INTEGRATED SIMULATION AND OPTIMIZATION FOR DECISION-MAKING UNDER UNCERTAINTY WITH APPLICATION TO HEALTHCARE

A Dissertation

by

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ABSTRACT

Many real applications require decision-making under uncertainty. These decisions occur at discrete points in time, influence future decisions, and have uncertainties that evolve over time. Mean-risk stochastic integer programming (SIP) is one optimization tool for decision problems involving uncertainty. However, it may be challenging to develop a closed-form objective for some problems. Consequently, simulation of the system performance under a combination of conditions becomes necessary. Discrete event system specification (DEVS) is a useful tool for simulation and evaluation, but simulation models do not naturally include a decision-making component. This dissertation develops a novel approach whereby simulation and optimization models interact and exchange information leading to solutions that adapt to changes in system data.

The integrated simulation and optimization approach was applied to the scheduling of chemotherapy appointments in an outpatient oncology clinic. First, a simulation of oncology clinic operations, DEVS-CHEMO, was developed to evaluate system performance from the patient and managements perspectives. Four scheduling algorithms were developed for DEVS-CHEMO. Computational results showed that assigning patients to both chairs and nurses improved system performance by reducing appointment duration by 3%, reducing waiting time by 34%, and reducing nurse overtime by 4%.

Second, a set of mean-risk SIP models, SIP-CHEMO, was developed to determine the start date and resource assignments for each new patients appointment schedule. SIP-CHEMO considers uncertainty in appointment duration, acuity levels, and resource availability. The SIP-CHEMO models utilize the expected excess

and absolute semideviation mean-risk measures. The SIP-CHEMO models increased throughput by 1%, decreased waiting time by 41%, and decreased nurse overtime by 25% when compared to DEVS-CHEMOs scheduling algorithms.

Finally, a new framework integrating DEVS and SIP, DEVS-SIP, was developed. The DEVS-CHEMO and SIP-CHEMO models were combined using the DEVS-SIP framework to create DEVS-SIP-CHEMO. Appointment schedules were determined using SIP-CHEMO and implemented in DEVS-CHEMO. If the system performance failed to meet predetermined stopping criteria, DEVS-CHEMO revised SIP-CHEMO and determined a new appointment schedule. Computational results showed that DEVS-SIP-CHEMO is preferred to using simulation or optimization alone. DEVS-SIP-CHEMO held throughput within 1% and improved nurse overtime by 90% and waiting time by 36% when compared to SIP-CHEMO alone.

DEDICATION

I dedicate this dissertation to the memory of the loving relatives that I lost while working on this research: Grandaddy, Uncle Odell, Aunt Mae, Grandad, Aunt Trudy, Grandma, and Mary Jane. I am sorry for missing many of your final moments, but I hope you are proud to have a "doctor" in the family.

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NOMENCLATURE

ASAP	As-Soon-As-Possible
ASD	Absolute Semi-Deviation
CHEMO	Chemotherapy
DEVS	Discrete Event System Specification
DM	Decision Maker
EE	Expected Excess
IV	Intravenous
SES	System Entity Structure
SIP	Stochastic Integer Programming

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1. INTRODUCTION

1.1 Motivation and Problem Statement

Simulation and mathematical optimization are useful modeling tools for many decision-making problems in science and engineering. In real complex systems, data uncertainties often evolve over time. Decision makers are sometimes required to make important system decisions prior to observing uncertain events. Often the decisions epochs occur during discrete times periods and influence future decisions. Consequently, modeling the system using an explicit mathematical formulation can be impossible, and simulation of the system performance under a combination of conditions becomes necessary in order to model uncertain events and evaluate possible decision options. Due to data uncertainties in the system, decision-making is *not* trivial and requires stochastic optimization to determine a combination of stochastic conditions that would result in best system performance.

This dissertation concerns such challenging decision-making problems under uncertainty. Motivation for this work stems from the lack of solution methods for the class of decision-making problems described above, which have many real life applications. For example, problems arising in healthcare regarding patient service management under limited resources (e.g. nurses, medical equipment, etc.) call for system *simulation* and *stochastic optimization* due to there complexity. These problems have uncertainty in several aspects of the decision problem such as the arrival of appointment scheduling requests, treatment duration, and resource availability.

Stochastic optimization has evolved into a viable approach for decision-making under uncertainty, much of the progress has been made under simplifying assumptions such as closed-form objective functions, precise knowledge of a static under-

lying probability distribution, and decisions do not influence future decisions. In many practical applications, however, these simplifying assumptions are not appropriate. For example, in oncology clinic operations performance measures such as throughput or overtime cannot be captured by a closed-form mathematical expression and the probability distribution of an appointment duration can change over time. Scheduling decisions made in one time period will impact future decisions and outcomes. Also, scheduling oncology clinic patients later than the oncologist's prescribed treatment start date can pose *risk* to the patient in terms how they respond to treatment. Therefore, simulation of the underlying system is necessary in order to make any data-driven decisions. Consequently, SIP alone is *not* adequate for optimal decision-making in this case.

Discrete event simulation has been shown to be a useful tool for evaluating complex systems under a given combination of conditions. However, simulation models are traditionally designed without knowledge of possible mathematical decision models. Therefore, simulation alone is generally not sufficient when it comes to making optimal decisions under uncertainty. A new framework for combining stochastic optimization with simulation is needed, whereby the stochastic optimization and system simulation models interact and exchange information leading to solutions that adapt to changes in system data.

The *objective* of this dissertation is to *develop and implement theory, models, and algorithms for integrated discrete event simulation and stochastic optimization with application to healthcare.* Specifically, this dissertation integrates discrete event system specification (DEVS) simulation and mean-risk stochastic integer programming (mean-risk SIP) under a new paradigm termed, DEVS-SIP.

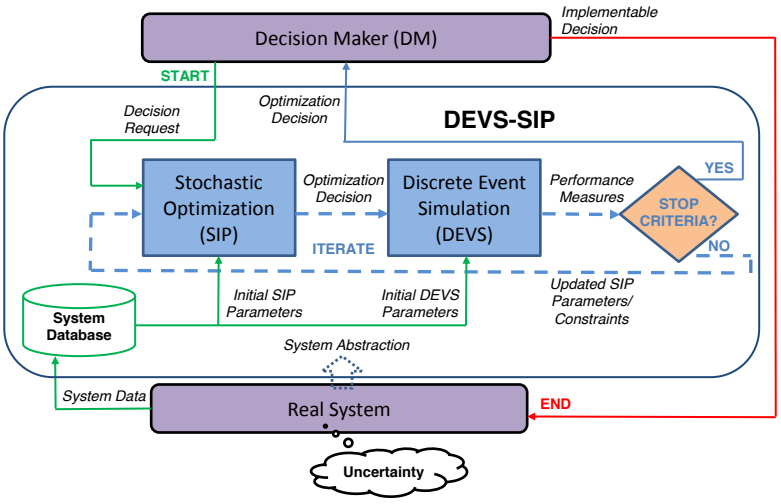


Figure 1.1: DEVS-SIP Framework for Decision-Making Under Uncertainty

In the DEVS-SIP framework (Figure 1.1), a decision maker (DM) of a real system uses simulation and optimization to make decisions. The simulation and optimization models are both abstractions of the real system and have access to system data, including uncertain system parameters. The DM uses a SIP model to make a decision when there is uncertainty in the problem's parameters. The SIP model decisions are only optimal for the current state of the system and the limited information used to formulate the model. By using SIP, the decisions should perform "good" under any realization of future uncertainty. However, a tractable formulation of the SIP model will not consider all problem parameters with as much granularity as a simulation model can. Furthermore, the future decisions and their impact on the current decision are difficult to incorporate into a SIP model.

The optimization decisions from the SIP model are implemented and evaluated using a DEVS simulation model that also simulates future decisions and outcomes. The DM determines practical levels of system performance which are then used

to established stopping criteria for the solution search process. If the performance measures from the DEVS simulation satisfy the stopping criteria established by the DM, then the SIP model's most recent optimization decision is provided to the DM. Otherwise, the performance measures that failed to meet the stopping criteria are used to modify the SIP model's parameters and constraints. The modifications (e.g., changing objective function coefficients, adding constraints, etc.) depend on the specific application and the targeted performance measures.

The revised SIP model is then solved to determine a new optimization decision for evaluation in the DEVS simulation model. This process is repeated until the stopping criteria are satisfied and the results are reported to the DM. The DM then determines an *implementable decision* for the real system. An implementable decision is a course of action that can be put into effect after careful consideration. The DM may implement the decision provided by DEVS-SIP, modify the decision, or even choose an alternative course of action.

In this dissertation, the integrated DEVS-SIP methodology is applied to the healthcare setting of oncology clinic operations management. Oncology clinics deal with scheduling patients and allocating limited resources such as treatment chairs and nurses. The decision-making process in this setting involves scheduling a series of appointments for each new cancer patient based on the oncologist's prescription. A scheduler is tasked with the responsibility of determining the appointment schedule for the patient and the resource assignments for each appointment in the patient's treatment regimen. The scheduler knows the new patient's treatment regimen, the clinic's resource characteristics, requirements for resource assignment, and past scheduling decisions.

Complicating the decision is the uncertainty in *appointment duration*, *patient acuity levels* and *nurse availability*. The realization of uncertain parameters and the

number and type of future appointment requests that will also compete for clinic resources are unknown. A simulation model of the oncology clinic can evaluate possible decisions under the realization of uncertainty. The performance measures from the simulation model can then be used to update the optimization model. This process will continue until a decision is identified that best satisfies the performance measure expectations determined by the DM. The nature of the oncology clinic setting is suitable for decision-making under uncertainty (mean-risk SIP) and system simulation (DEVS).

1.2 Research Tasks

Three research tasks were completed to achieve the objective of integrating discrete event simulation and stochastic optimization with application to healthcare. First, a simulation model of the underlying healthcare problem was designed and implemented. Next, the chemotherapy appointment scheduling decision was modeled using an optimization model. Finally, the simulation and optimization models were integrated using the DEVS-SIP framework. Next is an overview of each research task.

1.2.1 Simulation Model for Oncology Clinic Operations

In the first task (Chapter 3), a DEVS model of a real oncology clinic called DEVS-CHEMO was developed. The DEVS-CHEMO simulation model allows for modeling and simulating the arrival of appointment requests, the arrival process of the patients to the clinic on the day of their appointment, and the activities of clinic resources. DEVS-CHEMO was also designed to allow for assessing and evaluating different patient scheduling rules using performance measures from both the patient's and management's perspectives. DEVS-CHEMO was verified using a real oncology clinic setting through collaboration with the Scott & White Oncology Clinic in Temple,

Texas. Four scheduling algorithms were developed and implemented to determine which resources were important for chemotherapy appointment scheduling. Experiments were also conducted to demonstrate the effectiveness of DEVS-CHEMO in determining staffing levels for the oncology clinic.

1.2.2 Mean-Risk Stochastic Integer Programming Model for Oncology Clinic Appointment Scheduling

The second task (Chapter 4) was to develop mean-risk SIP models for the problem of scheduling patients, chairs, and nurses in an outpatient oncology clinic. The models produced in this task are the first optimization models for oncology clinic appointment scheduling that incorporate uncertainty in the problem parameters and addresses the concept of risk-averse decision-making. In the mean-risk SIP models, called SIP-CHEMO, appointments are scheduled for a patient based on recommendations from an oncologist. The models determine the appointment dates, start times, and resource assignments. Mean-risk SIP allows for modeling different levels of risk using mean-risk measures such as *expected excess* and *absolute semideviation*. Risk in this problem is associated with how likely an appointment schedule will cause scheduling conflicts such as overlapping appointments or overtime. Three SIP-CHEMO models were developed, implemented, and compared to current scheduling methods in a real oncology clinic.

1.2.3 Integrated Simulation and Optimization for Oncology Clinic Operations

The final task (Chapter 5) required the development of a new framework, termed DEVS-SIP, which enables interaction between simulation (DEVS) and optimization (mean-risk SIP). The real system is simulated using DEVS. In each decision period, the parameters for the mean-risk SIP model are computed via DEVS. The mean-risk SIP model is then solved to determine an optimal decision for the current state of

the system. The decisions are implemented in a second DEVS simulation model which incorporates future uncertainty for system performance evaluation. If the stopping criteria are satisfied, then the best decision is implemented in the original DEVS simulation model. Else, the mean-risk SIP model is updated to obtain a new decision that is also evaluated in the second DEVS simulation model. DEVS-SIP is a general framework designed to be tailored to different applications.

To demonstrate the DEVS-SIP framework, the mean-risk SIP-CHEMO optimization model and the DEVS-CHEMO simulation model were combined. This dissertation then applied DEVS-SIP to decision-making under uncertainty for oncology clinic operations management. This new methodology, called DEVS-SIP-CHEMO, enables data-driven decision-making for both strategic and operational planning in oncology clinics. Four stopping criteria and four modifications were developed for DEVS-SIP-CHEMO. The stopping criteria and modifications were implemented in different combinations to determine which was most effective in improving system performance.

1.3 Research Contributions

This dissertation advances the state-of-the-art in stochastic programming with simulation by contributing new concepts, models, and algorithms, for a variety of applications. Specific contributions are as follows:

- *DEVS simulation model of oncology clinic operations.* The DEVS-CHEMO simulation model allows for modeling and simulating the arrival of appointment requests, the arrival process of the patients to the clinic on the day of their appointment, and the activities of oncology clinic resources. DEVS-CHEMO provides managers with a tool for analyzing decision-making and operational policies within the oncology clinic.

