is in part dependent on the method of integration between visualisation and conventional OR/MS tools. This supports the practical use of the *Visual Systems Modelling Framework* by identifying how it can incorporate validation, and provides information on how the methods of integrating conventional OR/MS tools with visualisation (discussed in Section 8.3) may interfere with the ability to validate these techniques.

8.4.3 Limitations and Future Directions

While the case studies presented within this thesis demonstrated different approaches to how visualisation could be used to assist the validation of conventional OR/MS tools, the results presented here may be a result of other factors such the choice of conventional OR/MS tools, or some other decision that was made during model development which was not discussed in this thesis. Another application of the *Visual Systems Modelling Framework*, following the same methods for integrating visualisation with conventional OR/MS tools, may have found results different to those discussed within this thesis.

This limitation can be addressed by further research, using case studies which examine how visualisation can be used as a systems modelling tool. Such research would allow for recommendations to be developed on specific conventional OR/MS tools, and recommendations regarding how these tools can be integrated with visualisation. This

research would constitute a refinement of the *Visual Systems Modelling Framework* which was developed within this thesis.

8.5 Summary

The research contained within this thesis investigated how visualisation can be applied as a systems modelling tool. A systematic literature review on the use of visualisation within OR/MS literature identified a lack of discussion on visualisation as a systems modelling tool. The results of this literature review were then used to develop the *Visual Systems Modelling Framework*, a general method which supports the application of visualisation as a systems modelling tool. This thesis presented four case studies which applied the *Visual Systems Modelling Framework* to different operational contexts, and used the results of this application to develop recommendations for how this framework can be used within OR/MS practice. This thesis contributes to the OR/MS literature by providing a method for integrating visualisation into the systems modelling toolkit, along with examples of its use and recommendations for applying it to future systems modelling tasks.

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Ye, Jianguo David and Thomas Froese (2009). "Visualization Configuration Model for Integrating Presentation of Construction Project Management Data". In: *Construction Research Congress 2009: Building a Sustainable Future*, pp. 979–988.

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Appendices

Appendix A

List of papers reviewed in Chapter 2

A.1 List of papers included in review

Papers are listed in order with which they are cited within the systematic review

Andreinko, Gennady, et al. "Geovisualization and synergies from InfoVis and Visual Analytics." *2007 11th International Conference Information Visualization (IV'07)*. IEEE, 2007.
Jääskeläinen, Aki, and Juho-Matias Roitto. "Visualization techniques supporting performance measurement system development." *Measuring Business Excellence* 20.2 (2016): 13-25.
France, Stephen L., and Sanjoy Ghose. "Marketing analytics: Methods, practice, implementation, and links to other fields." *Expert Systems with Applications* (2018).
Mortenson, Michael J., Neil F. Doherty, and Stewart Robinson. "Operational research from Taylorism to Terabytes: A research agenda for the analytics age." *European Journal of Operational Research* 241.3 (2015): 583-595.
Hindle, Giles A., and Richard Vidgen. "Developing a business analytics methodology: A case study in the foodbank sector." *European Journal of Operational Research* 268.3 (2018): 836-851.
Wark, Steven, and Dale Lambert. "Presenting the story behind the data: Enhancing situational awareness using multimedia narrative." *MILCOM 2007-IEEE Military Communications Conference*. IEEE, 2007.
Eppler, Martin J., Jeanne Mengis, and Sabrina Bresciani. "Seven types of visual ambiguity: On the merits and risks of multiple interpretations of collaborative visualizations." *2008 12th International Conference Information Visualisation*. IEEE, 2008.
Wolf, David, Timothy W. Simpson, and Xiaolong Zhang. "A preliminary study of novice and expert users' decision-making procedures during visual trade space exploration." *ASME Design Engineering Technical Conferences—Design Automation Conference, ASME, San Diego, CA, Paper No. DETC2009/DAC-87294*. 2009.
Bacic, Dinko, and Raymond Henry. "The role of business information visualization in knowledge creation" *AMCIS 2012 Proceedings* (2012).
Remus, William. "A study of graphical and tabular displays and their interaction with environmental complexity." *Management Science* 33.9 (1987): 1200-1204.
Eick, Stephen G., and Graham J. Wills. "High interaction graphics." *European journal of operational research* 81.3 (1995): 445-459.
Chan, Yu-Hsuan, Kimberly Keeton, and Kwan-Liu Ma. "Interactive visual analysis of hierarchical enterprise data." *2010 IEEE 12th Conference on Commerce and Enterprise Computing*. IEEE, 2010.

Table A.1: Papers included from review in Chapter 2

Bieber, Michael. "On integrating hypermedia into decision support and other information systems." *Decision Support Systems* 14.3 (1995): 251-267.
Morin, Magnus, Johan Jenvald, and Mirko Thorstensson. "Computer-supported visualization of rescue operations." *Safety Science* 35.1-3 (2000): 3-27.
Heer, Thomas, Christoph Außem, and René Wörzberger. "Flexible Multi-Dimensional Visualization of Process Enactment Data." *International Conference on Business Process Management*. Springer, Berlin, Heidelberg, 2009.
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Matsatsinis, Nikolaos F., and Yannis Siskos. "MARKEX: An intelligent decision support system for product development decisions." *European Journal of Operational Research* 113.2 (1999): 336-354.
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Radovanovic, Sandro, et al. "Where will the next ski injury occur? A system for visual and predictive analytics of ski injuries." *Operational Research* (2019): 1-20.
Ye, Jianguo David, and Thomas Froese. "Visualization Configuration Model for Integrating Presentation of Construction Project Management Data." *Construction Research Congress 2009: Building a Sustainable Future*. 2009.
Dos Santos, C. Russo, et al. "Experiments in information visualization using 3D metaphoric worlds." *Proceedings IEEE 9th International Workshops on Enabling Technologies: Infrastructure for Collaborative Enterprises (WET ICE 2000)*. IEEE, 2000.
Jensen, Andrew, Justin Boyle, and Sankalp Khanna. "Visualising patient flow." *HIC*. 2012.
Tan, Joseph KH, and Izak Benbasat. "Processing of graphical information: A decomposition taxonomy to match data extraction tasks and graphical representations." *Information Systems Research* (1990): 416-439.
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Delias, Pavlos, Vassilios Zoumpoulidis, and Ioannis Kazanidis. "Visualizing and exploring event databases: a methodology to benefit from process analytics." Operational Research (2018): 1-22.
Burattin, Andrea, Marta Cimitile, and Fabrizio Maria Maggi. "Lights, camera, action! business process movies for online process discovery." International Conference on Business Process Management. Springer, Cham, 2014.
Bachhofner, Stefan, et al. "Towards a Multi-parametric Visualisation Approach for Business Process Analytics." International Conference on Advanced Information Systems Engineering. Springer, Cham, 2017.
Bolt, Alfredo, Massimiliano de Leoni, and Wil MP van der Aalst. "Process variant comparison: using event logs to detect differences in behavior and business rules." Information Systems 74 (2018): 53-66.
Gulden, Jens. "Visually comparing process dynamics with rhythm-eye views." International Conference on Business Process Management. Springer, Cham, 2016.
Fradi, Ahmed, et al. "Decision-Making Support in Engineering Design Based on Collaborative Dashboards: Integration of Business Intelligence Techniques." International Conference on Research into Design. Springer, Singapore, 2017.
Pieterse, J. L. "An Improved Approach Towards Business Intelligence Dashboards Through Automated Reporting." Computers and Industrial Engineering 42. 2012.
Nowak, Alexander, et al. ""Flexible information design for business process visualizations." 2012 Fifth IEEE International Conference on Service-Oriented Computing and Applications (SOCA). IEEE, 2012.
Dau, Frithjof, and Simon Andrews. "Combining business intelligence with semantic technologies: the CUBIST project." International Conference on Conceptual Structures. Springer, Cham, 2014.
Wasser, Avi, and Maya Lincoln. "ProcessGene view: an integrated visualization of business process models." OTM Confederated International Conferences" On the Move to Meaningful Internet Systems". Springer, Berlin, Heidelberg, 2010.

Table A.3: Papers included from review in Chapter 2

Shamsuzzoha, Ahm, et al. "Collaborative smart process monitoring within virtual factory environment: an implementation issue." International Journal of Computer Integrated Manufacturing 30.1 (2017): 167-181.
Cano, Rafael G., et al. "A hybrid GRASP heuristic to construct effective drawings of proportional symbol maps." Computers & Operations Research 40.5 (2013): 1435-1447. Liiv, Innar, et al. "Visual matrix explorer for collaborative seriation." Wiley Interdisciplinary Reviews: Computational Statistics 4.1 (2012): 85-97.
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Abbiw-Jackson, Roselyn, et al. "A divide-and-conquer local search heuristic for data visualization." Computers & operations research 33.11 (2006): 3070-3087. Feiner, S. K., and Clifford Beshers. "Visualizing n-dimensional virtual worlds with n-vision." ACM SIGGRAPH Computer Graphics. Vol. 24. No. 2. ACM, 1990.
Rose, Alan F., et al. "Using qualitative studies to improve the usability of an EMR." Journal of biomedical informatics 38.1 (2005): 51-60.
Suntinger, Martin, et al. "The event tunnel: Interactive visualization of complex event streams for business process pattern analysis." 2008 IEEE Pacific Visualization Symposium. IEEE, 2008.
Lee, Namhun, and Eddy M. Rojas. "Visual representations for monitoring project performance: developing novel prototypes for improved communication." Journal of construction engineering and management 139.8 (2013): 994-1005.
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Farrugia, Michael, and Aaron Quigley. "Enhancing airline customer relationship management data by inferring ties between passengers." 2009 International Conference on Computational Science and Engineering. Vol. 4. IEEE, 2009.
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Table A.4: Papers included from review in Chapter 2

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Wang, Lidong. "Big Data and IT Network Data Visualization." International Journal of Mathematical, Engineering and Management Sciences 3.1 (2018): 9-16.
Kusakabe, Takahiko, Takamasa Iryo, and Yasuo Asakura. "Data mining for traffic flow analysis: Visualization approach." Traffic Data Collection and its Standardization. Springer, New York, NY, 2010. 57-72.
Haspeslagh, Marc, and Luc Delesie. "A management tool to trace the clinical path of depressed patients." European journal of operational research 105.2 (1998): 332-345.
Park, Ji Hwan, et al. "C 2 A: Crowd consensus analytics for virtual colonoscopy." 2016 IEEE Conference on Visual Analytics Science and Technology (VAST). IEEE, 2016.
Liu, Kan, and Ping Liu. "Visual Analysis of Customer Data in Commercial Banks." 2009 International Conference on Business Intelligence and Financial Engineering. IEEE, 2009.
Ieva, Francesca, and Anna Maria Paganoni. "Detecting and visualizing outliers in provider profiling via funnel plots and mixed effect models." Health care management science 18.2 (2015): 166-172.
Thomas, T., et al. "Morphostat: A simple beach profile monitoring tool for coastal zone management." Ocean & Coastal Management 153 (2018): 17-32.
Osekowska, Ewa, Stefan Axelsson, and Bengt Carlsson. "Potential fields in maritime anomaly detection." Proceedings of the 3rd international conference on models and technologies for intelligent transport systems. TUD Press, 2013.
Crowe, Sonya, et al. "Combining qualitative and quantitative operational research methods to inform quality improvement in pathways that span multiple settings." BMJ Qual Saf 26.8 (2017): 641-652.
Sargent, Robert G. "Verification and validation of simulation models." Proceedings of the 2010 Winter Simulation Conference. IEEE, 2010.
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Gravel, Marc, et al. "A DSS for production planning." International Transactions in Operational Research 1.3 (1994): 363-373.
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Table A.6: Papers included from review in Chapter 2

Grignard, Arnaud, and Alexis Drogoul. "Agent-based visualization: a real-time visualization tool applied both to data and simulation outputs." Workshops at the Thirty-First AAAI Conference on Artificial Intelligence. 2017.
Ingram, Fred, and Roger John Brooks. "Simulating classroom lessons: an agent-based attempt." (2018): 230-240.
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Ardito, Carmelo, et al. "An information visualization approach to hospital shifts scheduling." International Conference on Human-Computer Interaction. Springer, Berlin, Heidelberg, 2009.
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Deasy, Joseph, et al. "A collaboratory for radiation therapy treatment planning optimization research." Annals of Operations Research 148.1 (2006): 55-63.
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Weber, Charles A., and Anand Desai. "Determination of paths to vendor market efficiency using parallel coordinates representation: a negotiation tool for buyers." European journal of operational research 90.1 (1996): 142-155.