- *Mean-Risk SIP model of oncology clinic decisions.* The mean-risk SIP-CHEMO optimization model is the first optimization model for the decision problem of scheduling oncology clinic patients, chairs, and nurses under uncertainty and considering risk. The inclusion of a suitable mean-risk measure in the objective function enables DMs to consider risk preferences in their scheduling decisions.

- *New simulation and optimization framework for many applications.* This contribution provides a new paradigm, DEVS-SIP, for decision-making under uncertainty for complex problem settings. DEVS and SIP are extended to a new level beyond some of the traditional impractical assumptions. The extensions include, **1**) formal coupling between DEVS and SIP, **2**) decision-making available in DEVS using an SIP model, **3**) non-static probability distributions for SIP (generated via DEVS), and **4**) non-closed-form objective functions for SIP (modeled, evaluated, and revised via DEVS). An important feature of DEVS-SIP is that it allows for automated online (or real-time) system data update for both DEVS and SIP models, thus enabling decision-making over time adapting to dynamic changes in the problem data. This kind of decision-making framework is necessary in many practical applications where a decisions have to be made at discrete time periods over a rolling horizon.

- *Integrated solution method for decision-making of oncology clinic operations management.* The integrated DEVS-SIP-CHEMO simulation and optimization model is a practical tool for decision-making of oncology clinic operations under uncertainty. DEVS-SIP-CHEMO enables data-driven decision-making for both strategic and operational planning in oncology clinics. Furthermore, the computational results for the DEVS-SIP-CHEMO show that integrating simulation and optimization yields better overall system performance results

that either method alone. Results also provide insight into the practicality and use of the DEVS-SIP framework in a real setting and for other applications.

DEVS-SIP has the potential to address many important decision problems in a variety of applications, such as extended attack response planning for large-scale escaped wildfires. Optimal decision-making for such a problem has the potential to save lives as well as billions of dollars in property damage and natural resources. For the case of oncology clinic appointment scheduling, optimal decisions under uncertainty provide an improved patient-centered experience and reduce clinic overtime.

1.4 Dissertation Organization

The rest of this dissertation is organized as follows: Chapter 2 reviews closely related work in simulation and optimization, oncology clinic operations, mean-risk SIP, and discrete event simulation. The DEVS-CHEMO simulation model for oncology clinic operations is developed, verified, and analyzed in Chapter 3. Mean-risk SIP-CHEMO models for scheduling oncology clinic appointments are developed and analyzed in Chapter 4. Chapter 5 develops an integrated simulation and optimization framework that combines the SIP-CHEMO optimization model and the DEVS-CHEMO simulation model and provides computational results. Finally, concluding remarks and future research directions are discussed in Chapter 6.

2. LITERATURE REVIEW

This chapter provides a literature review of simulation and optimization methodology, oncology clinic operations management, DEVS, and mean-risk SIP. Each section identifies gaps in the existing literature and further motivates the need for the proposed research. The first section discusses how simulation and optimization have been previously combined and describes specific applications in the healthcare setting. The second section discusses existing classification-based and optimization-based approaches for chemotherapy appointment scheduling problems. The third section examines the history of discrete event simulation, the development of DEVS, and the use of simulation in healthcare. Finally, a review of the development of mean-risk SIP is provided in the fourth section.

2.1 Simulation and Optimization Methodology

Simulation and optimization have been integrated to solve problems from various applications, including the healthcare setting. Table 2.1 summarizes three papers from other application areas and six papers from the healthcare setting. Although simulation and optimization in healthcare and other areas have shown promising results, the general methodology has never been formally developed. Additionally, most other works use the simulation model to evaluate the optimization decisions, generate scenarios for the optimization model, or compute parameters or objectives for the optimization model. None of these works have used the simulation model to revise the optimization model to improve the scheduling decisions for oncology clinic operations management.

Table 2.1: Simulation and Optimization Literature Review

Paper	Brief Description	Application
Cheung et al. [9]	Simulation and optimization applied to network service planning.	Other Applications
Ko et al. [21]	Hybrid simulation and optimization approach for a distribution network design.	
Acar et al. [1]	Simulation and optimization for combinatorial problems applied to a facility location problem.	
Kropp et al. [23]	Recursive simulation and optimization approach for staffing and facility plans.	Healthcare
Butler et al. [6]	Linkage of a simulation and optimization model for facilities strategic hospital planning.	
Baesler and Sepulveda [5]	Combine simulation, goal programming, and a genetic algorithm to examine the impact of resource capacities at an oncology clinic.	
Pérez et al. [29]	Stochastic online scheduling for appointments in nuclear medicine.	
Woodall et al. [48]	Simulation-optimization for daily nurse schedules at an outpatient oncology clinic.	
Gocgun and Puterman [13]	Use Markov decision processes and approximate dynamic programming to schedule chemotherapy patient appointments and evaluate the decisions with simulation.	
This work	Develops a general discrete event simulation and stochastic optimization framework applied to oncology clinic operations management.	

Simulation and optimization have been used for network service planning [9]. In a two-stage methodology, the optimization model determined the network configuration at the macro-planning level, then the simulation model verified and evaluated the performance at the operational level before sending feedback to the optimization model. Ko et al. [21] also used a "hybrid" simulation and optimization approach for the distribution network design of third-party logistics to evaluate the performance for warehouses. The framework of the "hybrid" model was such that the optimization model generated a network, then the simulation was used to evaluate warehouse capacities. If the simulation outputs satisfied the performances, then the procedure terminated. Otherwise, the design parameters and constraints were modified in the optimization model. The work by Cheung et al. [9] and Ko et al. [21] are different from this dissertation in that this work formally defines a DEVS and SIP framework for how the simulation and optimization models interact for multiple decisions over a planning horizon instead of only one decision period. Additionally, this dissertation is applied to a different application area.

Acar et al. [1] used an integer optimization model and a simulation to solve combinatorial problems. In their iterative approach, the optimization model was used to generate a solution. If the solution had already been simulated, then the iteration stopped. If not, then the simulation was used to evaluate the solution. The difference between the deterministic cost function and the average simulation cost was used to update the optimization formulation. The work by Acar et al. [1] differs from DEVS-SIP in that the DEVS-SIP optimization model also considers uncertainty from the decision problem and the system performance motivates the stopping criterion.

Early research using simulation and optimization for healthcare problems focused on facilities planning [6, 23]. Kropp et al. [23] used a mixed-integer program (op-

timization model) to generate staffing and facility plans and a simulation model to evaluate their day-to-day acceptability. The optimization model provided a decision-making component and reduced the number of alternatives for the simulation model to examine. The simulation model was designed to handle the system's complex relationships that were too cumbersome for the optimization model. A linear regression used the simulation results to add non-cost constraints to the optimization model. In the work by Butler et al. [6], simulation and optimization were used for multi-level strategic evaluation of hospital plans and decisions. The optimization model dealt with the facility layout and capacity allocation while the simulation model was used to capture the complexities of the hospital operations. Both works [6, 23] utilized simulation and optimization for a different type of healthcare problem than the research in this dissertation and both used deterministic optimization models.

Multi-objective simulation optimization was developed by Baesler and Sepulveda [5] for a cancer treatment center. Their work combined simulation, goal programming, and genetic algorithms. The goal was to find the optimal number of clinic resources that best improved a multi-objective formulation. The simulation model was a black box representing the objective functions for the problem and the genetic algorithm performed the search for improved solutions.

Both simulation and optimization have been used to address stochastic online appointment scheduling in nuclear medicine [29]. A stochastic online scheduling algorithm used an optimization model to determine patient and resource schedules. The simulation model obtained scenarios for the stochastic programming models and tested the performance. The computational study by Pérez et al. [29] considered both patient and clinic performance measures. They concluded that the stochastic online scheduling algorithm allowed more patients per year on average and decreased patient waiting time for an appointment by an average of two days. The research

in this dissertation is different because the simulation model is used to update the optimization models to find decisions that improve system performance.

A discrete event simulation model was used to predict patient waiting time and resource utilization at the Duke Cancer Institute [48]. A simulation analysis revealed that nurses are the limiting resource in the clinic. A mixed-integer programming model was used to optimize the nurse schedules on a weekly and monthly basis. Then a simulation-optimization approach optimized the daily schedule for the nurse shifts. The optimization model's objective was intractable so simulation was used to sample expected patient waiting times. Tabu search and other heuristics were used to find a near-optimal schedule. The work by Woodall et al. [48] is important because it analyzed the benefits of using detailed nurse schedules, included a combination of full-time and part-time nurses from different cancer disease groups, and incorporated varying start time shifts for nurses.

Finally, simulation and Markov decision processes (MDP) have been used together to dynamically schedule chemotherapy patient appointments [13]. Each appointment in the treatment regimen was assumed to have a time window, within a few days, of a target appointment date. A MDP and an approximate dynamic programming (ADP) model was developed to determine the date for each appointment. The simulation was used to evaluate the scheduling decisions of the ADP as compared to several heuristics. The research in this dissertation focuses on a different set of decisions and uses simulation to update the optimization model's decisions.

2.2 Oncology Clinic Operations Management

In the last decade research has developed in the area of scheduling of chemotherapy appointments. Hospital and clinic staff were the first approached the problem using various classification-based approaches. Classification-based approaches used

acuity levels [18, 24], next-day scheduling [12, 33], or patient classification systems [7]. It was not until the last two to three years that operations researchers began utilizing optimization-based techniques to schedule chemotherapy appointments [8, 36, 46]. None of the optimization-based techniques included uncertain problem parameters in the optimization model.

2.2.1 Classification-Based Chemotherapy Scheduling

Table 2.2 contains a summary of the literature on the chemotherapy appointment scheduling problem using classification-based approaches. A number of oncology clinics have tried to improve the scheduling of chemotherapy appointments using various classification approaches. Some clinics created schedules by classifying nurse tasks [24] or acuity levels [18] while others have used drug [12] or patient types [7]. Although none of these classification techniques used optimization or uncertainty, they were simple methods that were successfully implemented in practice. These works provide guidance on the key aspects of the decision problem (acuity levels, resource availability, treatment duration, etc.). In addition, many clinics [12, 24, 33] have noted considerable success using next-day scheduling. A *next-day*, or *split-scheduling*, method implies that patient arrives one day for blood work and returns the next day to receive their chemotherapy treatment.

One next-day scheduling system used nurse task classification based on the time required to complete the tasks [24]. The three-step process of (1) lab and x-ray, (2) oncologist visit, and (3) chemotherapy administration was scheduled over two or three days. This system assumed that the time between appointments was "free" and thus patients spent less time waiting. After implementation, the laboratory observed fewer inquiry calls, more balanced nursing workloads, and more time for preparation and assessment. Rosenburg [33] also used a split-scheduling system for

three out-patient chemotherapy centers. The new system allowed the clinic to order the chemotherapy drugs overnight. Analysis revealed more chair space, more efficient use of nurses, reduced inventory, and increased patient satisfaction.

Table 2.2: Literature Review on Classification-based Techniques for Chemotherapy Appointment Scheduling

Paper	Brief Description
Langhorn and Morrison [24]	Patient appointment scheduling using nine acuity levels.
Doblish [12]	Next-day scheduling system in an oncology center using a drug classification system.
Gruber et al. [14]	Identified a "perfect day" for cancer patients and oncology clinic staff.
Chabot and Fox [7]	Patient classification system in an outpatient infusion center.
Hawley and Carter [18]	Development of a scheduling system based on an acuity rating system.
Rosenburg [33]	Split-scheduling system for three out-patient chemotherapy centers.
Ahmed et al. [3]	Developed a scheduling template based on a best-scenario performance using a simulation model.
Kallen et al. [20]	Identified and prioritized four items (IV assessment, quick treatments, completion of chemotherapy orders, and pharmacy notification) to improve patient waiting times.

One next-day chemotherapy scheduling system used drug classification based on infusion times [12]. Rising demand for treatment caused overtime, long patient wait times, and high resource utilization. Patients were arriving early for their appointments hoping to get through the system faster, but this only led to congestion in the clinic. The next-day system allowed the pharmacy adequate preparation time before administration. After implementation, the quality of work-life improved for the clinic staff and patients accepted the changes. The repeated success of next-day scheduling systems motivated the decision to limit the scope of the chemotherapy scheduling problem to only the drug infusion appointment.

In one study, the "perfect day" for cancer patients and oncology clinic staff was developed at the Roswell Park Cancer Institute in Buffalo, NY [14]. The common goal was for patient appointments to begin on time. A series of improvements were implemented to achieve this goal. Some of the improvements included changing staff start times, cross-training nurses, revising the patient appointment schedule, and modifying prescribing practices. Prior to implementing the changes, only 11% of appointments began on time as compared to 94% afterwards.

A two-patient classification system (those with pre-medications and those without) was developed by Chabot and Fox [7]. Prior to this classification system, patients were often double-booked and had long waiting times, appointments rarely began on the recommended start date, and nurses had inadequate breaks. The new scheduling system required a minimum break time between appointments. After three years of implementation, the clinic observed an increase of 10% throughput, longer lunch breaks for the nurses, a decrease in late arrivals, increased job satisfaction, and increased patient satisfaction. An acuity rating system was developed at a Cleveland cancer center to address scheduling problems [18]. They developed a medical oncology five-level acuity rating system. After treatment lengths were

also incorporated in the scheduling template, the new system resulted in improved patient satisfaction scores.