Table A.7: Papers included from review in Chapter 2

Di Matteo, Michael, Graeme C. Dandy, and Holger R. Maier. "A multi-stakeholder portfolio optimization framework applied to stormwater best management practice (BMP) selection." Environmental modelling & software 97 (2017): 16-31.
Kasanen, Eero, Ralf Östermark, and Milan Zeleny. "Gestalt system of holistic graphics: new management support view of MCDM." Computers & Operations Research 18.2 (1991): 233-239.
Miettinen, Kaisa, et al. "Using box indices in supporting comparison in multiobjective optimization." European Journal of Operational Research 197.1 (2009): 17-24.
Trinkaus, Hans L., and Thomas Hanne. "knowCube: a visual and interactive support for multicriteria decision making." Computers & Operations Research 32.5 (2005): 1289-1309.
Roselli, Lucia Reis Peixoto, Adiel Teixeira de Almeida, and Eduarda Asfora Frej. "Decision neuroscience for improving data visualization of decision support in the FITradeoff method." Operational Research (2019): 1-21.
Vetschera, Rudolf. "A preference-preserving projection technique for MCDM." European Journal of Operational Research 61.1-2 (1992): 195-203.
Frej, Eduarda Asfora, Adiel Teixeira de Almeida, and Ana Paula Cabral Seixas Costa. "Using data visualization for ranking alternatives with partial information and interactive tradeoff elicitation." Operational Research (2019): 1-23.
Hudec, Miroslav, and Mirko Vujošević. "A fuzzy system for municipalities classification." Central European Journal of Operations Research 18.2 (2010): 171-180. Agarwal, Puneet, et al. "An exploratory analysis for performance assessment of state police forces in india: an eclectic approach." Operational Research (2019): 1-27.
Siskos, Yannis, Athanasios Spyridakos, and Denis Yannacopoulos. "Using artificial intelligence and visual techniques into preference disaggregation analysis: The MUDAS system." European Journal of Operational Research 113.2 (1999): 281-299.
Mareschal, Bertrand, and Jean Pierre Brans. "BANKADVISER: An industrial evaluation system." European Journal of Operational Research 54.3 (1991): 318-324.
El-Mahgary, Sami, and Risto Lahdelma. "Data envelopment analysis: visualizing the results." European Journal of Operational Research 83.3 (1995): 700-710.

Table A.8: Papers included from review in Chapter 2

Førsund, Finn R., Sverre AC Kittelsen, and Vladimir E. Krivonozhko. "Farrell revisited–Visualizing properties of DEA production frontiers." Journal of the Operational Research Society 60.11 (2009): 1535-1545.
Seidl, Immanuel, and Margit Sommersguter-Reichmann. "Visualizing production surfaces in 3D diagrams." Advances in Operations Research 2011 (2011).
Yang, Jian-Bo, Dong-Ling Xu, and Shanlin Yang. "Integrated efficiency and trade-off analyses using a DEA-oriented interactive minimax reference point approach." Computers & Operations Research 39.5 (2012): 1062-1073.
Ozcan, Yasar A., et al. "Evaluating the performance of Brazilian university hospitals." Annals of Operations Research 178.1 (2010): 247-261.
Lins, Marcos Pereira Estellita, et al. "Integrating the regulatory and utility firm perspectives, when measuring the efficiency of electricity distribution." European Journal of Operational Research 181.3 (2007): 1413-1424.
Bernatavičienė, Jolita, et al. "Optimal decisions in combining the SOM with nonlinear projection methods." European Journal of Operational Research 173.3 (2006): 729-745.
Dzemyda, Gintautas, and Olga Kurasova. "Heuristic approach for minimizing the projection error in the integrated mapping." European Journal of Operational Research 171.3 (2006): 859-878.
Cattinelli, Isabella, et al. "Use of Self-Organizing Maps for Balanced Scorecard analysis to monitor the performance of dialysis clinic chains." Health care management science 15.1 (2012): 79-90.
Zhuang, Zoe Y., et al. "Combining data mining and case-based reasoning for intelligent decision support for pathology ordering by general practitioners." European Journal of Operational Research 195.3 (2009): 662-675.
Seret, Alex, et al. "A new SOM-based method for profile generation: Theory and an application in direct marketing." European Journal of Operational Research 220.1 (2012): 199-209.
Lai, Daphne Teck Ching, et al. "A methodology for automatic classification of breast cancer immunohistochemical data using semi-supervised Fuzzy c-Means." Central European Journal of Operations Research 22.3 (2014): 475-499.

Table A.9: Papers included from review in Chapter 2

Powell, Guido, et al. "Multidimensional and Longitudinal Indicators in Population Health." Workshops at the Thirty-First AAAI Conference on Artificial Intelligence. 2017. Christodoulou, Georgina, and Gordon J. Taylor. "Using a continuous time hidden Markov process, with covariates, to model bed occupancy of people aged over 65 years." Health Care Management Science 4.1 (2001): 21-24.
Marshall, Adele H., and Barry Shaw. "Computational learning of the conditional phase-type (C-Ph) distribution." Computational Management Science 11.1-2 (2014): 139-155.
Riihimäki, Jaakko, Reijo Sund, and Aki Vehtari. "Analysing the length of care episode after hip fracture: a nonparametric and a parametric Bayesian approach." Health care management science 13.2 (2010): 170-181.
Au, Siu-Tong, et al. "A framework of irregularity enlightenment for data pre-processing in data mining." *Annals of Operations Research* 174.1 (2010): 47-66.

Table A.10: Papers included from review in Chapter 2

A.2 List of papers excluded from review after full-text reading

Article	Reason Excluded
Akhavian, Rez Computer Supported Cooperative Work in Design, 2007. CSCWD 2007. 11th International Conference on. a, and Amir H. Behzadan. "Knowledge-based simulation modeling of construction fleet operations using multimodal-process data mining." *Journal of Construction Engineering and Management* 139.11 (2013): 04013021.	Duplicate of Akhavian and Behzadan (2012).
Cerone, Antonio. "Process mining as a modelling tool: Beyond the domain of business process management." *International Conference on Software Engineering and Formal Methods*. Springer, Berlin, Heidelberg, 2015.	Discusses process mining, not visualisation.
Dodendorf, Diane M., et al. "Assessing the patient's mammogram experience." *Health care management review* 29.1 (2004): 77-87.	Discusses "Soft" OR/MS.
Fill, Hans-Georg, and Florian Johannsen. "A knowledge perspective on big data by joining enterprise modeling and data analyses." *2016 49th Hawaii International Conference on*. IEEE, 2016.	Discusses knowledge management, not visualisation.
Fisk, John. "An interactive game for production and financial planning." *Computers & Operations Research* 7.3 (1980): 157-168.	Discusses classroom education, not OR/MS practice or visualisation.
Jarke, Matthias, M. Tawfik Jelassi, and Melvin F. Shakun. "MEDIATOR: Towards a negotiation support system." *European Journal of Operational Research* 31.3 (1987): 314-334.	Discusses a program for collaborative decision making, not system modelling

Table A.11: Papers excluded from review in Chapter 2

Nunes, Vanessa Tavares, Flavia Maria Santoro, and Marcos RS Borges. "Capturing context about group design processes." *Computer Supported Cooperative Work in Design, 2007. CSCWD 2007. 11th International Conference on.* IEEE, 2007.	Discusses the importance of capturing contextual information, not visualisation.
Ranjan, Jayanthi. "Business justification with business intelligence." *Vine* 38.4 (2008): 461-475.	Discusses the commercial benefits from using Business Intelligence in a business setting, not visualisation
Stark, Robert F., Emilie M. Roth, and Michael P. Farry. "Incrementally formalizing graphical models for collaborative operations research." *Proceedings of the human factors and ergonomics society annual meeting.* Vol. 57. No. 1. Sage CA: Los Angeles, CA: SAGE Publications, 2013.	Discusses a process for applying OR/MS methodology. Visualisation is discussed in the context of Soft OR/MS.
Tekiner, Firat, and John A. Keane. "Big data framework." *Systems, Man, and Cybernetics (SMC), 2013 IEEE International Conference on.* IEEE, 2013.	Discusses the benefits and challenges arising from big data, not visualisation
Tian, Maoyi, et al. "Research and implementation of tunnel three-dimensional modeling algorithm based on java3D." *Artificial Intelligence, Management Science and Electronic Commerce (AIMSEC), 2011 2nd International Conference on.* IEEE, 2011.	Discusses mapping of mine shafts visualisation of them, not systems modelling
Welsch, Roy E. "Graphics for data analysis." *Computers & Graphics* 2.1 (1976): 31-37.	Discusses an online platform for data visualisation, not systems modelling
Agrež, Jernej, and Nadja Damij. "Knowledge dynamics assessment in complex organizational systems: a missing person investigation case study." *Central European Journal of Operations Research* 23.3 (2015): 527-545.	Discusses "Soft" OR/MS
Akter, Shahriar, and Samuel Fosso Wamba. "Big data and disaster management: a systematic review and agenda for future research." *Annals of Operations Research* (2017): 1-21.	Reviews literature on disaster management, no discussion of visualisation

Table A.12: Papers excluded from review in Chapter 2

Allen, Eric J., et al. "Reference-dependent preferences: Evidence from marathon runners." *Management Science* 63.6 (2016): 1657-1672.	Discusses bunching of performance data around reference points, not systems modelling
Basu, Amit, and Robert W. Blanning. "A graph-theoretic approach to analyzing knowledge bases containing rules, models and data." Annals of Operations Research 75 (1997): 3-23.	Discusses "Soft" OR/MS
Bonutti, Alex, et al. "Benchmarking curriculum-based course timetabling: formulations, data formats, instances, validation, visualization, and results." Annals of Operations Research 194.1 (2012): 59-70.	Mentions visualisation but does not discuss it in sufficient depth to contribute to review
Bornschlegl, Marco Xaver. "Advanced Visual Interfaces Supporting Distributed Cloud-Based Big Data Analysis." DCPD CHItaly. 2017.	Discusses infrastructure supporting visualisaiton, not visualisaiton itself
Hodgson, Anthony M. "Hexagons for systems thinking." European Journal of Operational Research 59.1 (1992): 220-230.	Discusses "Soft" OR/MS
Kapelko, Magdalena. "Measuring productivity change accounting for adjustment costs: evidence from the food industry in the European Union." *Annals of Operations Research* (2017): 1-20.	No discussion of visualisation
Kou, Gang, and Chunwei Lou. "Multiple factor hierarchical clustering algorithm for large scale web page and search engine clickstream data." *Annals of Operations Research* 197.1 (2012): 123-134.	No discussion of visualisation

Table A.13: Papers excluded from review in Chapter 2

Montaser, A. "WEB-BASED INTEGRATED PROJECT CONTROLS SYSTEM." ISARC. Proceedings of the International Symposium on Automation and Robotics in Construction. Vol. 34. Vilnius Gediminas Technical University, Department of Construction Economics & Property, 2017.	No discussion of visualisation
Murguia, Danny, et al. "Process integration framework for the design phase of a residential building." Procedia engineering 196 (2017): 462-469.	Discusses methodology for project management, not visualisation
Pärn, E. A., and D. J. Edwards. "Conceptualising the FinDD API plug-in: A study of BIM-FM integration." Automation in Construction 80 (2017): 11-21.	Discusses tools supporting visualisation, but does not discuss visualisation.
Poot, Alexander, Goossen Kant, and Albert Peter Marie Wagelmans. "A savings based method for real-life vehicle routing problems." Journal of the Operational Research Society 53.1 (2002): 57-68.	No discussion of visualisation
Qu, H., et al. "Virtual EP: a simulator of multi-agents-based virtual plant growth in response to environmental heterogeneity." Journal of Simulation 4.3 (2010): 181-195.	Not related to OR/MS
Satoh, Kenichi, and Hirokazu Yanagihara. "Estimation of varying coefficients for a growth curve model." American Journal of Mathematical and Management Sciences 30.3-4 (2010): 243-256.	No discussion of visualisation
Shaikh, Tahira Sumbal, Muhammad Sarfraz, and Malik Zawwar Hussain. "Shape preserving positive and convex data visualization using rational bi-cubic functions." Pakistan Journal of Statistics and Operation Research 8.1 (2012): 121-138.	Visualisation is not discussed in the context of OR/MS practice

Table A.14: Papers excluded from review in Chapter 2

Simon, Chihanga, et al. "Malaria control in Botswana, 2008–2012: the path towards elimination." Malaria journal 12.1 (2013): 458.	Visualisation of not discussed in the context of OR/MS practice
Tyagi, Rajesh, Laurence J. Moore, and Bernard W. Taylor III. "A decision support system for funds management in a Public University: Special focus article." Operations research 36.6 (1988): 864-881.	No discussion of visualisation
Veith, Tamie L., John E. Kobza, and C. Patrick Koelling. "Netsim: Java™-based simulation for the World Wide Web." Computers & operations research 26.6 (1999): 607-621.	No discussion of visualisation
Wu, Hongle, et al. "Personal sleep pattern visualization via clustering on sound data." Workshops at the Thirty-First AAAI Conference on Artificial Intelligence. 2017.	Not related to OR/MS
Zyoud, Shaher H., and Daniela Fuchs-Hanusch. "A bibliometric-based survey on AHP and TOPSIS techniques." Expert Systems with Applications 78 (2017): 158-181.	No discussion of visualisation
Cox Jr, Louis Anthony, Douglas A. Popken, and Richard X. Sun. "Descriptive Analytics for Public Health: Socioeconomic and Air Pollution Correlates of Adult Asthma, Heart Attack, and Stroke Risks." Causal Analytics for Applied Risk Analysis. Springer, Cham, 2018. 251-283.	No discussion of OR/MS