One study aimed to increase throughput and reduce patient waiting time in the chemotherapy treatment unit at CancerCare Manitoba [3]. Several scenarios were created that matched resource schedules with the clinics arrival pattern of patients. A simulation model analyzed each scenario's performance. The scenario with the best performance was used to create a scheduling template. The new template increased throughput by 22.5% and increased resource utilization without requiring more resources.

At the Ambulatory Treatment Center of the MD Anderson Cancer Center in Houston, TX, researchers implemented four new policies to improve patient wait time [20]. First, they began performing earlier evaluations on the appropriateness and accessibility of IV lines. Second, short-duration appointments were streamlined to a specific unit. The third modification began directly paging oncologists to complete drug orders. Finally, the fourth change notified the pharmacy earlier in the treatment process that a patient was ready for medication. In combination, the four changes showed a 25% improvement in the time patients waited on the day of treatment.

2.2.2 Optimization-Based Chemotherapy Scheduling

Table 2.3 contains a summary of the literature on the chemotherapy appointment scheduling problem using optimization-based approaches. In the past three years, researchers started using optimization models to address the chemotherapy scheduling problem. One model producing near optimal solutions was implemented in a real clinic setting [46], but the results are not necessarily applicable to other clinics. Although one study did consider uncertainty in real time decision requests [17], none of the works incorporated uncertainty in the problem parameters.

Table 2.3: Literature Review on Optimization-based Techniques for Chemotherapy Appointment Scheduling

Paper	Brief Description
Santibáñez et al. [36]	Developed chemotherapy appointment scheduling software (Chemo Smartbook) to determine near-optimal schedules.
Chan [8]	Used an inverse optimization model to determine nurses' preferences in the Chemo Smartbook.
Sadki et al. [35]	Oncology appointment scheduling with oncology and bed resources using lagrangian-based heuristic and local optimization heuristics.
Turkcan et al. [46]	Multi-period time horizon chemotherapy schedule with rolling horizon methodology.
Sevinc et al. [42]	Negative feed-back algorithm for laboratory scheduling and heuristic for multiple knapsack problem of scheduling infusion appointments.
Woodall et al. [48]	Mixed-integer programming model for nurse weekly and monthly scheduling and simulation-optimization model for daily nurse shifts.
Hahn-Goldberg et al. [17]	Dynamic template scheduling to accommodate online appointment requests and cancellations.
Gocgun and Puterman [13]	Used Markov decision processes and approximate dynamic programming to schedule patient appointments within specific time windows.
This work	Uses stochastic optimization and simulation to account for uncertainty in three problem parameters when scheduling chemotherapy appointments and clinic resources.

The paper-based scheduling system at the British Columbia Cancer Agency's (BCCA) Vancouver Cancer Centre was insufficient to handle increased demand and more complex treatments. A Chemo Smartbook [36] scheduling system was developed as an innovative software approach that offered customized, flexible scheduling and considered patient time preferences, appointments from different departments, system capacity, nurse workload, and staff schedules. The implementation of the Chemo Smartbook led to 58% reduction in late patient appointment confirmations and a wait list reduction of 84%. Overall patient satisfaction increased, staff workload became more balanced, and stress levels were reduced. Furthermore, the wait-list size decreased by 84% and the number of days to first appointment decreased from eleven days to five days. Later, Chan [8] used an inverse optimization model to determine nurses' preferences in order to create better schedules in the Chemo Smartbook.

Another study also addressed the appointment scheduling problem in an outpatient oncology clinic [35]. Their work is one of the few that consider the oncologist consultation in the problem setting. After mathematically modeling this problem, two solution methods were considered: a Lagrangian relaxation-based heuristic and local optimization heuristic. Numerical tests showed the Lagrangian relaxation-based heuristic to be best.

A multi-period time horizon approach to address the problem of scheduling patients and resources for an oncology outpatient clinic was developed by Turkcan et al. [46]. The objectives were to minimize the treatment delay, patient waiting times, and staff overtime while simultaneously maximizing the staff utilization. In this two-stage problem, the first stage determined the treatment start day for the patients. In the second stage of the problem, the daily schedule was determined for all patients. Turkcan et al. [46] proposed an algorithm for solving their two-stage problem and used a rolling horizon methodology. The optimization model is closely related to

the one presented in this dissertation, but it did not include mean-risk measures or uncertain problem parameters.

Algorithms for scheduling chemotherapy regimens were developed by Sevinc et al. [42] with the goal of maintaining the treatment regimen specifications, minimizing patient waiting time, and optimizing chair utilization. This was one of the few papers to consider lab appointments along with infusion appointments. The plan for laboratory tests used an adaptive negative-feedback algorithm and target infusion chair utilization to control the load on the system. If the laboratory test results were approved by the oncologist, the second-phase determined infusion seat allocation. The second-phase was modeled using a multiple knapsack problem and solved using on-line heuristics. A simulation model was used to evaluate the scheduling methods. The main contribution of [42] was that this work addressed infusion appointment cancellations and delays due to poor laboratory test results.

Recall that Woodall et al. [48] used a mixed-integer programming model to optimize nurse schedules on a weekly and monthly basis. The problem considered a combination of full-time and part-time nurses from different cancer disease groups. A simulation-optimization model determined a near-optimal daily schedule for the nurse shifts with the objective of minimizing the expected patient wait time. Because the model's objective was intractable, a simulation was used to sample expected patient waiting times.

Recently, a dynamic optimization model was developed by Hahn-Goldberg et al. [17] to schedule chemotherapy appointments. Their work considered uncertainty through real-time requests for appointments and uncertainty due to last-minute scheduling changes. This work used a scheduling template and online optimization in a novel technique they refer to as dynamic template scheduling. A sample of appointments were used in a deterministic optimization model to create a schedul-

ing template for the day. As appointment requests arrived, the appointments were allocated to available slots in the template. When a request arrived that did not fit the template, a new, smaller sample of appointments were generated and the open time slots were once again optimized to include the latest scheduling request. To accommodate last minute cancellations and requests, a shuffling algorithm moved appointment start times within a predefined time limit. Results show that their approach improved the makespan by 20% compared to the current practice.

Finally, recall that Gocgun and Puterman [13] used simulation and Markov decision processes (MDP) to dynamically schedule chemotherapy patient appointments. In their problem, each appointment in the treatment regimen was assumed to have a time window, within a few days, of a target appointment date. The scheduling problem determined the date for each appointment using a MDP. The MDP was intractable so a linear-programming approximate dynamic programming (ADP) model was used to obtain an approximate solution. The simulation was implemented in GAMS and used to evaluate the scheduling decisions of the ADP as compared to several heuristics. Although the ADP solution approach was valid, the earliest policy heuristic, which schedules patients on the earliest available day within each appointment's respective time window, also worked well and was faster computationally.

2.3 Discrete Event Simulation

Discrete event simulation first emerged in the 1950s and is now a well-known tool for operations research analysts in various applications such as manufacturing, finance, and healthcare. Tocher and Owen [45] is generally credited with creating the first simulator called the general simulation program. Over time, simulation has become popular in computational techniques such as Monte Carlo methods and random number generation. Additionally, discrete event simulation has been used

in various modeling approaches such as queuing theory, stochastic processes, and DEVS. This section discusses the history of the DEVS formalism and the use of discrete event simulation in healthcare.

The DEVS formalism was developed by Zeigler et al. [51]. Many DEVS extended formalisms have been introduced with their own purposes such as P-DEVS for parallel discrete event simulation [11] and RT-DEVS for realtime discrete event simulation [10]. The DEVS formalism and its variations have been used to simulate fire spread, nuclear medicine departments, and manufacturing systems. The text by Zeigler et al. [52] provides theory and modeling for the integration of discrete event simulation and continuous complex dynamic systems. For an introduction to DEVS modeling and simulation methodology, see Zeigler and Sarjoughian [50], which defines the concepts of experimental frame, models, state transitions, etc. used in the DEVS formalism and provides minimal working examples.

In the past several decades, discrete event simulations have been used as a tool for analyzing healthcare problems. Many of the contributions in this area are summarized in Jun et al. [19]'s extensive taxonomy of research using discrete-event simulations in healthcare clinics between 1978-1997. The taxonomy identified a void in research on complex integrated systems, such as multi-facility healthcare delivery systems. Additionally, Jun et al. [19] specified the combination of simulation and optimization as a future research direction. The taxonomy identified five papers that used optimization to arrive at parameters for a simulation model, but none of them used the simulation to improve decision making criteria for the optimization model. At the time of the taxonomy's publication, many simulation software packages were just beginning to provide an optimization add-on to the software to provide special search algorithms to guide a simulation model to an optimal or near-optimal solution.

A survey by Günal and Pidd [15] indicated that there has been a notable in-

crease in the number of papers published on discrete event simulation in healthcare since 2004. They concluded that few simulation papers propose or illustrate general approaches, but instead focus on specific healthcare applications such as an intensive care unit or emergency room. There have been several authors who have used discrete event simulations in outpatient clinics. Guo et al. [16] presented a discrete event simulation framework for the evaluation and optimization of outpatient clinic scheduling rules. Takakuwa and Katagiri [43] used simulation for the modeling of patient flows in a large-scale outpatient hospital ward using electronic medical records. More recently, Weerawat et al. [47] modeled the orthopedic outpatient department in a large public hospital.

A DEVS simulation model for multi-step sequential nuclear medicine procedures was developed in Pérez et al. [28], Pérez-Roman [30]. This work also included stochastic online scheduling algorithms where the appointment requests were revealed one at a time. The characteristics of the nuclear medicine problem differs from the chemotherapy scheduling problem. For example, the nuclear medicine requires strict time windows due to the short half-life of radio-pharmaceuticals and resources are not shared among multiple patients.

A number of simulation models have been used for oncology clinics (Table 2.4). The first simulation model identified in the literature for an outpatient oncology clinic was developed by Sepulveda and Cahoon [41]. The simulation model analyzed the impact of alternate floor layouts on resource and patient flow. The results indicated that a relocation of the clinic's pharmacy and laboratory, along with scheduling changes, would allow an increase of 30% in patient throughput using the same number of clinic resources. The performance measures in their study were patient waiting times and clinic closing time.

Table 2.4: Literature Review on Oncology Clinic Simulations

Paper	Brief Description
Sepulveda and Cahoon [41]	Developed an ARENA simulation model to analyze the layout of an outpatient oncology clinic.
Ahmed et al. [3]	Used an ARENA simulation model to analyze the performance of a scheduling template in an outpatient oncology clinic.
Yokouchi et al. [49]	Developed an ARENA simulation model of blood exams, oncologist visits, and chemotherapy infusions at an outpatient oncology clinic.
Sevinc et al. [42]	Used Micorsoft SQL to simulate the scheduling and postponement of lab tests and infusion appointments.
Woodall et al. [48]	Used an ARENA simulation model to sample expected patient waiting times for the objective of an optimization model.
Gocgun and Puterman [13]	Used a GAMS simulation to evaluate the proposed scheduling policies for chemotherapy patient appointments.
This work	Uses simulation to generate requests for appointments by cancer patients, to evaluate the scheduling decisions made by a mean-risk SIP optimization model, and to update the optimization model for improved decisions.

A simulation model developed by Ahmed et al. [3] was used to analyze the performance of a scheduling template in an oncology clinic. Using ARENA Rockwell Simulation Software, the simulation modeled five stations in the chemotherapy unit and two main resources, chairs and nurses. The oncologist visit and laboratory tests were excluded from the simulation model. Yokouchi et al. [49] developed a simulation

model of an outpatient oncology clinic to explore appointment scheduling based on properties of the treatments. The ARENA simulation model included blood exams, oncologist visit, and chemotherapy infusion. The results indicated that a scheduling method based on infusion time was necessary.

Recall that some simulation models of the oncology clinics have been used as analysis tools for scheduling methods [42]. Other simulation models of oncology clinics have been previously discussed in combination with simulation-optimization [13, 48]. This dissertation uses DEVS integrated with mean-risk SIP to generate requests for appointments, evaluate the scheduling decisions, and update the optimization model for improved decisions.

2.4 Mean-Risk Stochastic Integer Programming

This research uses mean-risk SIP for optimal decision-making under uncertainty. Mean-risk stochastic programming [34] was first developed for financial risk analysis and began with the axiomatic principles of stochastic dominance, a form of stochastic ordering. In a two-stage mean-risk SIP, the first-stage decision variables represent the "here and now" decisions while the second-stage decisions represent the "recourse" decisions made after uncertainty is realized. Historically, SIP used the expected value of the first-stage objective function, which is appropriate for the risk-neutral case or when the law of large number can be applied. But in certain applications it may be more appropriate to explicitly model risk within its objective. *Mean-Risk SIP models* represent risk using both the expected value and a mean-risk measure in the objective function to more accurately reflect the inherent uncertainty in a problem.

Early risk measures such as variance and value-at-risk (VaR) did not provide suitable properties for analysis. Artzner et al. [4] defined four properties of coherent risk measures: translation invariance, subadditivity, monotonicity, and positive ho-

mogeneity. Ogryczak and Ruszczynski [27] discussed the transition from stochastic dominance to mean-risk as a means of quantifying risk-aversion using both the mean and a measure of risk. Pflug [31] presented some properties and comparisons of VaR and conditional value-at-risk (CVaR). The analysis concluded that CVaR is a coherent risk measure. Pflug [31] also defined the VaR optimization problem and the CVaR optimization problem for portfolio optimization. The VaR optimization problem is nonconvex in general, but the CVaR risk measure provides either a singleton or a convex polyhedron solution.