Table A.15: Papers excluded from review in Chapter 2

Appendix B

Detailed results for validation of Marshall and McClean (2004) Clustering

B.1 CART trees

B.1.1 2 phase systems

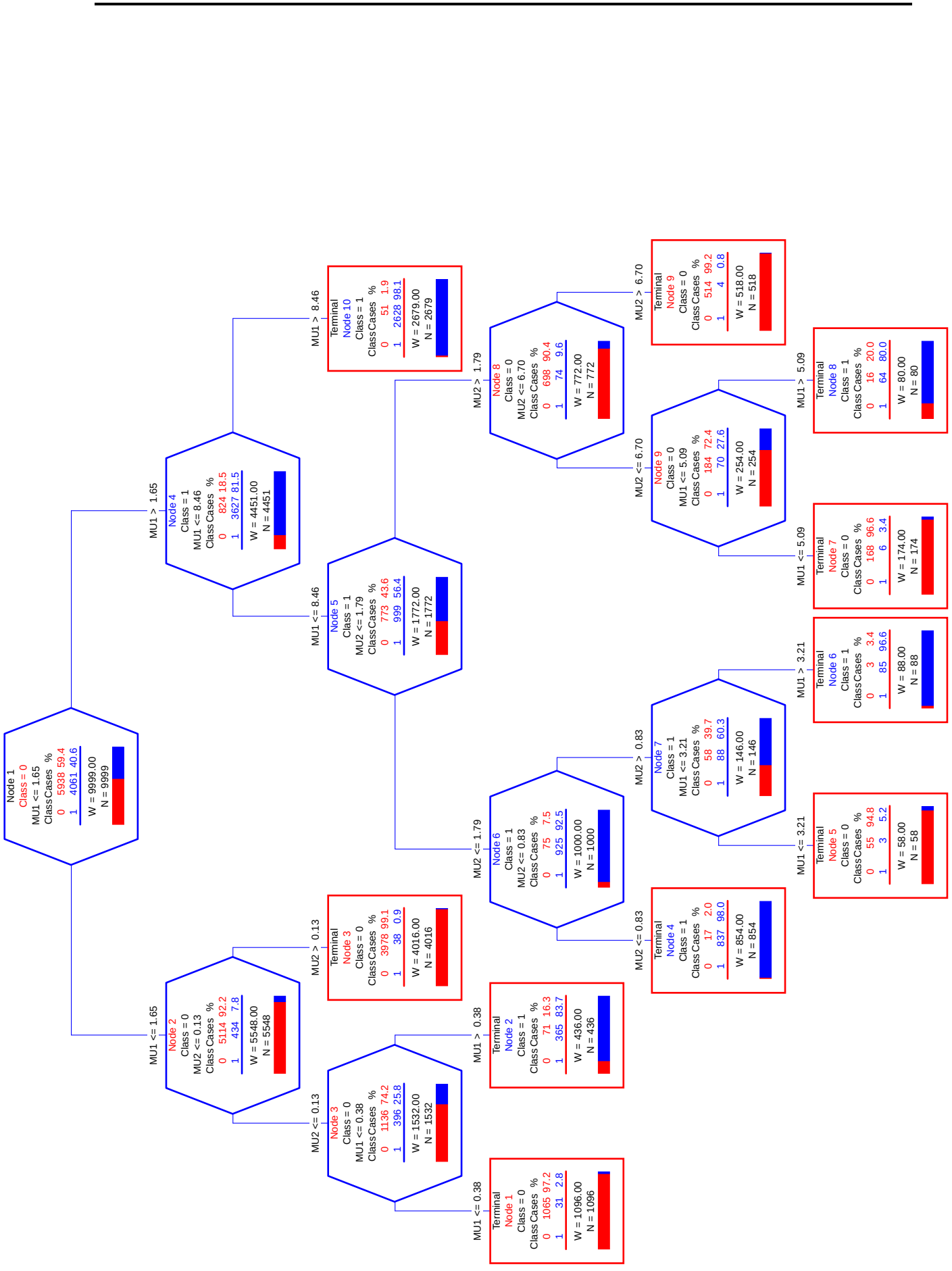

Figure B.1: CART tree for 2 phases with kappa ≥ 70

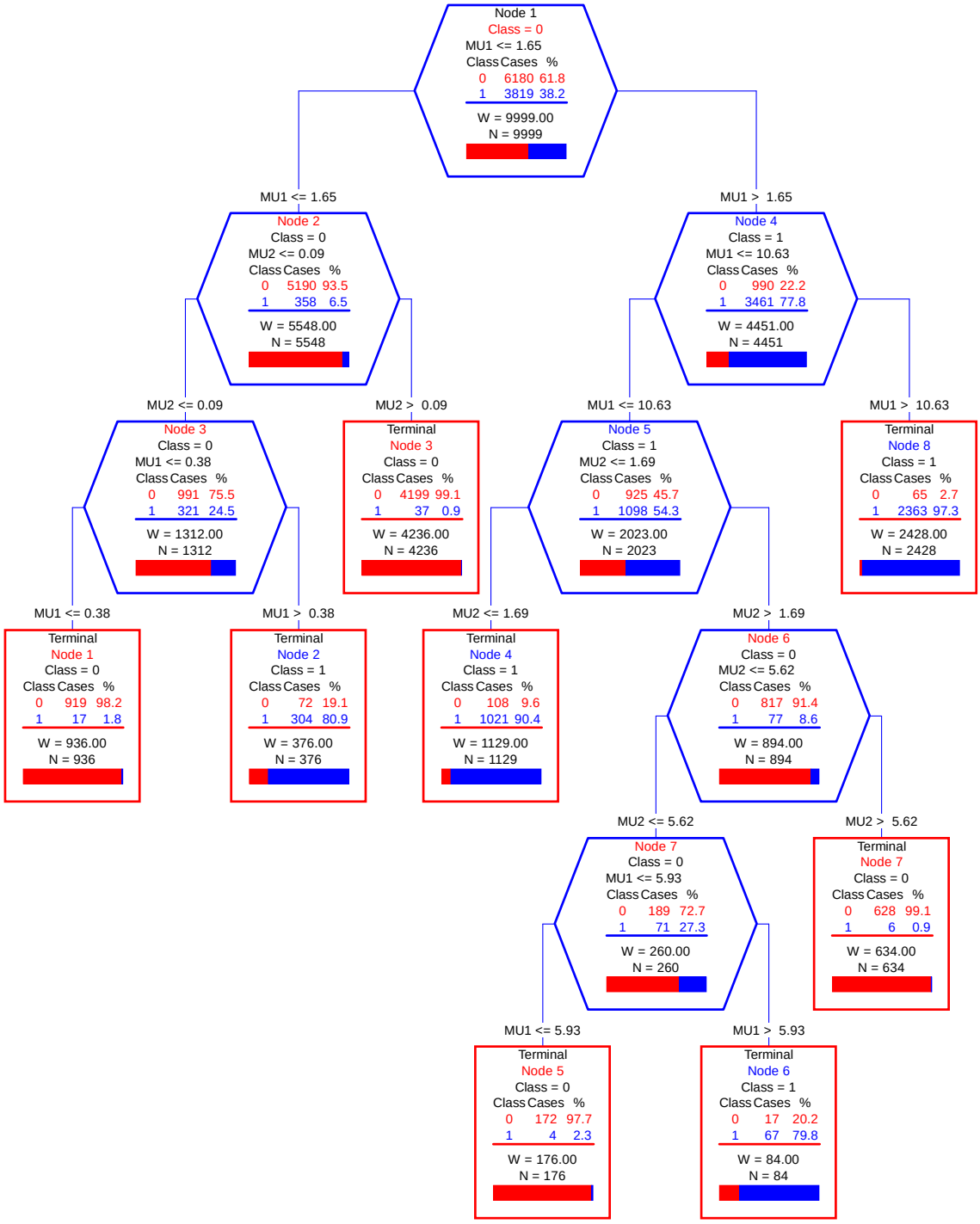

Figure B.2: CART tree for 2 phases with kappa ≥ 75

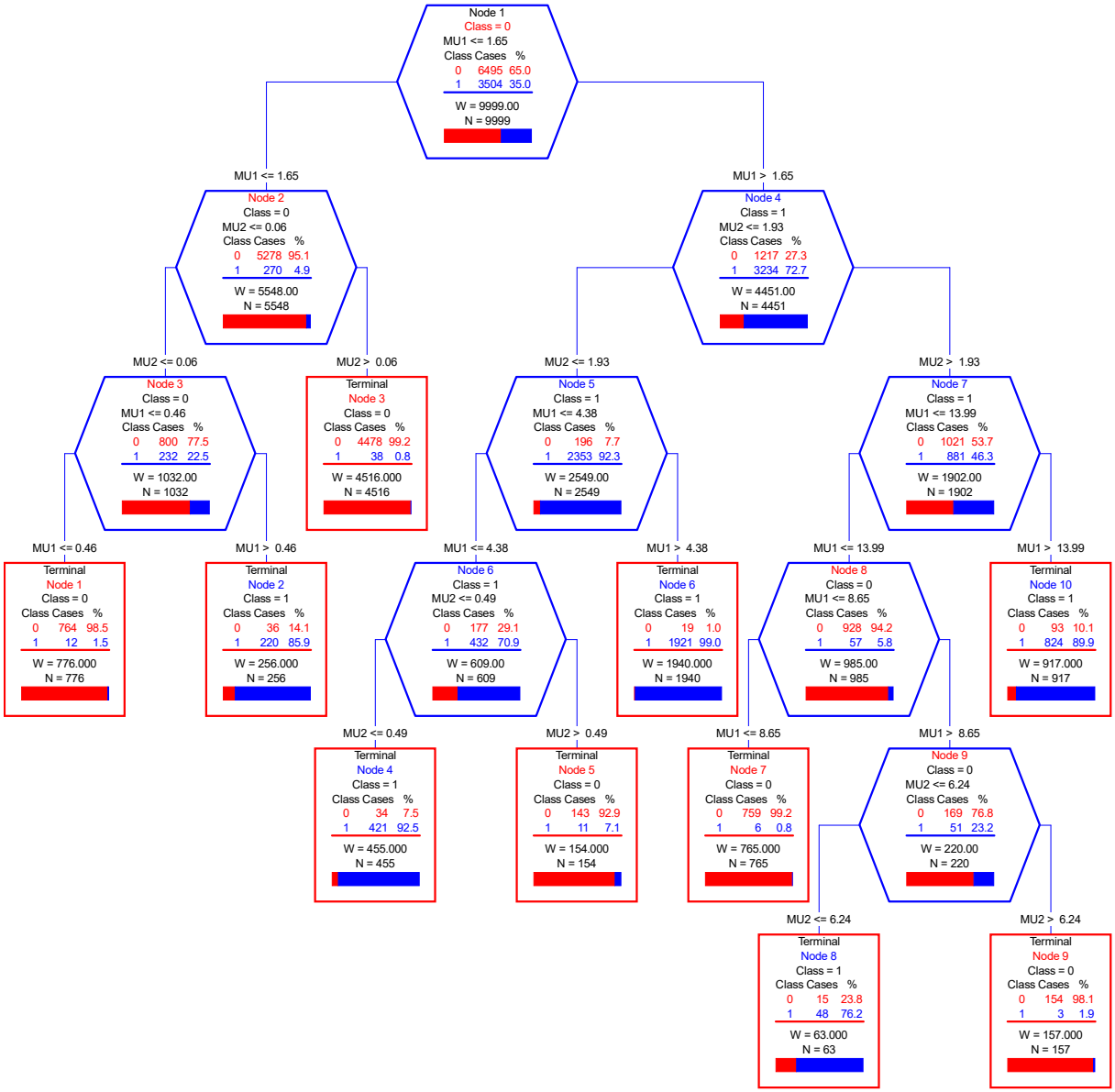

Figure B.3: CART tree for 2 phases with kappa ≥ 80

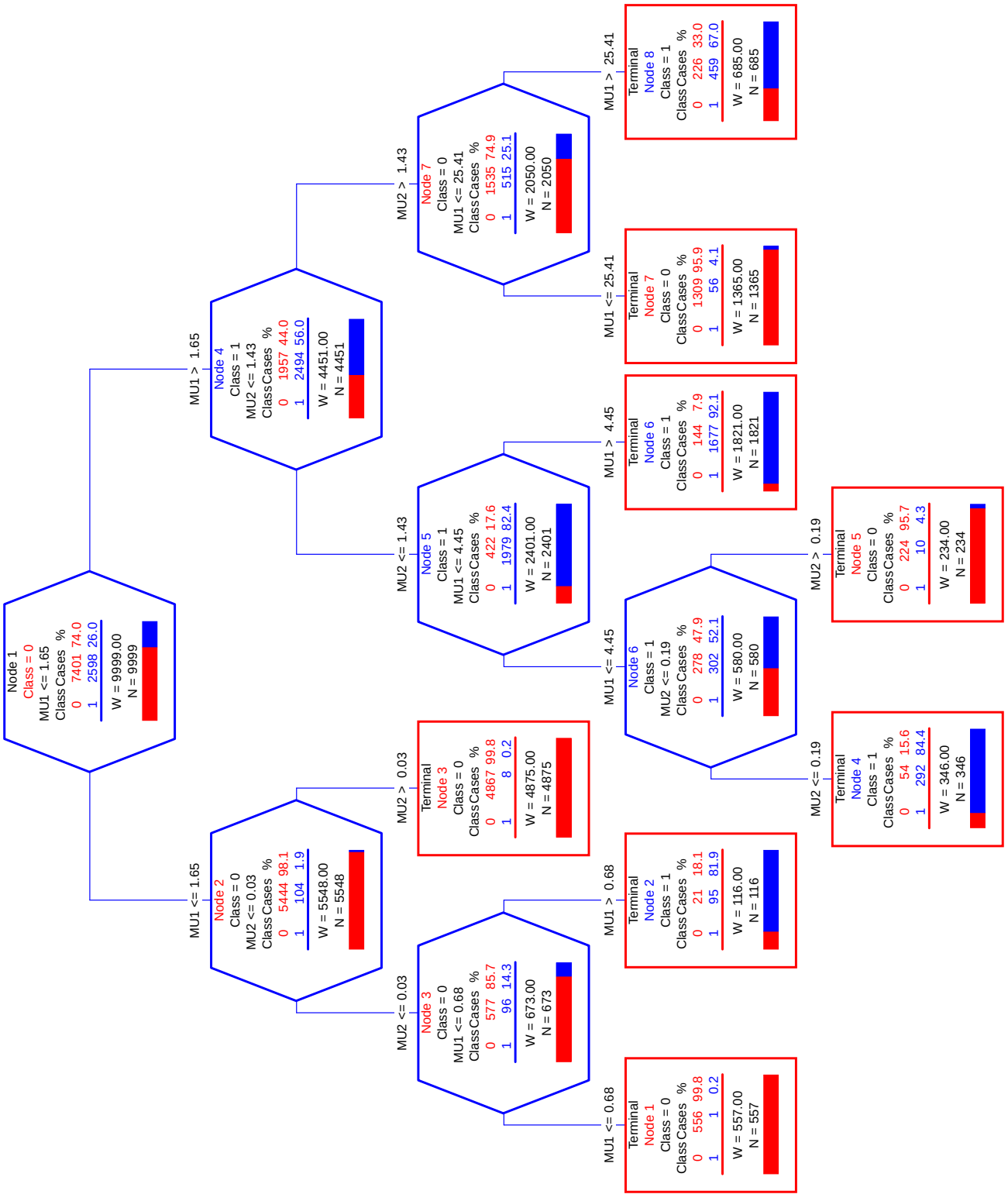

Figure B.4: CART tree for 2 phases with kappa ≥ 90

B.1.2 3 phase systems

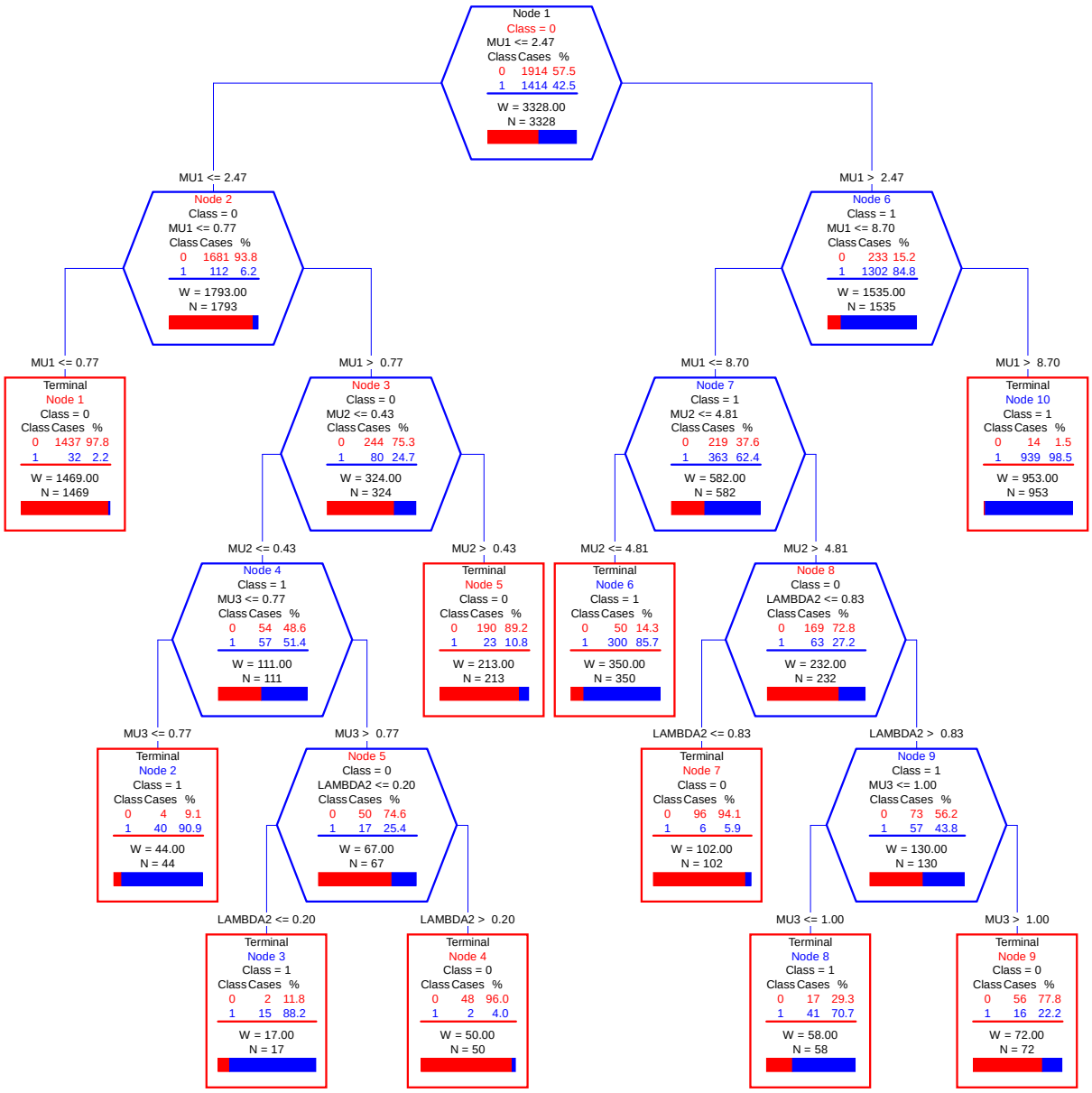

Figure B.5: CART tree for 3 phases with kappa ≥ 70

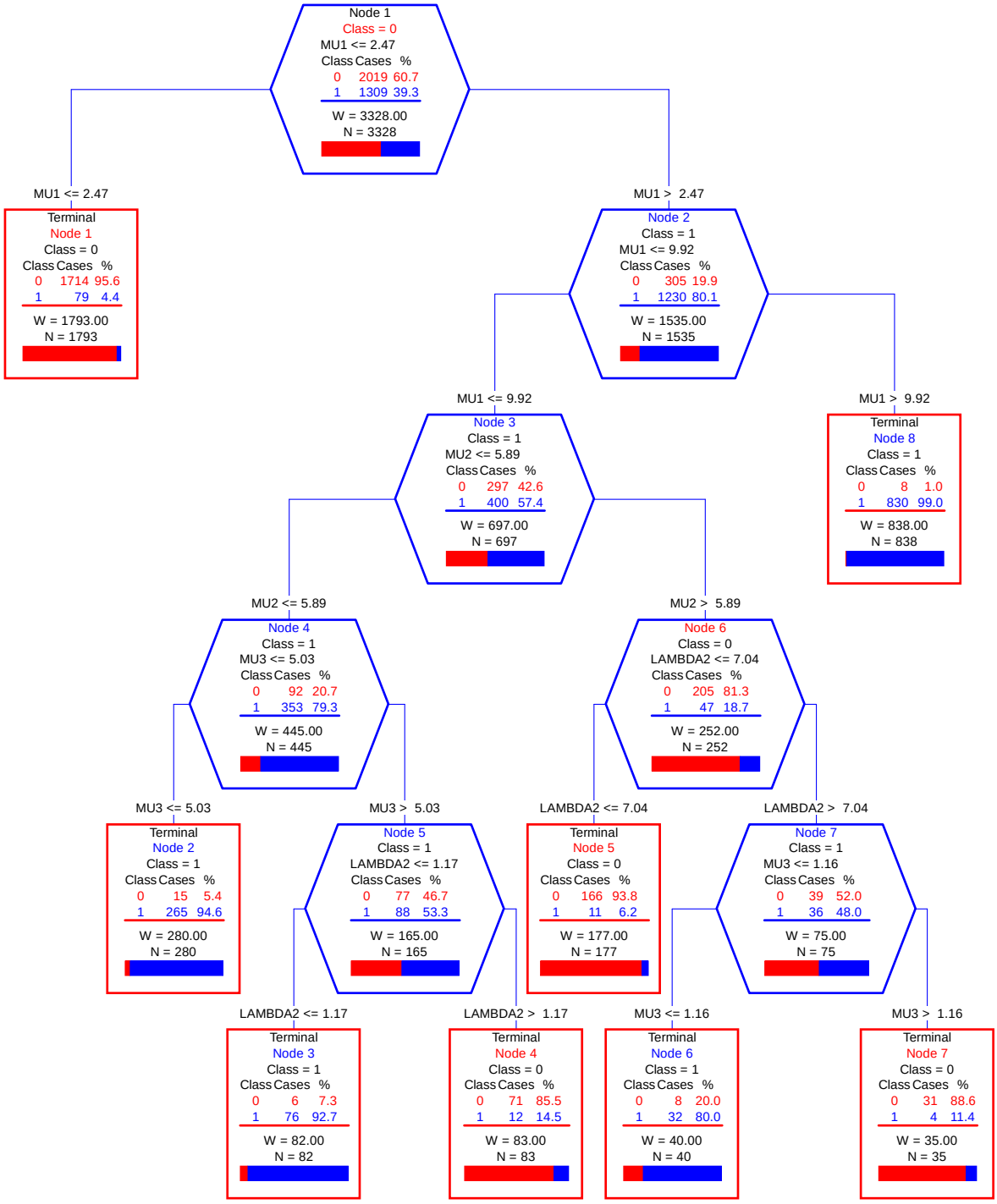

Figure B.6: CART tree for 3 phases with kappa ≥ 75

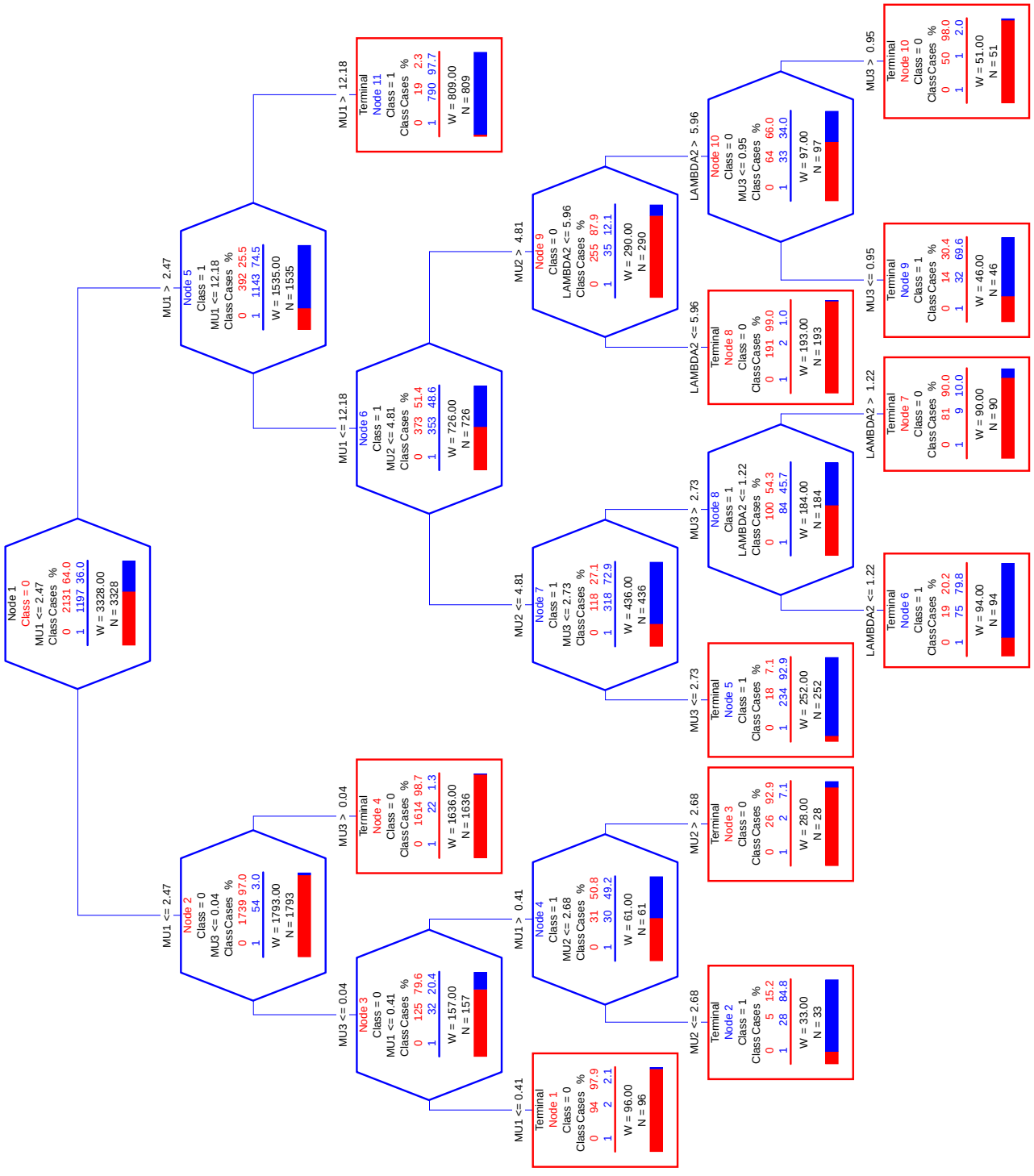

Figure B.7: CART tree for 3 phases with kappa ≥ 80

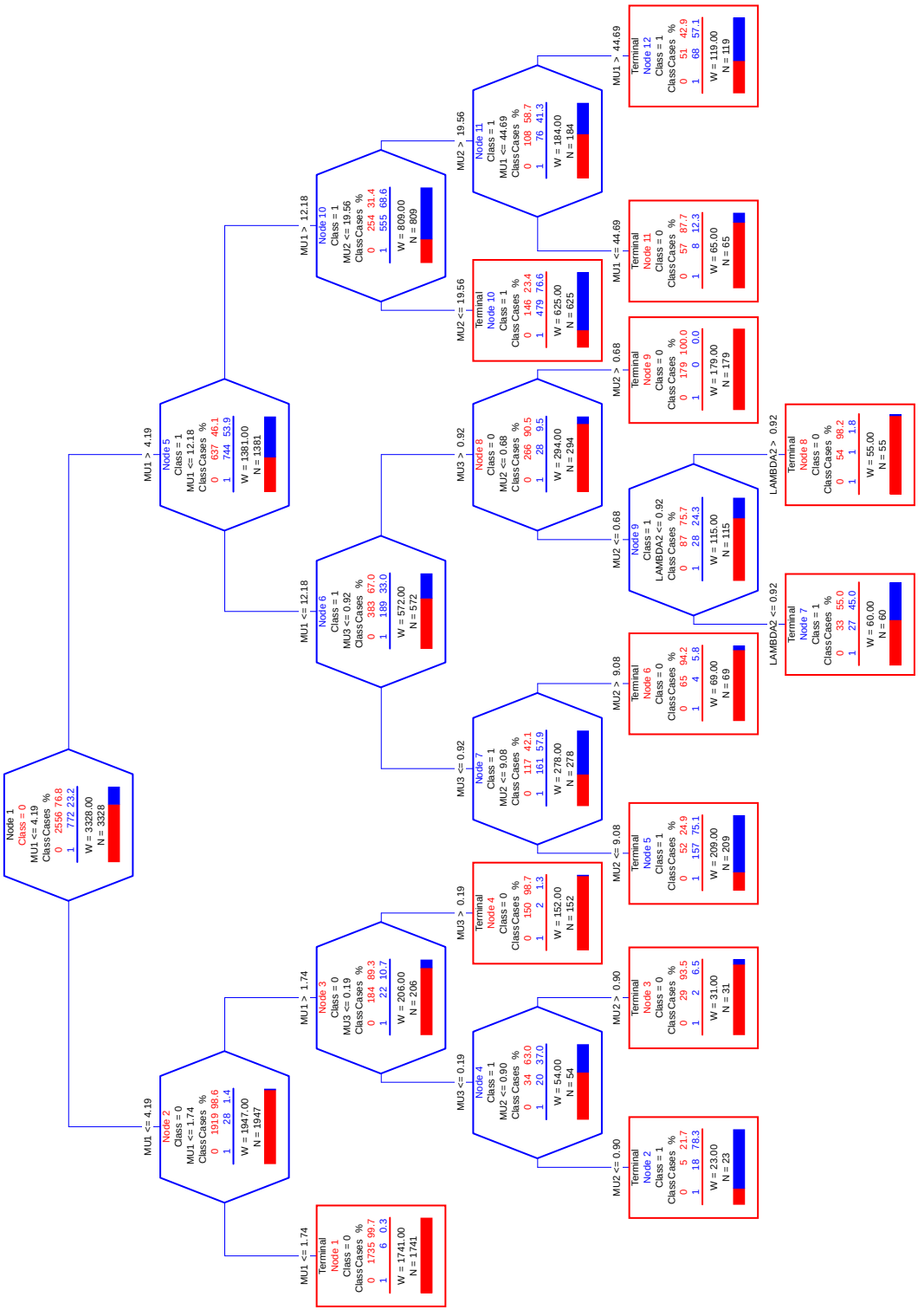

Figure B.8: CART tree for 3 phases with kappa ≥ 90

B.1.3 4 phase systems

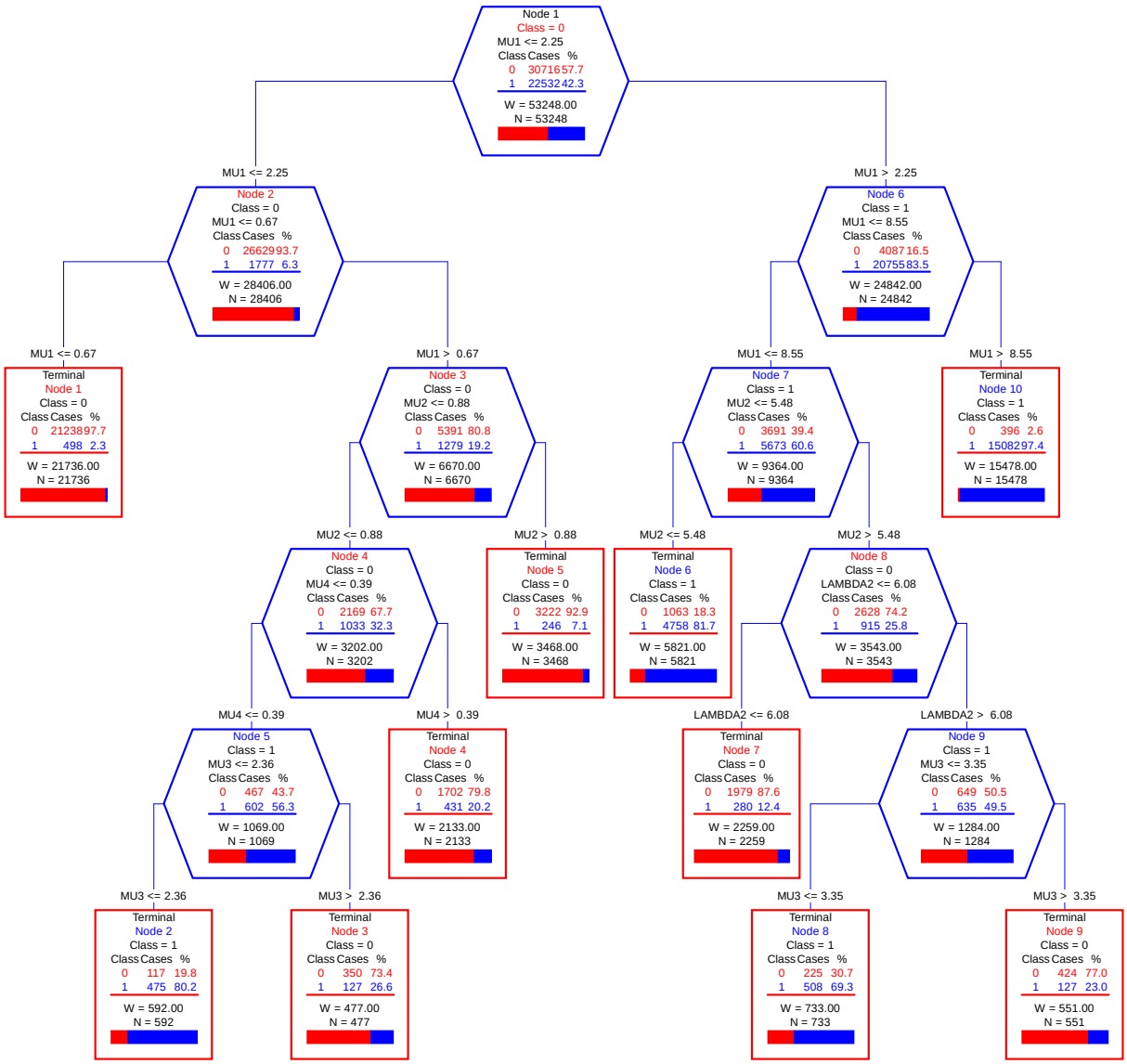

Figure B.9: CART tree for 4 phases with kappa ≥ 70

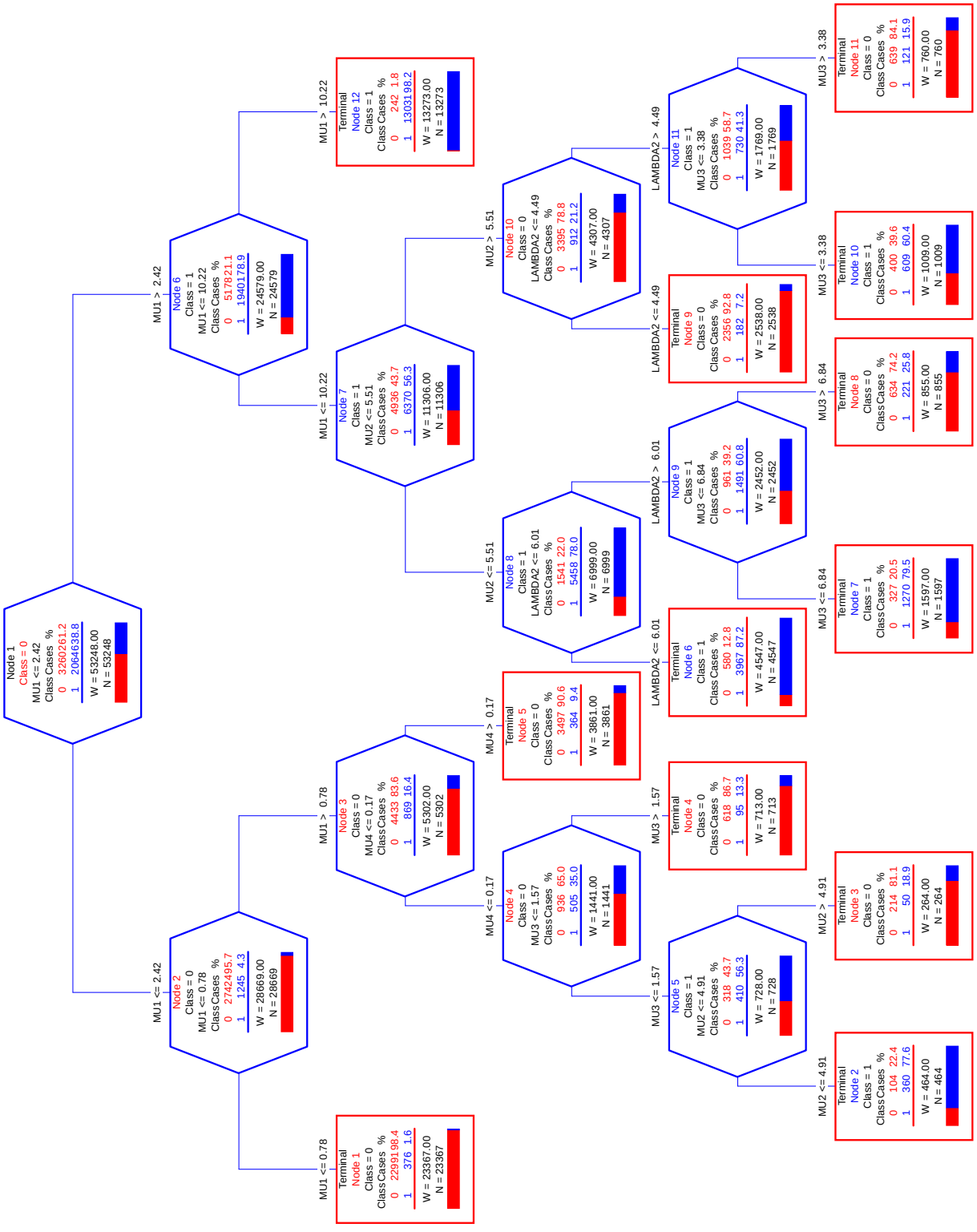

Figure B.10: CART tree for 4 phases with kappa ≥ 75

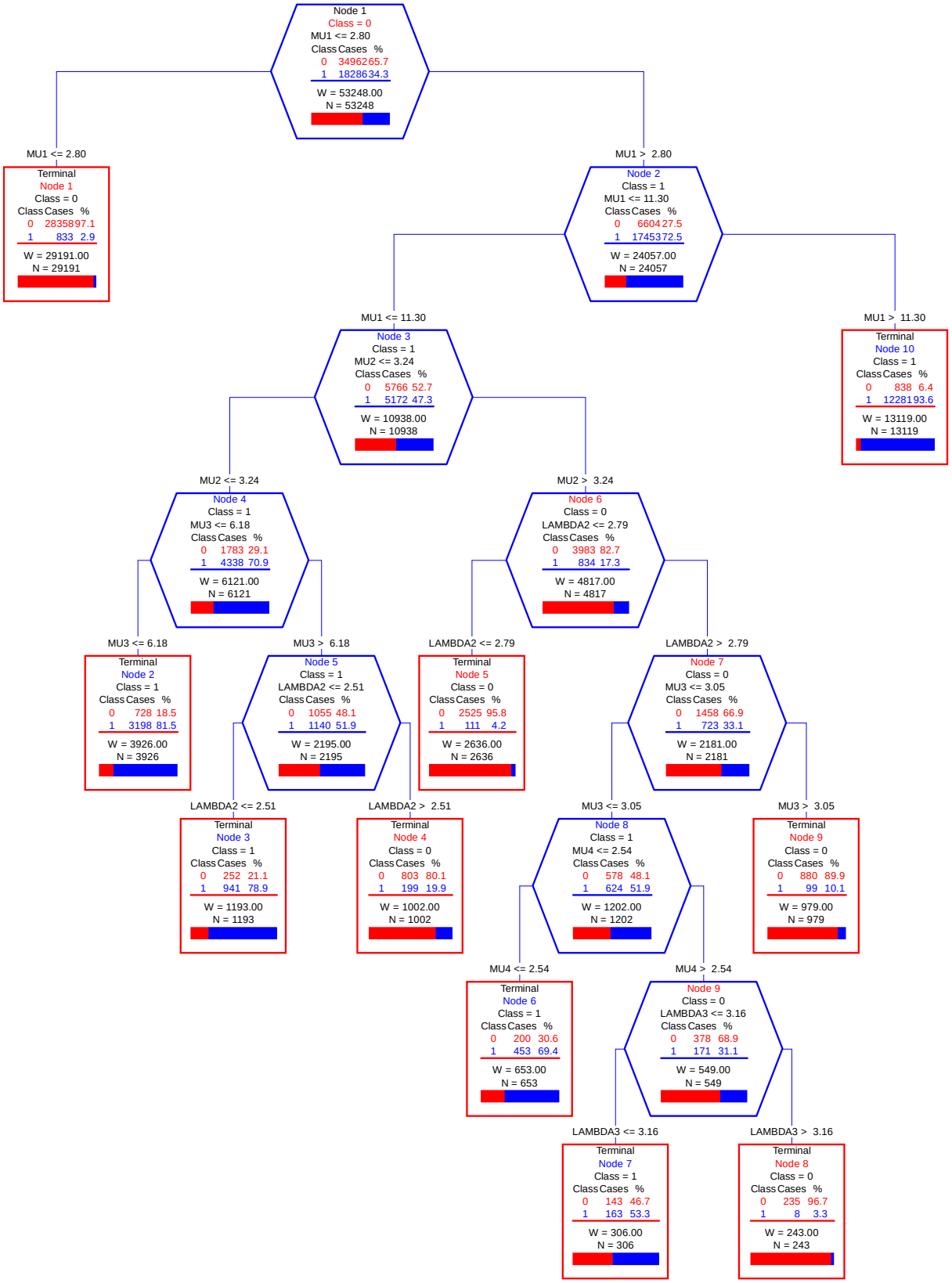

Figure B.11: CART tree for 4 phases with kappa ≥ 80

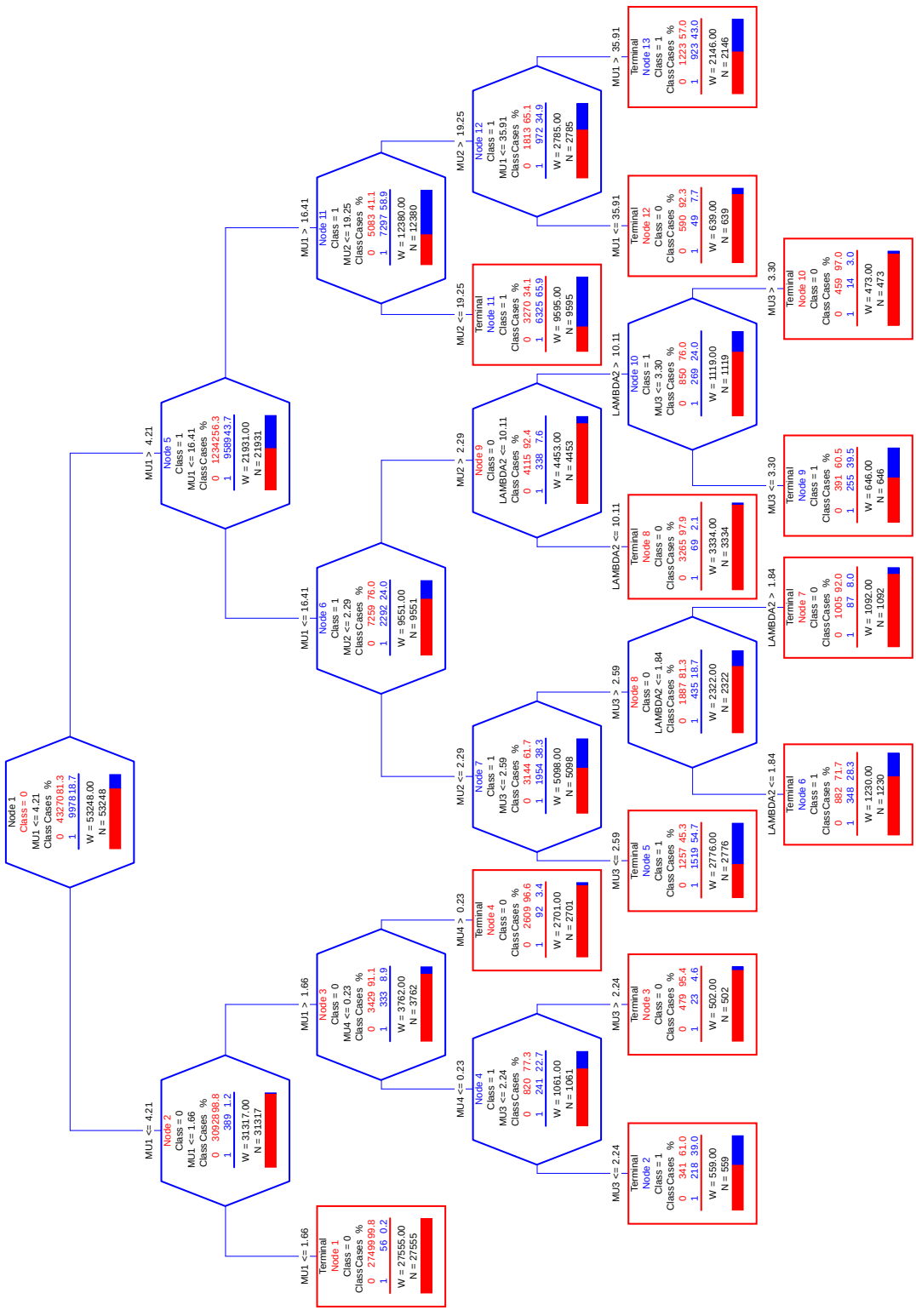

Figure B.12: CART tree for 4 phases with kappa ≥ 90

B.1.4 5 phase systems

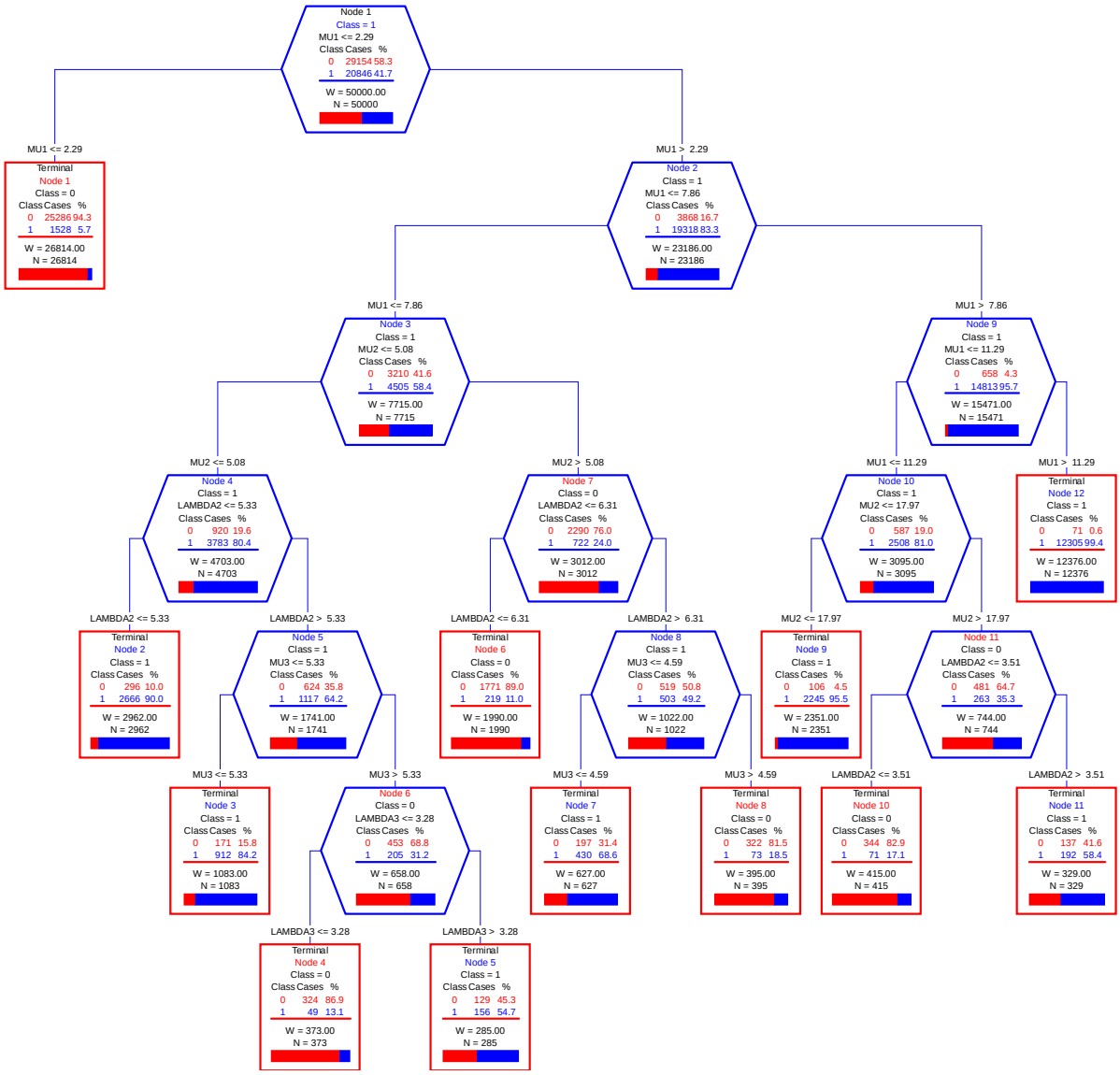

Figure B.13: CART tree for 5 phases with kappa ≥ 70

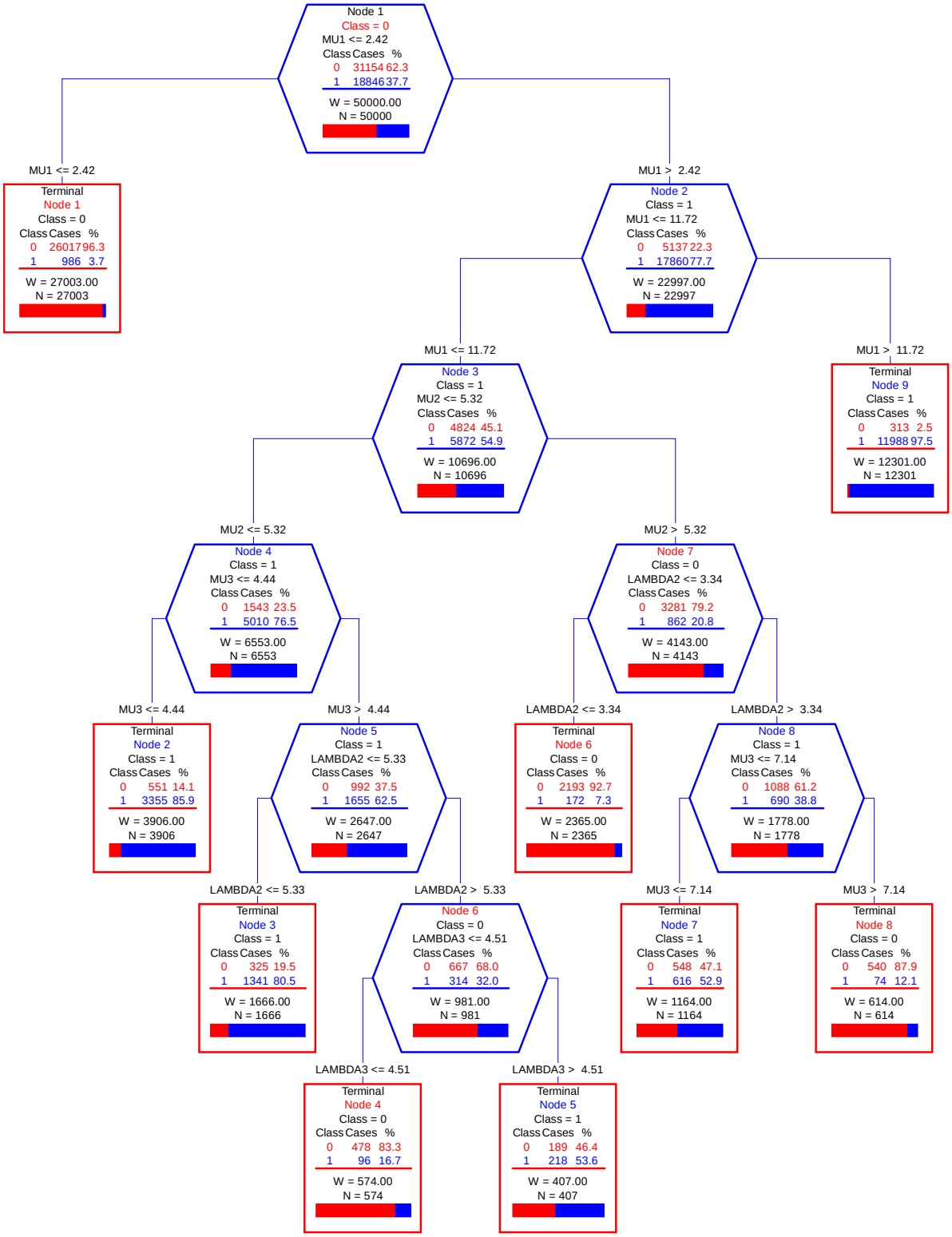

Figure B.14: CART tree for 5 phases with kappa ≥ 75

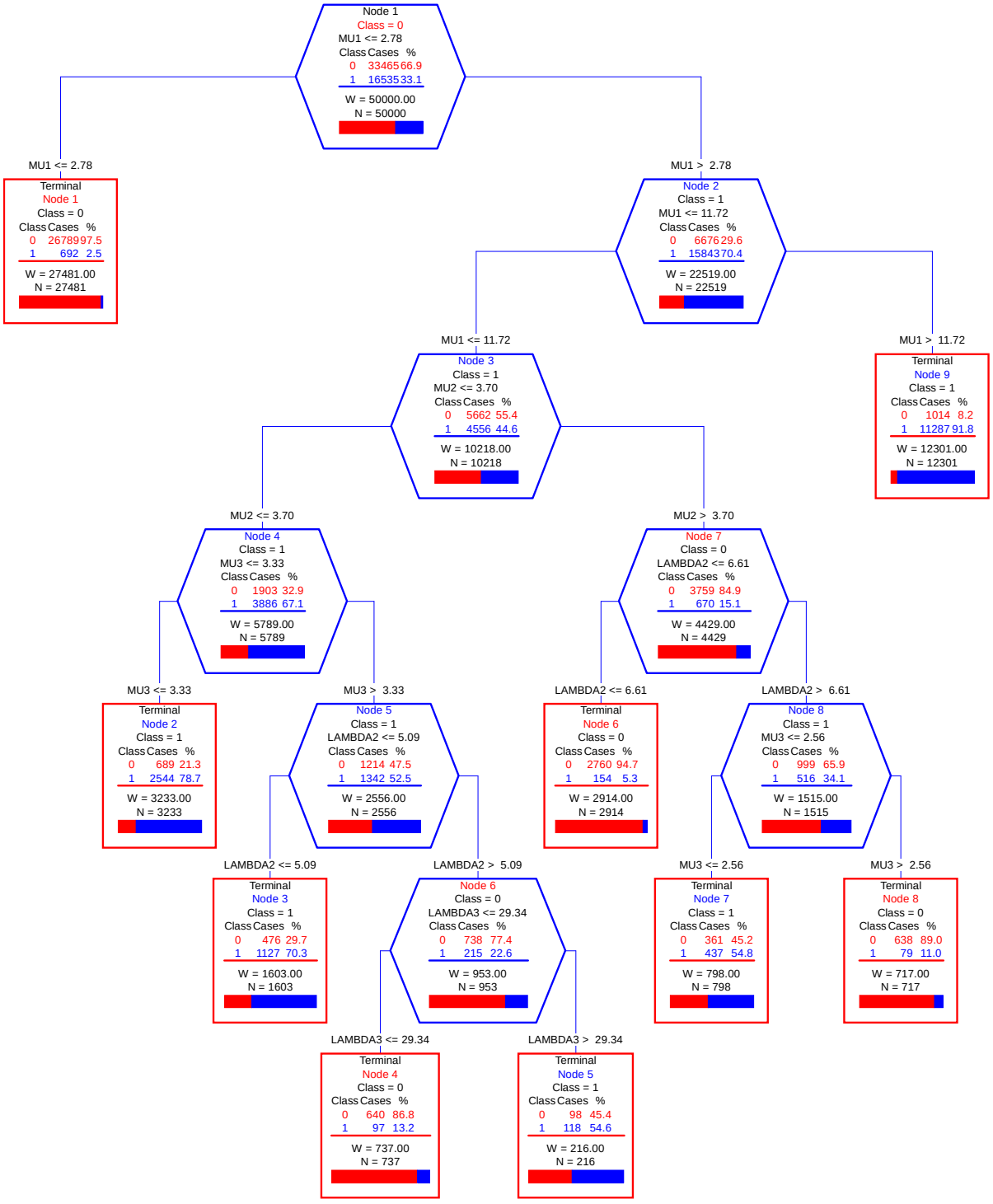

Figure B.15: CART tree for 5 phases with kappa ≥ 80

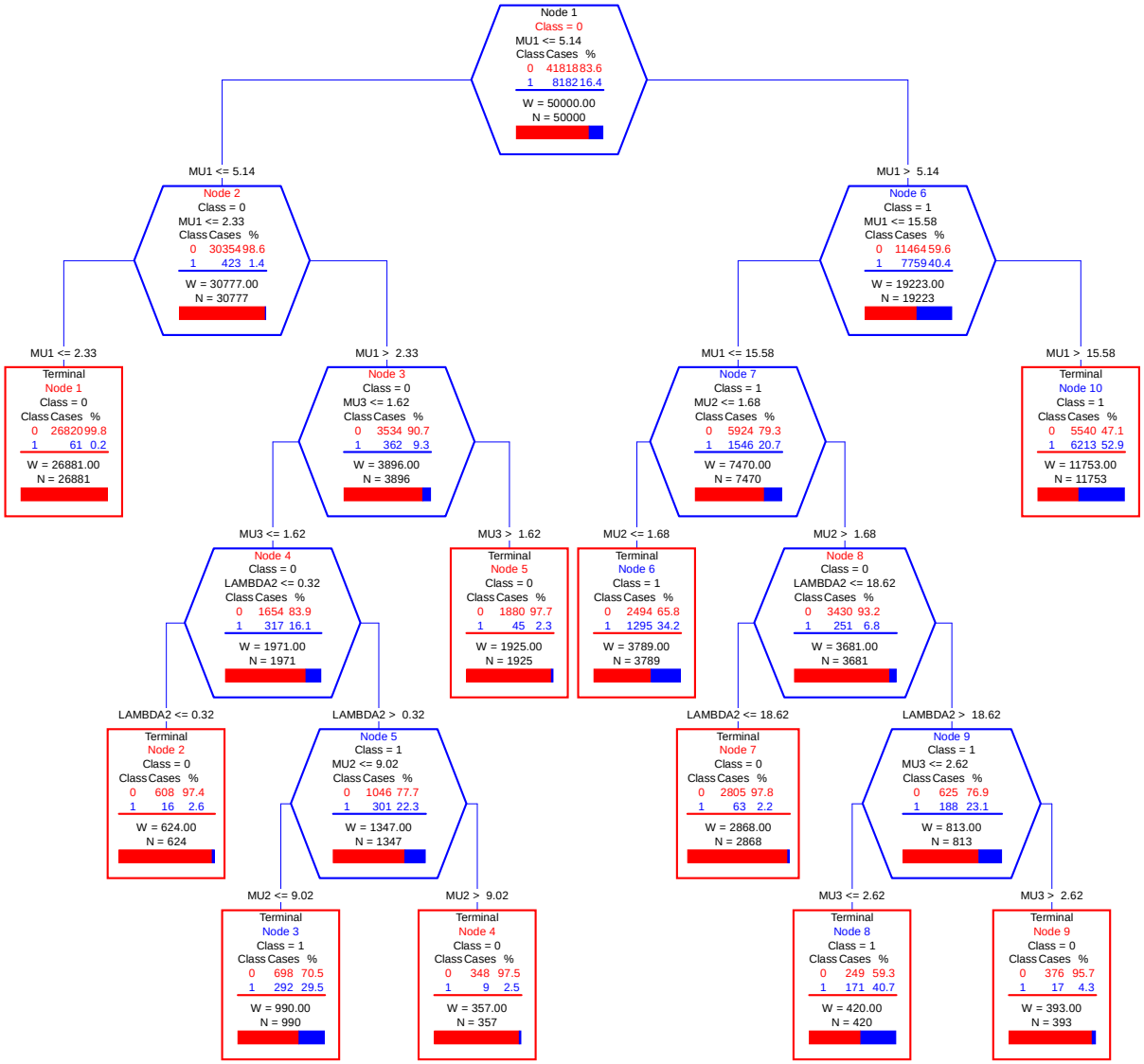

Figure B.16: CART tree for 5 phases with kappa ≥ 90

B.2 GLM Model Quality

Table B.1: Regression model quality at various penalties

2			3		
auc	λ	npars	auc	λ	npars
50			50		
0.968225776	0.265221839	1	0.958746266	0.149006716	1
0.998208939	0.01482805	2	0.962219805	0.112718116	2
0.999529696	9.76E-05	3	0.985368986	0.023180619	6
60			0.991154675	0.004767123	11
0.965155508	0.260931577	1	0.99343746	0.000105121	15
0.998446255	0.01103543	2	60		
0.999598005	8.75E-05	3	0.965387184	0.137792135	1
70			0.971510242	0.094974774	3
0.960675002	0.276628007	1	0.981136851	0.049519926	5
0.998743636	0.007347483	2	0.99035913	0.007019322	8
0.999583431	8.45E-05	3	0.993830863	8.86E-05	15
75			70		
0.95715746	0.294860584	1	0.96506178	0.162435682	1
0.998741419	0.005924436	2	0.971065548	0.122876636	2
0.999509006	0.000108461	3	0.990616668	0.025269731	5
80			0.995748583	0.002049706	11
0.951664241	0.308416808	1	0.996559613	9.51E-05	15
0.998157242	0.003891779	2	75		
0.998664173	7.82E-05	3	0.964513248	0.173976302	1
90			0.978577522	0.099555636	3
0.923015235	0.32223086	1	0.984501937	0.068619838	4
0.988889284	0.002326767	2	0.990911313	0.032599983	5
0.989041014	0.001007202	3	0.995155127	0.010675025	7
			0.997710308	0.000101898	15
			80		
			0.961576244	0.183621748	1
			0.979430004	0.095740532	3
			0.984172735	0.072424201	4
			0.991555113	0.034407363	5
			0.995447693	0.012365365	6
			0.99751	0.000206267	15
			90		
			0.919897606	0.186703527	1
			0.92092047	0.1701173	2
			0.956472613	0.0808195	3
			0.96138097	0.055705746	6
			0.970294085	0.003751309	9
			0.971223087	0.000702927	14

Table B.2: Regression model quality at various penalties (cont'd)

4			5		
auc	λ	npars	auc	λ	npars
50			50		
0.950011324	0.110211039	1	0.950130203	0.110206822	1
0.961611492	0.069215745	6	0.960322856	0.057461928	6
0.97490581	0.036089147	11	0.970783375	0.032881828	15
0.981251842	0.020651537	17	0.980572187	0.014233758	30
0.990116468	0.00167511	50	0.989718774	8.53E-05	238
0.991103297	0.000135873	63	60		
60			0.961282184	0.113377258	1
0.959478358	0.124003641	1	0.97216029	0.044718327	7