The structural properties of the expectation in the objective function such as real valuedness and lower semicontinuity are derived in Schultz [37]. Relatively recently, Märkert and Schultz [26] and Schultz [38] obtained similar results for the mean-risk measures based on either *quantiles* or *deviations* from some target. The quantile measures include *excess probability* and *CVaR*, while the deviation measures include *expected excess* and *absolute semideviation*.

Structural and algorithmic properties of two-stage stochastic linear programs (SLP) with deviation measures were derived in Kristoffersen [22]. Similar results for excess probability were obtained in Riis and Schultz [32]. Risk aversion for SLP was addressed in Ahmed [2] with a focus on convexity properties and subgradient decomposition. Stochastic mixed-integer programs with risk functionals based on the semideviation and value-at-risk (VaR) were studied in Märkert and Schultz [26] and in a thesis by Tiedmann [44]. Schultz and Tiedemann [39] studied SIP based on excess probabilities, while Schultz and Tiedemann [40] studied SIP2 based on conditional value-at-risk (CVaR). Although SIP has been used to schedule appointments in nuclear medicine [29], the complexities and constraints were quite different than those seen in oncology clinics. To the best of our knowledge, this dissertation is the first to use mean-risk SIP for oncology clinic appointment scheduling.

3. SIMULATION MODEL FOR ONCOLOGY CLINIC OPERATIONS

Chemotherapy is a common treatment method for cancer patients. Chemotherapy treatments are administered orally or intravenously at outpatient oncology clinics. Reports have shown that cancer costs in the U.S. exceeded $124 billion in 2010 and are expected to increase 27% by 2020 [25], while the demand for oncology services is projected to increase by 48% between 2005 and 2020 [46]. Cancer patients receiving chemotherapy treatment require a series of appointments over several weeks or months and the timing of these appointments is critical to the treatment's effectiveness. Oncology clinics deal with the problem of scheduling the cancer patients' appointments using limited clinic resources. The timing sensitivity as well as the rising costs and demand motivate the need for efficient chemotherapy appointment schedules.

This chapter describes the design, verification, and testing of a simulation model for an outpatient oncology clinic using DEVS. The simulation, termed DEVS-CHEMO, models the scheduling process of clinic resources (chairs and nurses) and chemotherapy patients, the arrival process of the patients to the clinic for each appointment, and the oncology clinic operations as patients receive chemotherapy treatment. DEVS-CHEMO was also designed to enable oncology clinic managers to evaluate different patient scheduling algorithms and operations planning decisions using performance measures from the patient and management perspectives.

Chemotherapy appointment scheduling decisions involve a complex problem setting due to high level of interaction among patients, nurses, and other resources in the system. Because of this complexity, oncology clinic managers find it challenging to assess the impact of their scheduling decisions on overall clinic operations and per-

formance. Modeling and simulation is a viable approach to addressing this aspect of the chemotherapy appointment scheduling problem. In this chapter, modeling and simulation are used to develop a discrete event simulation model, DEVS-CHEMO, using the DEVS formalism. The DEVS formalism allows for hierarchical and modular construction and uses well-defined concepts for coupling components. The modular construction allows the user to design and construct models independently. By coupling components, the individual models can interact with one another and even combine to create a hierarchy of models.

DEVS-CHEMO is a useful tool that allows the oncology clinic managers to address the chemotherapy scheduling problem by evaluating different appointment scheduling algorithms and implementation policies. The testing of DEVS-CHEMO in this chapter focuses on how patients should be scheduled and the impact of the number of nurse resources in the clinic. DEVS-CHEMO has been designed to capture performance measures from both the patient and management perspectives in order to identify scheduling policies that achieve high levels of patient service and satisfy the clinic's business objectives.

The contributions of this dissertation include a discrete event simulation of outpatient oncology clinic operations, an innovative tool that can assist oncology clinic managers in determining appointment scheduling and operational policies. Additionally, DEVS-CHEMO not only allows assessment from the management perspective, but the patient perspective as well. Thus DEVS-CHEMO provides an advance toward higher levels of patient service in healthcare. The DEVS-CHEMO simulation results provide insight for oncology clinic managers on how to schedule chemotherapy appointments and determine staffing needs.

The rest of the chapter is organized as follows: section 3.1 provides background information on outpatient oncology clinic scheduling. The DEVS formalism is first

reviewed in section 3.2, then the DEVS-CHEMO simulation model is presented including the system objects, model abstraction, performance measures, hierarchical design, and implementation. Simulation results are reported in section 3.3 while section 3.4 summarizes the chapter.

3.1 Background on Outpatient Oncology Clinics

In an oncology clinic, once a patient is diagnosed with cancer, an oncologist prescribes a unique *treatment regimen*, or series of chemotherapy appointments, to each cancer patient based on the patient's current state of health. A treatment regimen (Table 3.1) consists of a prescribed *start date* for the patient, frequency of appointments (*treatment days*), the suggested *duration* (in minutes), *acuity level* (values of 1, 2, or 3), and *drug name* for each appointment. The start date is the number of days into the future that the patient's oncologist recommends for the first treatment to begin. Treatment days specifies the spacing between each appointment. In the example in Table 3.1, the patient has three treatments spaced two days apart. Duration is the total time that the appointment is expected to take from the time the patient arrives to the clinic until they are discharged from the clinic. The acuity level is a relative measure of the nurse's attention required by a patient during an appointment. Finally, the drug name is a list of the chemotherapy drugs the patient will receive during the appointment. Treatment regimens depend on the patient's type of cancer, stage of the cancer growth, and current health. Therefore treatment regimens are unique to each individual patient.

Table 3.1: Example Treatment Regimen

Start Date	Treatment Days*	Duration (mins.)	Acuity Level	Drug Name
1	1	118	1	Alimta, Carboplatin
	3	540	3	Carboplatin, Taxol
	5	320	2	Carboplatin, Taxol

*Oncologist specifies start date

Figure 3.1 illustrates the chemotherapy scheduling process. The treatment regimen prescribed by the oncologist is sent to a scheduler to determine the appointment schedule and to allocate clinic resources for each appointment in the treatment regimen. All appointments in the treatment regimen need be scheduled at this time to guarantee the availability of the later appointments. To maximize treatment effectiveness, these appointments should be scheduled as close to the state date recommended by the oncologist as possible. Delay from the prescribed start date is referred to as *type I delay*. Delays patients experience in the waiting room is referred to as *type II delay*. The time elapsed between the patient being seated in their chemotherapy chair until the infusion begins is referred to as the *type III delay*. The scheduler uses a model or algorithm to make a *chemotherapy scheduling decision*, which allocates a specific date, time, and set of clinic resources (chair and nurse) to each appointment in the patient's treatment regimen. Then the scheduler sends the patient appointment schedule to the patient and the chair and nurse resource schedules to the oncology clinic.

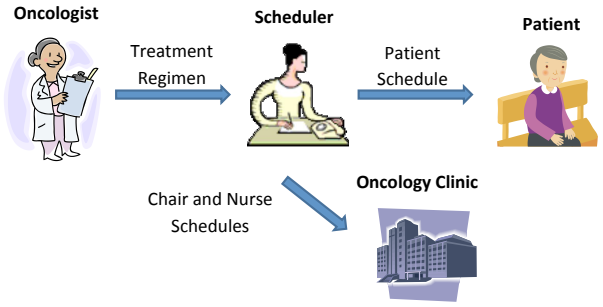


Figure 3.1: Chemotherapy Scheduling Process

Before a chemotherapy treatment is given, a cancer patient sometimes has an appointment for laboratory blood work. Afterward, the patient then meets with their oncologist to discuss their lab results and whether to proceed with the scheduled chemotherapy treatment. Although this is common practice, many oncology clinics have a separate laboratory for blood work or use next-day scheduling (discussed in the literature review Section 2.2.1), which allows the appointment for the chemotherapy treatment to be considered independent of the laboratory blood work appointment. The oncology clinic that contributed to this dissertation uses an an external laboratory for blood work. Because of this and considering the repeated success of next-day scheduling systems, the scope of the oncology clinic operations management problem examined in this dissertation excludes blood work and lab results. Instead, this dissertation focuses on the oncology clinic operations that occur during the chemotherapy appointment and the patient appointment flow depicted in Figure 3.2.

Chemotherapy scheduling decisions are also challenging because of the nature of the patient appointment flow (Figure 3.2) in the oncology clinic. When a patient arrives for a chemotherapy appointment, the patient first checks-in with a receptionist

and then waits in the waiting room for an available nurse and chair. Once both a chair and a nurse are available, the available nurse escorts the patient to the available chair, orders the patient's chemotherapy drug from the pharmacy, and checks the patient's vital signs. While waiting for the drug to be prepared in the pharmacy, the nurse starts the patient's intravenous (IV) drug infusion. When the chemotherapy drug is ready at the pharmacy, the patient's identity is verified and the nurse starts the patient's chemotherapy drug infusion. The entire process (escorting the patient to starting the infusion) takes around 15 minutes and the nurse is fully dedicated to a single patient during this time. Therefore, nurses can only start one patient during this 15 minute time period. Afterwards, the nurse is free to continue monitoring all patients as the chemotherapy infusion can take anywhere from one-half to eight hours. Stopping an infusion and discharging a patient generally takes a few minutes.

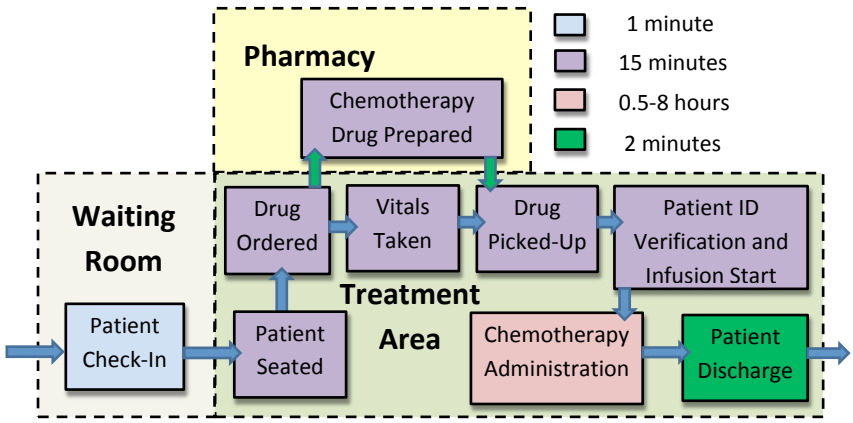


Figure 3.2: Oncology Clinic Patient Appointment Flow

Chemotherapy treatments are well-known for causing nausea and the cancer weakens the immune system, both of which can severely deteriorate a patient's state

of health. The side-affects can occur suddenly during the chemotherapy administration. Depending on the type and intensity of the treatment, nurses must pay close attention to patients in order to monitor the patient's condition and reactions to these side-affects. It is possible for each nurse to simultaneously monitor the chemotherapy treatments of several patients at the same time. However, it is crucial that the nurses are not over-utilized since they must be available to assist patients experiencing adverse reactions to the chemotherapy drugs. To account for this, the concept of acuity levels is used. An *acuity level* is a relative measure of the nurse's attention required by a patient during an appointment. Acuity levels are assigned a value of 1, 2, or 3, where an acuity level of 3 represents the maximum attention required by the patient from the nurse. Each nurse can monitor several patients at once, provided that the sum of the acuity levels for all patients is less than or equal to a pre-determined maximum acuity level for that nurse.

Figure 3.3 provides an example of limitations associated with scheduling a patient appointment using acuity levels and patient starts when scheduling a nurse. A *patient start* is the process a nurse completes to start a new patient's infusion. A patient start includes the steps shown in Figure 3.2 from seating a patient in a chemotherapy chair to starting the infusion. This example assumes one nurse and 15 minute time slots. Patient 1 begins treatment during time slot 1 and continues for 60 minutes (4 time slots). Patient 2 begins treatment during time slot 2 and continues for 60 minutes (4 time slots). Therefore, the nurse has a patient start during time slots 1 and 2. This single nurse could not have started both patients in the same time slot. The acuity levels of each patient are summed to compute the total acuity. The nurse can handle multiple patients as long as the total acuity does not exceed a pre-determined maximum acuity level.

Time Slots	1	2	3	4	5
Patient 1	Acuity Level: 2	Acuity Level: 2	Acuity Level: 2	Acuity Level: 2	
Patient 2		Acuity Level: 1	Acuity Level: 1	Acuity Level: 1	Acuity Level: 1
Patient Starts (1)	1	1	-	-	-
Total Acuity (2)	2	3	3	3	1

(1) Each nurse can only start one patient in each time slot
(2) Each nurse's total acuity for all patients cannot exceed a pre-determined maximum acuity level (e.g., 4).

Figure 3.3: Example Acuity Level and Patient Start Limitations for a Nurse Schedule Using 15 Minute Time Slots

In chemotherapy appointment scheduling, no-shows and cancellations are not a problem because the cancer patients rarely miss appointments. However, rescheduling of appointments is one issue that does pose a challenge for the scheduler. When the patient's health status deteriorates or the results of the blood test are not within the normal range, the oncologist may delay or modify the remaining appointments in the patient's treatment regimen. When such circumstances arise, the scheduler most cancel some or all of the remaining appointments and schedule the new treatment regimen. Although rescheduling is important in oncology clinic operations, it is beyond of the scope of work presented in this dissertation.

3.2 DEVS-CHEMO Simulation Model

This section describes the DEVS formalism, objects in the oncology clinic, discusses performance measures of interest, and then derives the corresponding models for the DEVS-CHEMO simulation model. The hierarchical organization of the models are also described using a system entity structure and the end of the section

discusses software implementation.

3.2.1 Overview of the DEVS Formalism

DEVS-CHEMO is modeled using the DEVS formalism. The DEVS formalism allows for hierarchical and modular construction and uses well-defined concepts for coupling components. The modular construction allows the user to design and construct models independently. By coupling components, the individual models can interact with one another and even combine to create a hierarchy of models. There are three objects in the conceptual framework of the DEVS formalism: *model*, *simulator*, and *experimental frame* [50]. The model is a set of instructions for generating data comparable to the real system. The simulator exercises the model's instructions to actually generate behavior. The experimental frame captures how the modeler's objectives impact the model construction, experimentation, and validation.

The DEVS formalism consists of two *model* types: *atomic* and *coupled*. An *atomic* model is the simplest class and forms the building block for the simulation model. Atomic models contain a set of input and output ports, state variables and parameters, a time advance function, transition functions, and output function. The *internal transition function* specifies which state the system will transition to after the time given by the time advance function has elapsed. The *external transition function* specifies how the system will change state when an input is received. The *confluent transition function* is used when an input is received at the same time an internal transition is to occur. The *output function* generates an external output just before an internal transition takes place.

The *coupled* model links other component models and specifies how to couple (connect) the component models together. A coupled model can be used as a component of a larger coupled model, thus giving rise to hierarchical construction. Cou-

pled models specify the set of component models, set of input and output ports, and coupling specifications. A coupling specification consists of 1) external input coupling (EIC) which connects the input port of the coupled model to an input port of a component model 2) internal coupling (IC) of the output port of a component model to the input port of another component model and 3) external output coupling (EOC) which connects the output port of a component model to the output port of the coupled model.

3.2.2 Objects in the Real System

The oncology clinic setting involves human resources, patients, clinic stations, and performance measures. There are ten types of objects in the real oncology clinic setting (Table 3.2). An object is a material thing that can be seen and touched. In DEVS, objects can be modeled as atomic models, coupled models, or entities. Atomic and coupled models are used when the behavior, or current state and reaction to events in the system, of the object is needed in the simulation. The atomic models are used for simple objects with behavioral properties and coupled models are used when the object has behavior properties and is composed of other objects. An entity is used when the behavior of the object is not relevant to the simulation. Because entities has attributes and methods, then properties of the entity objects can still be modeled.

Table 3.2: Objects in the Real Oncology Clinic Setting

Human Resources	Oncologist
	Scheduler
	Receptionist
	Registered Nurse
	Charge Nurse
Patients	Chemotherapy Patients
Clinic Stations	Waiting Room
	Pharmacy
	Chemotherapy Chairs
	Oncology Clinic

A human resource is an individual who makes up part of the workforce at an organization. There are five types of human resource objects in an oncology clinic: oncologist, scheduler, receptionist, charge nurse, and registered nurse. The *oncologist* is the doctor who treats cancer patients and prescribes a treatment regimen and start date for the cancer patient. Because the oncologist is not present during the chemotherapy treatment, the behavior of the oncologist is not explicitly modeled. However, the behavior of the remaining four human resources is important and therefore they are represented using atomic models. The *scheduler* receives an appointment request for a patient and works to schedule the patient's treatment regimen based on the availability of clinic resources. The *receptionist* assists patients upon arrival to the clinic for an appointment. The *registered nurse* performs many tasks during the patient's chemotherapy treatment including seating the patient, ordering the drug, checking vitals, etc. The *charge nurse* is considered the "head

nurse" and oversees the clinic operations and availability of the two primary clinic resources (registered nurses and chairs). The chemotherapy *patients* are also objects in the oncology clinic. Although the chemotherapy patients have important properties (patient identification number, treatment regimen, schedule, etc.), their behavior is assumed to not have an impact the other models in the system. Therefore, patients are represented as entities in the oncology clinic instead of atomic models.

A clinic station is a location within the clinic where a specified activity or service is based. The oncology clinic is composed of three clinic stations: waiting room, pharmacy, and chemotherapy chairs. The *waiting room* is the location where patients wait after check-in with the receptionist before the nurse assists them to a chemotherapy chair. The *pharmacy* is the location where drug orders are received from the registered nurse and prepared for the patient. The behavior of the waiting room and the pharmacy is captured using atomic models. However, the *chemotherapy chairs*, this is the location where patients sit to receive a drug infusion, are similar to the patients in that they do not have behavior relevant to the other models in the system. Thus, chemotherapy chairs are represented as entities in the system and not atomic models. The fourth clinic station is the oncology clinic itself. The *oncology clinic* is the location where chemotherapy patients are given treatment and it is composed of other clinic stations (waiting room, pharmacy, chemotherapy chairs) and human resources (receptionist, charge nurse, registered nurse). The oncology clinic is modeled as a coupled model.

Table 3.3: Performance Measures

Patient Perspective	
Type I Delay	Time (days) between the first scheduled appointment start date and the state date recommended by the oncologist
Type II Delay	Time (minutes) between the patient arriving to waiting room and the patient being called by the nurse to start the appointment
Type III Delay	Time (minutes) the patient waits in the chemotherapy chair before the nurse starts the patient's chemotherapy treatment
System Time	Time (minutes) the patient spends at the oncology clinic from arrival to the waiting room to discharge from the clinic
Management Perspective	
Patient Throughput	Number of patients served in the oncology clinic in a day
Chair Utilization	Percentage of time the chair is occupied during clinic operating hours
Nurse Utilization	Percentage of time the nurse has one or more patients during clinic operating hours
Nurse Overtime	Time (minutes) that the nurse must work beyond normal clinic operating hours

This dissertation aims to improve oncology clinic management by evaluating clinic scheduling rules and operational policies from both patient and management perspectives. Table 3.3 lists and describes three patient performance measures used in DEVS-CHEMO. Part of patient service satisfaction in oncology clinics is to improve

the patient's overall experience. The first performance measure of interest from the patient's perspective is type I delay. *Type I Delay* is the time between the first scheduled appointment start date and the start date recommended by the oncologist. This performance measure is measured in days and is important because the timing of the chemotherapy treatment regimens is crucial to the patient's health status and recovery. Scheduling algorithms aim to begin the treatment regimen close to the start date prescribed by the patient's oncologist and the type I delay captures how well the scheduling algorithm was able to accomplish this task.

Type II delay and type III delay are performance measures that capture the delay that patients experience at the oncology clinic on the day of an appointment. *Type II Delay* is the time between the patient arriving to the waiting room and the patient being called by the nurse to start the appointment. *Type III Delay* is the time the patient waits in the chemotherapy chair before the nurse starts the patient's chemotherapy treatment. Minimizing the three types of delay can improve the overall patient service experience in the oncology clinic. The *system time*, that is, the time a patient spends at the clinic, is important to minimize as well. Type II and type III delay are both components of system time.

In addition to providing a high quality of service to patients, oncology clinics must also operate from a business perspective. Table 3.3 also lists and describes four management perspective performance measures used in DEVS-CHEMO. *Patient throughput, chair utilization, and nurse utilization* are performance measures used to assess the efficiency of the oncology clinic in a single day. *Nurse overtime*, the amount of time each nurse must work beyond normal clinic operating hours, is a performance measure that was particularly important to the industry professionals who collaborated on this dissertation. Clinics with low nurse overtime can keep overhead costs down and increase employee satisfaction.

3.2.3 Model Abstraction

The DEVS-CHEMO simulation model is composed of nine *atomic models* and three *coupled models*. Next are descriptions of the role of each model and whether the model is classified as atomic or coupled.

CGENR (Atomic).

The call generator (CGENR) is an atomic model that creates a new chemotherapy patient and sends a message to the scheduler requesting an appointment schedule for the new patient. CGENR mimics the behavior of the chemotherapy patient calling into the oncology clinic to request a chemotherapy appointment schedule based on the treatment regimen prescribed by the oncologist.

SCHED (Atomic).

The scheduler (SCHED) is an atomic model that schedules all chemotherapy appointments in the treatment regimen using a scheduling algorithm. SCHED imitates the behavior of the scheduler human resource.

PGENR (Atomic).

The patient generator (PGENR) is an atomic model that generates patient arrivals to the oncology clinic at their scheduled appointment date and time. PGENR is used to model the arrival process of the patient for each appointment.

TRANSD (Atomic).

The tranducer (TRANSD) is an atomic model that captures data from other atomic models and computes patient and system performance measures. TRANSD is essential for analysis of clinic operations.

EF (Coupled).

The experimental frame (EF) is a coupled model that defines the environment

for testing and evaluating the DEVS-CHEMO simulation model. EF couples the CGENR, SCHED, PGENR, and TRANSD atomic models together.

RECEPT (Atomic).

The receptionist (RECEPT) is an atomic model that receives each patient who arrives at the oncology clinic for an appointment, directs the patient to the waiting room, and notifies the charge nurse of the patient's arrival to the clinic. RECEPT models the behavior of the receptionist human resource.

WAITROOM (Atomic).

The waitroom (WAITROOM) is an atomic model that represents the location where patients wait after check-in until their assigned registered nurse is available to begin their chemotherapy treatment. WAITROOM models the behavior of the waiting room clinic station.

PHARM (Atomic).

The pharmacist (PHARM) atomic model receives orders and prepares the chemotherapy drugs for the patient's chemotherapy treatment. PHARM imitates the behavior of the pharmacy clinic station.

CHARGENURSE (Atomic).

The charge nurse (CHARGENURSE) atomic model oversees the clinic operations, manages patients and resources, assigns patients who are ready for treatment to an available chemotherapy chair and registered nurse, and notifies the appropriate registered nurse that their next patient is ready for treatment. The CHARGENURSE atomic model also has the ability to reassign a patient to a different clinic chair or nurse as needed. CHARGENURSE serves the role of the charge nurse human resource.

REGNURSE (Atomic).

The registered nurse (REGNURSE) atomic model retrieves a patient from the waiting room, seats the patient in their assigned chemotherapy chair, orders drugs from the pharmacy, checks the patient's vital signs, picks up drugs from the pharmacy, starts the patient's chemotherapy drug infusion, monitors the patient, and stops the patient's chemotherapy drug infusion. The REGNURSE is the most involved atomic model because it models the behavior of the most active human resource, the registered nurse.

CHEMO (Coupled).

The chemotherapy clinic (CHEMO) is a coupled model that imitates the behavior of the oncology clinic on the day of the patient's appointment. CHEMO consists of the essential oncology clinic human resources and clinic stations used on the appointment day. Therefore CHEMO couples the RECEPT, WAITROOM, PHARM, CHARGENURSE, and REGNURSE atomic models.

EF_CHEMO (Coupled).

The EF_CHEMO is a coupled model that defines the DEVS-CHEMO simulation model. EF_CHEMO couples the CHEMO coupled model and the EF coupled model.

3.2.4 Performance Measures

The DEVS-CHEMO simulation model capture performance measures (listed in Table 3.3) from the patient and management perspectives. Next is a discussion on which atomic models these performance measures are associated with and how they are collected. A few of these performance measures are treated as *entities*, which represent a user-defined class with attributes and methods. An *entity* is different from an *atomic* model because the behavior (state transitions and response to system

events) of entity classes is not modeled.

Type I Delay.

Type I delay is modeled as a *Wait1Time* entity. This entity is created in the SCHED atomic model after the scheduler finds an appointment schedule for the patient. At this point, the SCHED has access to the information for computing Type I Delay and passes the Wait1Time entity to the TRANSD for analysis. The Wait1Time entity communicates the patient identification number and Type I Delay to the TRANSD.

Type II Delay.

Type II delay is modeled as a *Wait2Time* entity. This entity is created in the WAITROOM atomic model when the patient departs the waiting room. The Wait2Time entity contains the patient identification number and clinic arrival time and is passed to the TRANSD atomic model for analysis. The TRANSD atomic model notes the time the message is received and uses the clinic arrival time to compute the Type II Delay.

Type III Delay.

Type III delay is modeled as a *Wait3Time* entity. This entity is created by the REGNURSE atomic model at the time the patient is discharged from the clinic and sent to the TRANSD atomic model. The Wait3Time entity contains the patient identification number, chair identification number, and chair arrival time. The TRANSD atomic model notes the time the message is received and uses the chair arrival time to compute the Type III Delay.

System Time.

System Time is computed in the TRANSD atomic model. The REGNURSE atomic model creates a *PatientChair* entity at the time the patient is discharged

from the oncology clinic and communicates it to the TRANSD atomic model. The PatientChair entity contains the patient identification, chair identification, and an indicator for whether the chair is unoccupied by a patient or not. Using the PatientChair message, the TRANSD uses the patient identification number to look up what time the patient arrived at the clinic and then compute the system time for that patient.

Throughput.

Throughput is computed in the TRANSD atomic model. The REGNURSE atomic model creates a *PatientChair* entity at the time the patient is discharged from the oncology clinic and communicates it to the TRANSD atomic model. The PatientChair entity contains the patient identification, chair identification, and an indicator for whether the chair is unoccupied by a patient or not. When the TRANSD receives this message, it increments the daily throughput counter to indicate that another patient has been processed through the oncology clinic.

Chair Utilization.

Chair Utilization is computed in the TRANSD atomic model. The REGNURSE atomic model creates a *PatientChair* entity at the time the patient is discharged from the oncology clinic and communicates it to the TRANSD atomic model. The PatientChair entity contains the patient identification, chair identification, and an indicator for whether the chair is unoccupied by a patient or not. Using the PatientChair message, the TRANSD uses the patient identification number to look up what time the chair became occupied and then update the chair's utilization for the day.