0.962121938	0.093804207	2	0.982231283	0.01763783	20
0.970921459	0.058911776	6	0.990044031	0.003627241	69
0.981000264	0.027987866	13	0.99271397	8.78E-05	237
0.99026028	0.005244415	31	70		
0.993340921	8.75E-05	61	0.962972245	0.146520577	1
70			0.970409803	0.083844461	2
0.961590232	0.16094857	1	0.980303694	0.033069983	11
0.971959197	0.07646361	3	0.990162215	0.005646212	46
0.980865171	0.043755289	7	0.994008297	8.58E-05	233
0.990131027	0.011895261	16	75		
0.995040743	0.000417665	59	0.961332587	0.14139028	1
0.995375441	8.59E-05	63	0.970544639	0.073721009	3
75			0.980178451	0.029077085	13
0.961673935	0.156769496	1	0.990043122	0.001958095	103
0.971220907	0.089709269	2	0.991869783	9.09E-05	236
0.982080529	0.042619171	7	80		
0.990212591	0.011586398	16	0.953899529	0.131103035	1
0.994744725	8.37E-05	61	0.962115363	0.075021977	2
80			0.970956469	0.035641517	9
0.956818491	0.161845957	1	0.980329679	0.008044361	47
0.966939015	0.084386616	2	0.985765663	7.68E-05	238
0.970202501	0.070059251	5	90		
0.98067795	0.030326977	9	0.903682916	0.09574436	1
0.990044462	7.87E-05	62	0.912244065	0.065992873	3
0.989962197	0.000150938	63	0.920502433	0.049921189	6
90			0.932783425	0.031351961	13
0.906427608	0.116966594	1	0.941004904	0.016346939	26
0.912989607	0.097107721	2	0.949762445	6.15E-05	239
0.9311805	0.060986479	6			
0.941165514	0.042035614	11			
0.951876459	0.013764769	21			
0.956511185	0.00022961	61			

B.3 Selected GLM Models

Before applying these models, all parameters must first be scaled by $\frac{1}{\lambda_1}$, then then transformed to a $\log_{10}$ scale.

κ	Model (2-phase)
70	$-4.437605 + 10.182409\mu_1 - 5.073068\mu_2 + 0.99253\mu_1\mu_2$
75	$-6.686979 + 12.455666\mu_1 - 6.55256\mu_2 + 1.24759\mu_1\mu_2$
80	$-7.073288 + 10.875399\mu_1 - 5.920741\mu_2 + 0.840106\mu_1\mu_2$
90	$-5.957541 + 5.746463\mu_1 - 3.617085\mu_2 + 0.531336\mu_1\mu_2$
κ	Model (3-phase)