Nurse Utilization.

Nurse Utilization is computed in the TRANSD atomic model. The REGNURSE

atomic model creates a *NurseTime* entity at the time the patient is discharged from the oncology clinic and communicates it to the TRANSD atomic model. The NurseTime entity contains the nurse identification number and nurse start time for the day. The TRANSD notes the time the message is received and uses the nurse start time to compute nurse utilization for the current day.

Nurse Overtime.

Nurse Overtime is computed in the TRANSD atomic model. The REGNURSE atomic model creates a *NurseTime* entity at the time the patient is discharged from the oncology clinic and communicates it to the TRANSD atomic model. The NurseTime entity contains the nurse identification number and nurse start time for the day. The TRANSD notes the time the message is received and uses the nurse start time to compute nurse overtime if the clinic operating hours are over.

3.2.5 Atomic Models

Next is a description of the atomic model input ports, output ports, and states. Additionally, the SCHED, CHARGENURSE, and REGNURSE atomic model state transitions are described. The DEVS mathematical functions for these three same atomic models are given in Appendix A.1.

CGENR Atomic Model

The CGENR (call generator) atomic model represents the oncologist identifying a new cancer patient, prescribing a unique treatment regimen, and the patient requesting a series of appointments for the prescribed treatment regimen. In the DEVS-CHEMO model, CGENR creates a new chemotherapy patient and sends a message to

the scheduler requesting an appointment schedule for the new patient. CGENR has no input ports but has one output port "out_ApptRequest". The "out_ApptRequest output port sends information to the SCHED atomic model. CGENR has two states: "Idle" and "Generating".

SCHED Atomic Model

The SCHED (scheduler) atomic model schedules all patient appointments in the *treatment regimen* using a scheduling algorithm selected by the user. The SCHED atomic model in shown in Figure 3.4. It has one input port "in_ApptRequest" and two output ports, "out_ApptTimes and "out_Wait1Time. The "out_ApptTimes output port sends information to the PGENR atomic model and the "out_Wait1Time" output port sends information to the TRANSD atomic model.

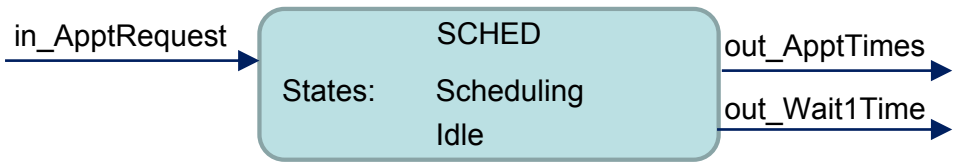


Figure 3.4: SCHED Block Diagram

The state transition of the SCHED atomic model is depicted in Figure 3.5. The model has two states: "Idle" and "Scheduling". The model is initialized in the "Idle" state. A transition to the "Scheduling" state occurs when the model is in the "Idle" state and a message *ApptRequest* is received at the "in_ApptRequest" input port. A method, *Algorithm*(); takes the information provided by the patient and performs

the scheduling using the algorithm chosen by the user. Upon completion of this task (*processingTime* time has elapsed) and if there are no more appointment requests (*schedQueue.isEmpty*() == *true*), the model transitions to the "Idle" state. Mathematical details of the SCHED atomic model are given in Appendix A.1.

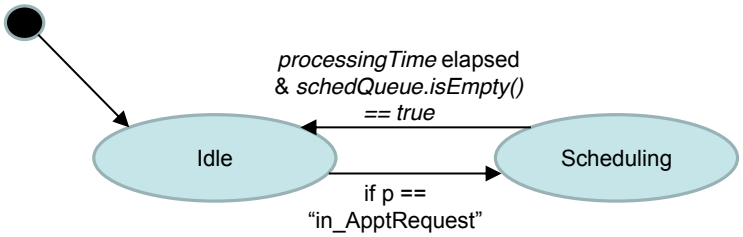


Figure 3.5: SCHED State Transition Diagram

PGENR Atomic Model

The PGENR (patient generator) atomic model generates patient arrivals to the oncology clinic at their scheduled appointment date and time. PGENR has one input port, "in_ApptTimes", and one output port, "out_PatientAppt". The "in_ApptTimes" input port receives information from the SCHED atomic model and the "out_PatientAppt output port allows for transmitting information to the RECEPT atomic model. PGENR has two states: "Idle" and "Generating".

TRANSD Atomic Model

The TRANSD (transducer) atomic model captures data points from other atomic models and computes the performance measures from Section 3.2.4. TRANSD has

six input ports and zero output ports. The six input ports are "in_Wait1Time", "in_Wait2Time", "in_Wait3Time", "in_WaitRoomCapacity", "in_NurseTime", and "in_PatientDepart". The "in_Wait1Time", "in_Wait2Time", and "in_Wait3Time" input ports receive information from the SCHED, WAITROOM, and REGNURSE atomic models respectively. The "in_WaitRoomCapacity" input port receives information from the WAITROOM while the "in_NurseTime" and "in_PatientDepart" receive information from a REGNURSE atomic model. TRANSD has two states: "Idle" and "Processing".

RECEPT Atomic Model

The RECEPT (receptionist) atomic model receives each patient who arrives at the oncology clinic for an appointment, directs the patient to the waiting room, and notifies the charge nurse of the patient's arrival to the clinic. RECEPT has one input port "in_PatientAppt" and one output port "out_PatientAppt". The "in_ApptTimes" input port receives information from the PGENR atomic model and the "out_PatientAppt output port sends information to the CHARGENURSE and WAITROOM atomic models. RECEPT has three states: "Available", "ServingPatient", and "Closed".

WAITROOM Atomic Model

The WAITROOM (waitroom) atomic model holds patients after they have left the receptionist until the registered nurse calls the patient to begin their chemotherapy treatment. WAITROOM has two input ports, "in_PatientAppt" and "in_PatientSeated", and two output ports, "out_Wait2Time" and "out_WaitRoomCapacity". The

"in_ApptTimes" input port receives information from the RECEPT atomic model and the "in_PatientSeated" output port receives information from the REGNURSE. The "out_Wait2Time and "out_WaitRoomCapacity" output ports send information to the TRANSD. RECEPT has three states: "Open", "Processing", and "Closed".

PHARM Atomic Model

The PHARM (pharmacy) receives drug orders from the registered nurse, prepares the chemotherapy drugs, and notifies the registered nurse when the drugs are ready. PHARM has one input port, "in_DrugOrder" and n output ports of type "out_DrugOrder$n$" where n is the number of registered nurses in the oncology clinic. The "in_DrugOrder" input port receives information from the REGNURSE atomic model and each "out_DrugOrder$i$" output ports send information to the corresponding REGNURSEi atomic model. PHARM has two states: "Idle" and "PreparingOrder".

CHARGENURSE Atomic Model

The CHARGENURSE (charge nurse) atomic model manages patients and clinic resources. The primary responsibility of the CHARGENURSE is to assign patients who are ready for treatment to an available chemotherapy chair and registered nurse. CHARGENURSE has two input ports, "in_PatientAppt" and "in_NurseTask", and n output ports of type "out_PatientAppt$n$" where n is the number of registered nurses in the oncology clinic. The "in_PatientAppt" input port receives information from the RECEPT atomic model and the"in_NurseTask" input port receives information from the REGNURSE atomic model. Each "out_PatientAppt$i$" output port sends a

message to the corresponding REGNURSEi atomic model to notify the nurse that a patient is available to begin their appointment. The CHARGENURSE atomic model's block diagram is shown in Figure 3.6.

Figure 3.6: CHARGENURSE Block Diagram

The state transitions of the CHARGENURSE atomic model are depicted in Figure 3.7. The model has three states: "Available", "ProcessingPatient", and "ChairAvailable". The model is initialized in the "Available" state. A transition to the "ProcessingPatient" state occurs when the model is in the "Available" state and a message *PatientAppt* is received at the "in_PatientAppt input port. A transition to the "ChairAvailable state occurs when the model is in the "Available" state and a message $NurseTask$ is received at the "in_ChairAvailable input port. Both the "ChairAvailable" and "ProcessingPatient" states have a processing time $processingTime$. Once the processing time has elapsed in the "ChairAvailable" state, the model transitions to the "Available" state if there are no more NurseTask entities waiting ($NTQueue.isEmpty() == true$) or transition to the "ProcessingPatient" state if there are PatientAppt entities waiting ($CNQueue.isEmpty() == false$). Once the processing time has elapsed in the "ProcessingPatient" state, the model transitions to the "Available" state if there are no more PatientAppt entities waiting ($CNQueue.isEmpty() == true$) or transition to the "ChairAvailable" state if there

are PatientAppt entities waiting ($NTQueue.isEmpty() == false$). Mathematical details of the CHARGENURSE atomic model can be found in Appendix A.1.

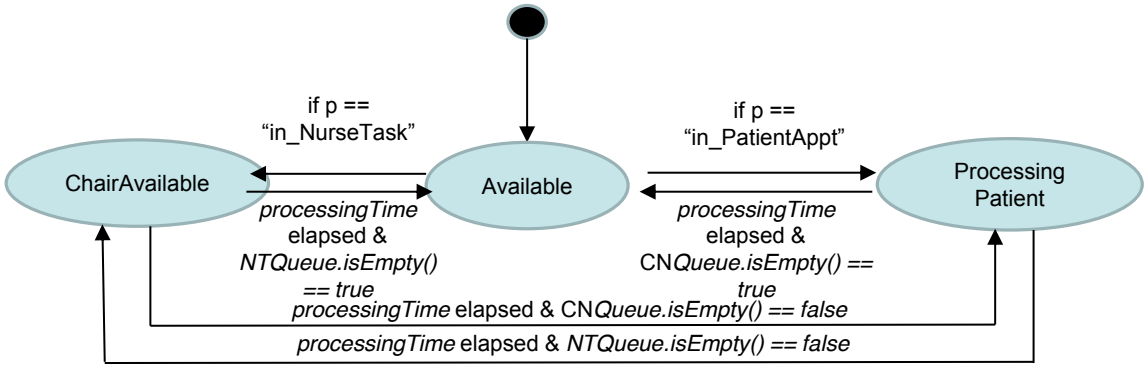


Figure 3.7: CHARGENURSE State Transition Diagram

REGNURSE Atomic Model

The REGNURSE (registered nurse) atomic model is the most involved atomic model in DEVS-CHEMO. The registered nurse retrieves a patient from the waiting room, seats the patient in their assigned chemotherapy chair, orders drugs from the pharmacy, checks the patient's vital signs, picks up drugs from the pharmacy, starts the patient's chemotherapy drug infusion, monitors the patient, and stops the patient's chemotherapy drug infusion. REGNURSE has two input ports, "in_PatientAppt" and "in_DrugOrder", and six output ports, "out_DrugOrder", "out_NurseTime", "out_Wait3Time", "out_PatientSeated", "out_PatientDepart", "out_NurseTask". The "in_PatientAppt" input port receives information from the RECEPT atomic model and the "in_DrugOrder" input port receives information from the PHARM atomic model. The "out_DrugOrder" output port sends information

to PHARM, the "out_NurseTask" output port sends information to the CHARGENURSE, the "out_PatientSeated" and "out_PatientDepart" output ports sends information to the WAITROOM and the TRANSD respectively. Finally, the "out_NurseTime" and "out_Wait3Time" output ports send messages to the TRANSD. The REGNURSE atomic model in shown in Figure 3.8. The state transitions of the REGNURSE atomic model are depicted in Figure 3.9. The model has twelve states: "Available", "CheckingWaitList", "GettingPatient", "SeatingPatient", "OrderingDrug", "CheckingVitals", "WaitingOnDrug", "StartingInfusion", "MonitoringPatients", "StoppingInfusion", "UpdateTRANSD", and "Home".

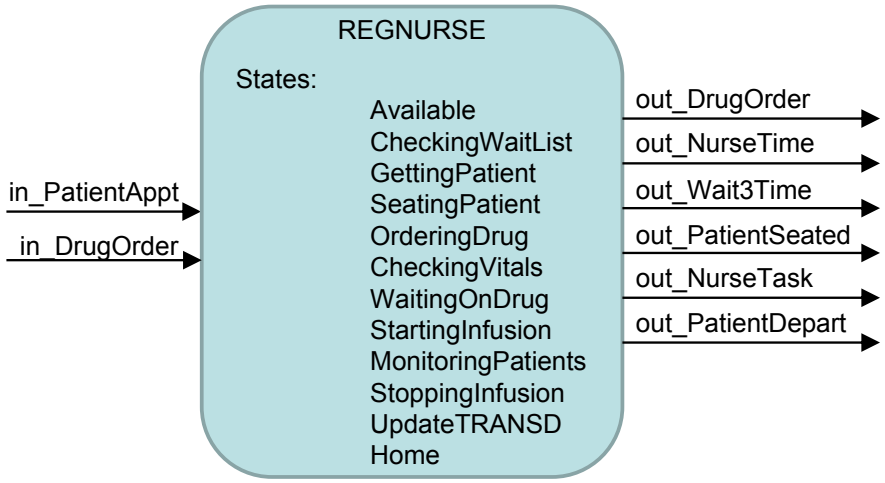


Figure 3.8: REGNURSE Block Diagram

The model is initialized in the "Home" state. A transition to the "Available" state occurs when the oncology clinic opens. A message received on the "in_PatientAppt" input causes the REGNURSE to transition to the "CheckingWaitList" state. In the "CheckingWaitList" state, if there is a patient waiting to start treatment ($WaitList$.-

$isEmpty() == true$) and there is adequate time and capacity to start the patient's treatment ($inadTimeCap() == false$), then the REGNURSE transitions to "GettingPatient". From here, the REGNURSE transitions to a series of phases based on elapsed times include "SeatingPatient", "OrderingDrug", and "CheckingVitals". If REGNURSE is in the "CheckingVitals" state and the drug order from the pharmacy is ready ($DrugReadyList.isEmpty() == false$), then REGNURSE transitions to "StartingInfusion". Otherwise (if $DrugReadyList.isEmpty() == true$), REGNURSE transitions to "WaitingOnDrug" until a message is received on the "in_DrugOrder" input port before transitioning to "StartingInfusion". After the $infStartTime$ has elapsed, REGNURSE returns to "CheckingWaitList".