70	$-1.816624 + 4.485771\mu_1 - 1.250766\mu_2 - 1.047059\mu_3 - 0.097858\lambda_2 - 0.145224\mu_1\mu_2 + 0.474228\mu_1\mu_3 + 0.140154\mu_2\mu_3 + 0.564145\mu_2\lambda_2 - 0.578532\mu_3\lambda_2 + 0.020248\mu_2\mu_3\lambda_2 + 0.058879\mu_1\mu_2\mu_3\lambda_2$
75	$-1.599673 + 2.998788\mu_1 - 0.816548\mu_2 - 0.615694\mu_3 + 0.057133\mu_1\mu_3 + 0.114055\mu_2\mu_3 + 0.264054\mu_2\lambda_2 - 0.327777\mu_3\lambda_2$
80	$-1.734529 + 2.565957\mu_1 - 0.701419\mu_2 - 0.46754\mu_3 + 0.086546\mu_2\mu_3 + 0.219284\mu_2\lambda_2 - 0.244218\mu_3\lambda_2$
90	$-2.180178 + 1.639036\mu_1 - 0.411212\mu_2 - 0.43417\mu_3 - 0.040729\mu_1\mu_2 - 0.036996\mu_1\mu_3 + 0.052424\mu_1\lambda_2 - 0.100106\mu_3\lambda_2 - 0.002589\mu_1\mu_3\lambda_2 - 0.02885\mu_1\mu_2\mu_3\lambda_2$

κ	Model (4-phase)
70	$-1.181308 + 2.827548\mu_1 - 0.689835\mu_2 - 0.37336\mu_3 - 0.320165\mu_4 - 0.017191\mu_1\mu_2 + 0.072286\mu_1\mu_3 + 0.147784\mu_1\mu_4 + 0.057049\mu_3\mu_4 + 0.287737\mu_2\lambda_2 - 0.219432\mu_3\lambda_2 - 0.10136\mu_4\lambda_2 + 0.097879\mu_3\lambda_3 - 0.156916\mu_4\lambda_3 + 0.061982\mu_3\lambda_2\lambda_3 - 0.0661\mu_4\lambda_2\lambda_3 - 0.003493\mu_2\mu_4\lambda_2\lambda_3$
75	$-1.545783 + 2.791171\mu_1 - 0.684503\mu_2 - 0.327746\mu_3 - 0.273757\mu_4 - 0.016541\lambda_3 - 0.003452\mu_1\mu_2 + 0.004784\mu_1\mu_3 + 0.044128\mu_1\mu_4 + 0.052769\mu_3\mu_4 + 0.231006\mu_2\lambda_2 - 0.207617\mu_3\lambda_2 - 0.091406\mu_4\lambda_2 + 0.085125\mu_3\lambda_3 - 0.159554\mu_4\lambda_3 + 0.059248\mu_3\lambda_2\lambda_3 - 0.067327\mu_4\lambda_2\lambda_3$
80	$-1.534312 + 1.980621\mu_1 - 0.395422\mu_2 - 0.154424\mu_3 - 0.13944\mu_4 + 0.033915\mu_2\lambda_2 - 0.108835\mu_3\lambda_2 - 0.015843\mu_4\lambda_2 - 0.091908\mu_4\lambda_3 - 0.009406\mu_4\lambda_2\lambda_3$
90	$-2.635265 + 1.683745\mu_1 - 0.366529\mu_2 - 0.283532\mu_3 - 0.236561\mu_4 + 0.016674\lambda_2 - 0.003733\lambda_3 - 0.007781\mu_1\mu_2 + 0.003053\mu_3\mu_4 + 0.115102\mu_1\lambda_2 - 0.146953\mu_3\lambda_2 - 0.060441\mu_4\lambda_2 - 0.090973\mu_4\lambda_3 - 0.081332\mu_1\mu_2\lambda_2 - 0.013898\mu_1\mu_3\lambda_2 - 0.01657\mu_1\mu_4\lambda_2 - 0.025633\mu_1\mu_4\lambda_3 + 0.020173\mu_3\lambda_2\lambda_3 - 0.026666\mu_4\lambda_2\lambda_3 - 0.010001\mu_1\mu_2\mu_4\lambda_2 - 0.010605\mu_1\mu_4\lambda_2\lambda_3 - 0.002364\mu_1\mu_2\mu_4\lambda_2\lambda_3$
κ	Model (5-phase)
70	$-0.930268 + 1.972912\mu_1 - 0.356563\mu_2 - 0.141244\mu_3 - 0.044066\mu_4 - 0.032394\mu_5 + 0.103777\mu_2\lambda_2 - 0.080003\mu_3\lambda_2 + 0.002582\mu_3\lambda_3 - 0.017022\mu_4\lambda_3 - 3.9e-05\mu_5\lambda_3 - 0.002138\mu_5\lambda_4$
75	$-1.290258 + 2.044235\mu_1 - 0.380456\mu_2 - 0.146066\mu_3 - 0.04921\mu_4 - 0.044617\mu_5 + 0.074061\mu_2\lambda_2 - 0.105263\mu_3\lambda_2 - 0.006768\mu_4\lambda_2 - 0.034001\mu_4\lambda_3 - 0.014358\mu_5\lambda_3 - 0.017589\mu_5\lambda_4 + 0.003429\mu_3\lambda_2\lambda_3 - 0.003278\mu_4\lambda_2\lambda_3$
80	$-1.516492 + 1.74582\mu_1 - 0.27043\mu_2 - 0.086199\mu_3 - 0.021999\mu_4 - 0.021075\mu_5 - 0.079799\mu_3\lambda_2 - 0.022277\mu_4\lambda_3 - 0.000168\mu_5\lambda_3 - 0.001079\mu_5\lambda_4$
90	$-2.766946 + 1.599676\mu_1 - 0.282602\mu_2 - 0.19298\mu_3 - 0.106194\mu_4 - 0.111089\mu_5 + 0.033543\lambda_2 - 0.020681\lambda_3 - 0.001549\lambda_4 + 0.074665\mu_1\lambda_2 - 0.127076\mu_3\lambda_2 - 0.032928\mu_4\lambda_2 - 0.013344\mu_5\lambda_2 - 0.067159\mu_4\lambda_3 - 0.019604\mu_5\lambda_3 - 0.042072\mu_5\lambda_4 - 0.098745\mu_1\mu_2\lambda_2 - 0.010908\mu_1\mu_3\lambda_2 - 0.008824\mu_1\mu_4\lambda_3 - 0.009873\mu_1\mu_5\lambda_3 - 0.021611\mu_4\lambda_2\lambda_3 - 0.01604\mu_1\mu_5\lambda_4 - 0.00717\mu_5\lambda_2\lambda_4 + 0.003574\mu_1\mu_2\mu_3\lambda_3 - 0.010166\mu_1\mu_2\lambda_2\lambda_3 - 0.005661\mu_1\mu_5\lambda_2\lambda_4 - 0.00289\mu_1\mu_5\lambda_3\lambda_4$