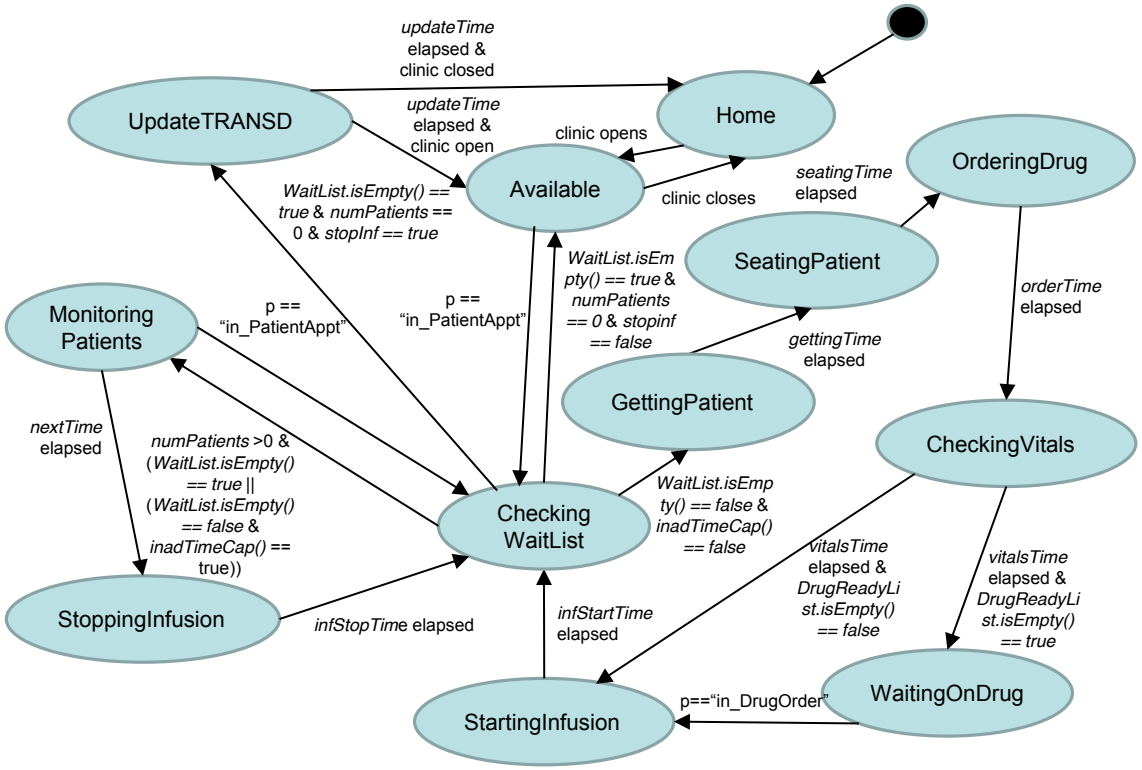


Figure 3.9: REGNURSE State Transition Diagram

From the "CheckingWaitList" state, if there are existing patients ($numPatients > 0$) and the REGNURSE is unable to start a patient's treatment regimen ($WaitList.isEmpty() == true$ OR ($WaitList.isEmpty() == false$ & $inadTimeCap() == true$)), then REGNURSE transitions to "MonitoringPatients". If the model is "MonitoringPatients", an input on "in_PatientAppt" triggers a transition back to "CheckingWaitList"; otherwise, the nurse eventually needs to discharge a patient ($nexttime$ elapses) and transition to "StoppingInfusion" and then "CheckingWaitList". If the model is in "CheckingWaitList" and there are no patients ($numPatients == 0$), no patients are waiting ($WaitList.isEmpty() == true$), and no patients were recently discharged ($stopInf == false$), then the model transitions to "Available". If the model is in "CheckingWaitList" and there are no patients ($numPatients == 0$) and no patients are waiting ($WaitList.isEmpty() == true$) but one or more patients were recently discharged ($stopInf == true$), then the model transitions to "UpdateTRANSD". After updating the transducer, REGNURSE transitions to "Available" if the clinic is still open or transition to "Home" if the clinic is closed. Finally, if the model is already in the "Available" state when the clinic closes, then REGNURSE transitions to "Home". Mathematical details of the REGNURSE atomic model can be found in Appendix A.1.

3.2.6 Coupled Models

The DEVS-CHEMO simulation model is defined by the EF-CHEMO coupled model which is composed of the the EF coupled model and the CHEMO clinic coupled model. Next is a description of each coupled model's input and output ports.

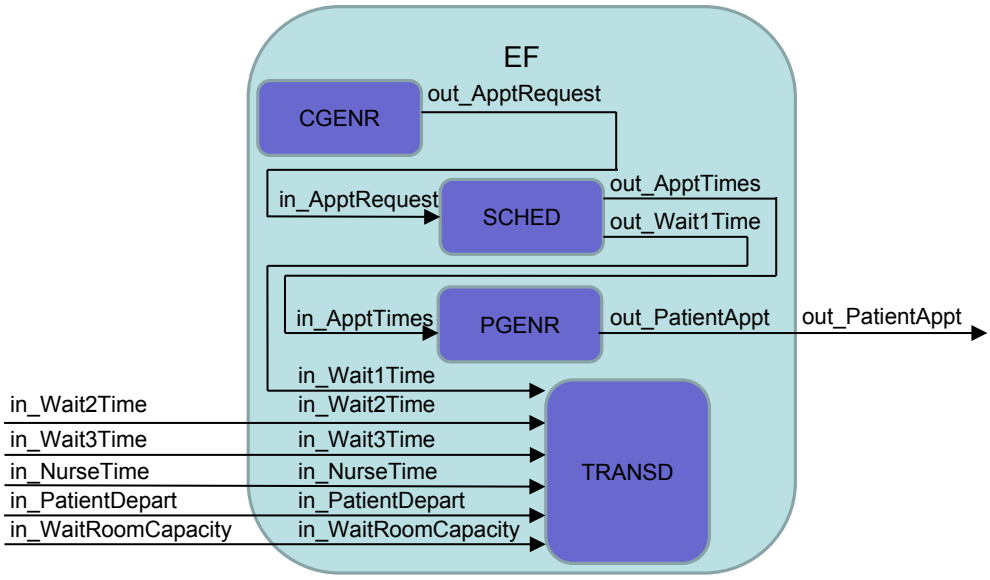


Figure 3.10: EF Block Diagram

EF Coupled Model

The EF (experimental frame) coupled model defines the environment for testing and evaluating the DEVS-CHEMO simulation model. EF couples the CGENR, SCHED, PGENR, and TRANSD atomic models as shown in Figure 3.10. EF has five input ports ("in_PatientChair", "in_Wait2Time", "in_Wait3Time", "in_NurseTime", and "in_WaitRoomCapacity") and one output port ("out_PatientAppt"). EF has five external input couplings. One of the external input couplings is the coupling between EF's "in_Wait2Time" input port and TRANSD's "in_Wait2Time" input port. There are three internal couplings (e.g., CGENR's "out_PatientAppt" output port is coupled to SCHED's "in_PatientAppt" input port). Finally, EF has one external output coupling where PGENR's "out_PatientAppt" output port is coupled to EF's "out_PatientAppt" output port.

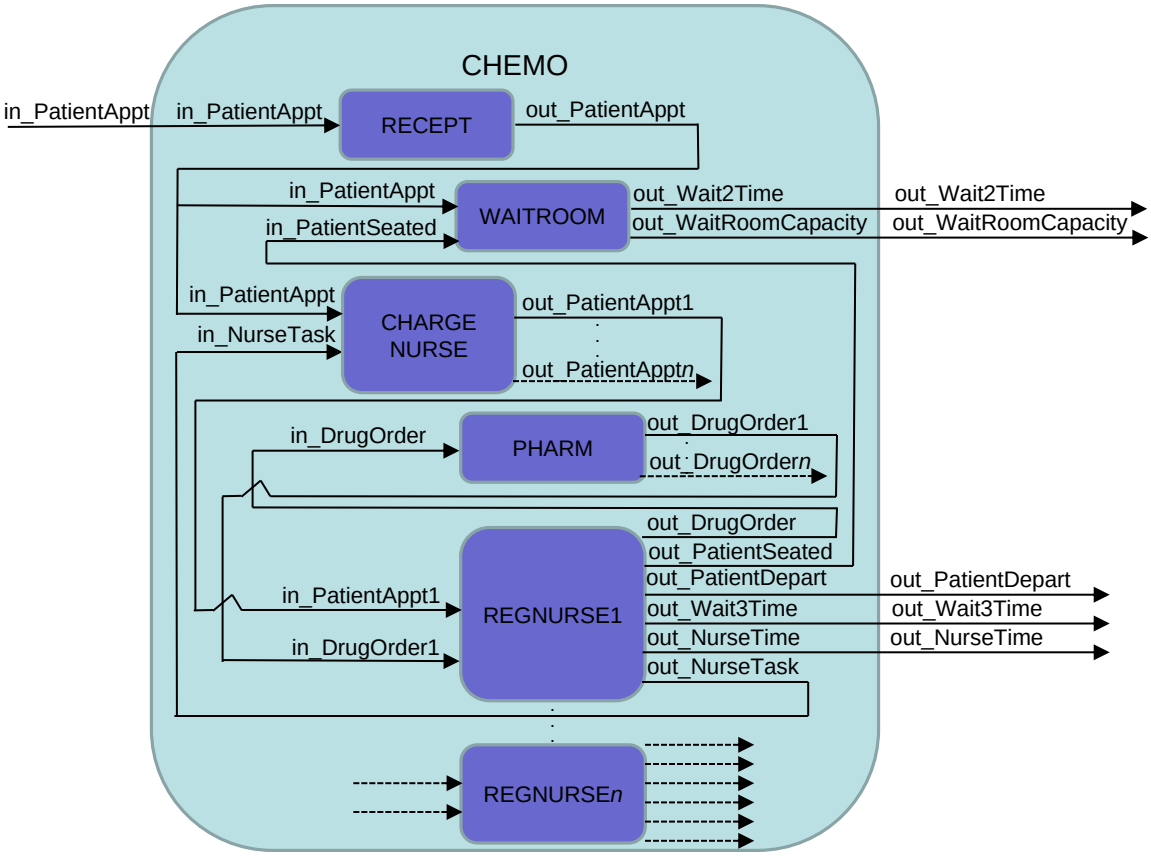


Figure 3.11: CHEMO Block Diagram

CHEMO Coupled Model

The CHEMO (chemotherapy clinic) coupled model imitates the behavior of the oncology clinic on the day of the patient's appointment. CHEMO couples the RECEPT, WAITROOM, PHARM, CHARGENURSE, and n REGNURSE atomic models as shown in Figure 3.11. CHEMO has one input port ("in_PatientAppt") and five output ports ("out_NurseTime", "out_PatientDepart", "out_Wait2Time", "out_Wait3Time", and "out_WaitRoomCapacity"). CHEMO has one external input coupling where CHEMO's "in_PatientAppt" input port is coupled to RECEPT's

"in_PatientAppt" input port. If n is the number of REGNURSE atomic models, then there are $(2+5n)$ internal couplings within CHEMO. The coupling between CHARGENURSE's "out_PatientAppt$i$" output port and REGNURSEi's "in_PatientAppt" input port is one of the internal couplings. Finally, CHEMO has $(2+3n)$ external output couplings such as the one between REGNURSEi's "out_Wait3Time" output port and CHEMO's "out_Wait3Time" output port.

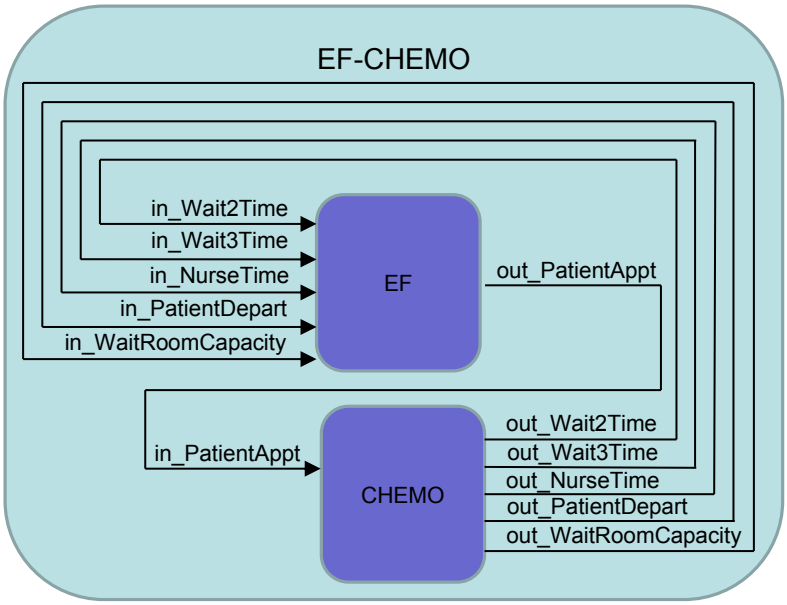


Figure 3.12: EF-CHEMO Block Diagram

EF-CHEMO Coupled Model

The EF-CHEMO coupled model defines the DEVS-CHEMO simulation model. EF-CHEMO couples EF and CHEMO as shown in Figure 3.12. EF-CHEMO does not have input or output ports and therefore does not have any external input couplings

or external output couplings. However, the coupling between EF's "out_PatientAppt" output port and CHEMO's "in_PatientAppt" input port is one of the six internal couplings in EF-CHEMO.

3.2.7 System Entity Structure

The system entity structure (SES) in Figure 3.13 is used to design simulation-based sytems and shows the hierarchy associated with DEVS-CHEMO models. Using the SES, a modeler can visualize the relationships between atomic and coupled models. In Figure 3.13, "x_dec" implies that the model x can be decomposed into smaller models. For example, "ef_chemo_dec" shows that EF_CHEMO can be decomposed into EF and CHEMO. Also in Figure 3.13, "y_spec" means that model y is specialized and thus contains children that are variants of itself. For example, "genr_spec" shows that GENR has two specialized models: PGENR and CGENR.

EF_CHEMO appears at the top of the SES which indicates that it is the highest level coupled model and can be decomposed into two other coupled models EF and CHEMO. The EF coupled model can decompose into four atomic models while the CHEMO coupled model decomposes into five atomic models. Furthermore, note that CHEMO is actually composed of HR (human resource) atomic models and STATION (clinic station) atomic models. The HR models are specialized as the receptionist (RECEPT) and nurse (NURSE) atomic models. The NURSE atomic models are further specialized as the charge nurse (CHARGENURSE) and registered nurse (REGNURSE) atomic models. The STATION atomic models are specialized as the pharmacy (PHARM) and wait room (WAITROOM) atomic models.

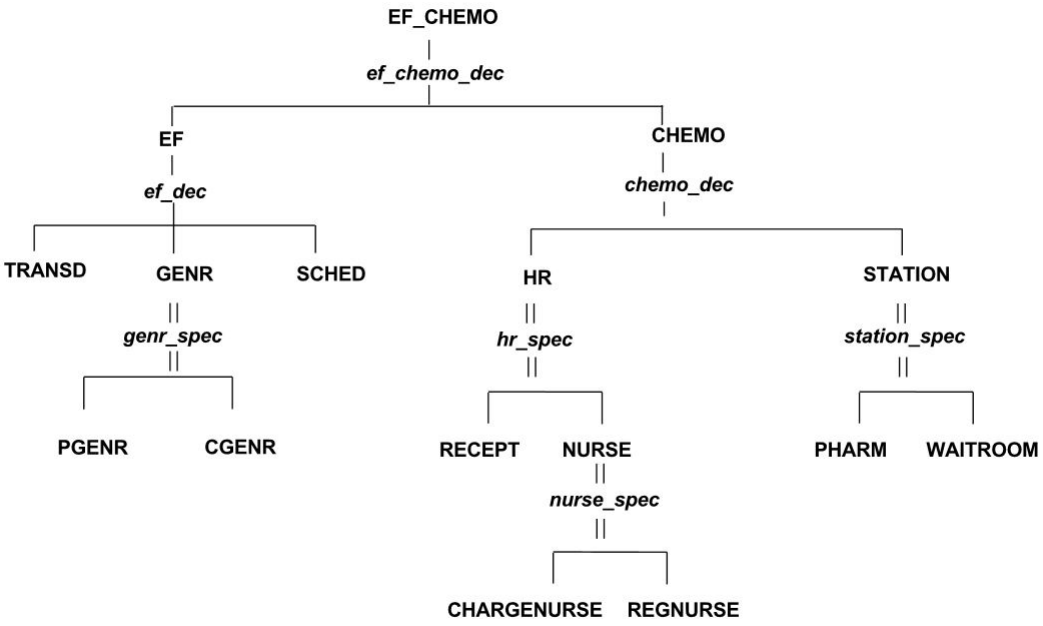


Figure 3.13: System Entity Structure (SES) of DEVS-CHEMO

3.2.8 Software Implementation

DEVS-CHEMO was implemented in DEVSJAVA [50], a Java-based modeling and simulation software using the DEVS formalism. The DEVS-CHEMO model was implemented using the Eclipse Standard environment. Each atomic and coupled model was tested individually using Simulation View Version (SimView) 1.2. SimView allows the modeler to visually inspect the model behavior by using test inputs and by starting, stopping, or slowing the simulation run to view the simulation clock and parameter values.

3.3 Application

The DEVS-CHEMO simulation model was verified using historical data from a five-month period at a real oncology clinic. In this section, a description of the

real oncology clinic setting at Scott & White Hospital is first given in Section 3.3.1. Results of the DEVS-CHEMO model verification are reported in Section 3.3.2. Three sets of experiments using DEVS-CHEMO are described and reported in Section 3.3.3. The first set of experiments implemented several scheduling algorithms to gain insight into oncology clinic management and operations. The second set of experiments examined the impact that the number of nurses had on system performance. The third set of experiments analyzed the sensitivity of system performance results to the probability distributions for type II + III delay. Results are discussed for all experiments in Section 3.3.5.

3.3.1 Real Oncology Clinic Setting

DEVS-CHEMO was used to build a simulation model of the outpatient oncology clinic at Scott & White Hospital in Temple, Texas, USA. This clinic operates five days a week from 08:00 to 17:00, Monday through Friday and typically has one charge nurse and four to eight registered nurses on duty at any given time. This clinic has 20 chemotherapy chairs in the oncology clinic, three of which are reserved for emergencies and special appointments. Therefore, only 17 chairs are actively used for "regular" scheduling purposes. There is always at least one receptionist and one scheduler available in the oncology clinic. The number of oncologists who refer patients to the clinic is not relevant to this study because their behavior was not modeled in DEVS-CHEMO. The clinic treats an average of 23.5 patients a day.

When patients call the scheduler to get an appointment schedule, patients provide their treatment regimen and start date. The scheduler then uses the *As-Soon-As-Possible* (ASAP) algorithm to schedule chemotherapy patient appointments. The scheduler begins with the recommended start date and ensures that the first appointment and all subsequent appointment dates can be accommodated by the availability

of the chemotherapy chairs. The availability of the registered nurses are ignored in the ASAP algorithm. If any appointment in the treatment regimen cannot be satisfied, the scheduler moves all appointments by one day and checks again. This process is repeated until all appointments are successfully scheduled. If possible, the patient's time preference is considered. However, DEVS-CHEMO ignores this aspect of the problem since historical data on how and when this occurs was unavailable.

One important scheduling issue discussed at the time of this study is related to the availability of the registered nurses. Under the ASAP algorithm, the oncology clinic can have as many as 17 patients scheduled to begin treatment at 08:00 hours. However, if six nurses are on duty, the one-to-one relationship between registered nurses and patients during the first fifteen minutes of the appointment implies that only six patients can be started on time, which delays the schedule for the rest of the day. On the day of a patient's chemotherapy appointment, the patient arrives at the scheduled time (previously determined by the availability of a chemotherapy chair), but the oncology clinic ignores the specific chair assignment and allows the patient to be seated in any available chair.

3.3.2 Model Testing and Verification

The design of experiments utilized historical patient data from a five-month period at the Scott & White Oncology Clinic. The raw data came from a nineteen week period between April and September 2012. The clinic has 17 chemotherapy chairs and historical data indicated that the number of registered nurses in the clinic varied daily from 4 to 8 registered nurses (average: 5.64). The experiments assumed one charge nurse, one receptionist, one scheduler, and three pharmacists in the pharmacy.

The clinic was assumed to operate for nine hours. Processing times in the CGENR, SCHED, PGENR, TRANSD, WAITROOM, and CHARGENURSE atomic

models were assumed to be zero. This is because the CGENR, PGENR, and TRANSD models in the EF were doing data upkeep whereby information was stored, sent, or received instantly. The scheduler (SCHED) does take time to make a scheduling decision, but since all appointments were assumed to start the following day, the time required to make a decision did not impact the system performance. In the WAITROOM, a processing time was not needed (set to zero) because no one is there to greet the patient. Finally, the CHARGENURSE was used to reassign patients to new chairs and nurses upon arrival; this happens automatically in the real clinic setting based on current availability so a processing time was not utilized in the experiments. The receptionist was assumed to check-in one patient every minute. In the REGNURSE atomic model, the data processing times were also assumed to be zero because the models were also doing data upkeep when processing times were used.

Historical data provided the time elapsed between the patient's arrival to the clinic and the infusion start time (type II + type III delay) for each appointment. The DEVS-CHEMO model required this time to be broken into several steps. Using input from interviews with the charge nurse as well as experimentation, it was determined that the total time would be broken down as follows in the DEVS-CHEMO model: 10% for getting a patient from the waiting room, 20% seating a patient, 10% ordering a drug, 15% for checking the patient's vitals, 30% for preparing the drugs in the pharmacy, and 10% for starting an infusion. The total does not sum to 100% because another step, waiting for the drug to be ready from the pharmacy, is uncertain.

The model assumes a fixed time for each drug preparation in the pharmacy, but a large queue of drug orders may require additional time since there are only three pharmacists available. Stopping an infusion (discharge) was assumed to take two minutes based on discussions with the charge nurse. It was assumed that all

patients had an acuity level of one since information about the actual patient's acuity levels was unavailable. To ensure that acuity levels did not substantially impact the system performance for model verification, the maximum acuity level for a nurse was assumed to be five. This value was determined by dividing the number of chairs (17) by the minimum number of nurses (4) and rounding up.

The model was verified by simulating the actual patient appointments from the historical data. In this verification, 505 patients were scheduled from the historical data at their actual appointment times and the system was analyzed for the 2070 resulting appointments. One hundred simulation runs of the historical events (arrivals, infusions, discharges, etc.) were implemented and are referred to as HIST. Each appointment in the historical data contained information on the patient's appointment date, appointment time, arrival time, IV start time, IV stop time, drug name(s), and each individual drug start and stop time(s). Data on type II and type III delay was only available as the sum of the two measures in the historical data, and is compared as type II + III delay. The actual values for the appointment duration, arrival time, and arrival to IV time for each appointment were used in HIST. The number of chairs and number of nurses available each day was also available. Data type I delay, resource assignments, and resource utilization were not available for analysis.

Table 3.4: Performance Results for Model Verification Using Historical Data

Data Source	Performance Measure (units)	AVG	STDEV	90% CI
Historical	Total Throughput (appts.)	2070.0	-	-
Data	Daily Throughput (appts.)	23.5	-	-
(1 instance)	Nurse Overtime (min.) (59)	19.00	14.91	-
	Type II + III Delay (min.)	50.41	6.21	-
	System Time (min.)	206.87	21.94	-
HIST:	Total Throughput (appts.)	2070.0	0.0	(2070.0,2070.0)
Simulation	Daily Throughput (appts.)	23.5	0.0	(23.5,23.5)
of Historical	Nurse Overtime (min.) (60.89)	23.64	0.81	(23.51,23.77)
Events (100	Type II + III Delay (min.)	50.77	0.14	(50.75,50.80)
instances)	System Time (min.)	206.98	0.05	(206.97,206.98)

HIST was conducted to demonstrate that the DEVS-CHEMO simulation could reproduce the events in the historical data with relative accuracy. The throughput, type II + type III delay, system time, and nurse overtime were compared to the simulation results in Table 3.4. For each result, the average (AVG), standard deviation (STDEV), and 90% confidence interval (90% CI) are given. Entries with dash marks (-) indicate that there was no need to compute the data value. The 90% CI's for the HIST data were calculated because the resource assignments in the historical data were not known and thus the charge nurse randomly assigned patients to any available registered nurse in HIST. Because these assignments were different for each simulation run, the average nurse overtime, type II+III delay, and system time values were different each time. HIST results reproduced results that were identical to the

total and daily throughput with values of 2070 appointments and 23.5 appointments, respectively. These results provide a cross-check that HIST used the exact number of patients in the simulation runs as were present in the historical data.

For the three performance measures, type II + type III delay, system time, and nurse overtime (all measured in minutes), results should be compared with caution. In the historical data, the AVG column shows the average of the 2070 patient appointments while the STDEV column gives the standard deviation. However, in HIST, the AVG column is the average of the one hundred simulations runs while the STDEV column shows the standard deviation of the average of the hundred simulation runs and the 90% CI column containing the confidence interval for those averages. HIST reproduced averages within 1% for the delay and system time. For Nurse Overtime, there were 59 instances where patients were discharged after the clinic's closing time and the average of those instances was 19 minutes with a STDEV of 15. HIST had an average of 61 instances where nurses stayed overtime and the average of those instances was 24 minutes. These nurse overtime values are only 4 minutes apart and we consider that to be an acceptable difference considering information about the nurse assignments were unknown. Thus, DEVS-CHEMO does provide a reasonably accurate representation of the Scott & White oncology clinic operations.

3.3.3 Design of Experiments and Algorithms

The design of experiments sought to answer three questions. First, how should patients be scheduled? Second, how does the number of nurses impact system performance for a 20% increase in demand? Third, how do different distribution assumptions change the system performance results? To find these answers, three different experiments were designed and conducted. This section first describes the simulation parameters and design set-up, then gives the results of the three experiments.

The simulation runs for the experiments with DEVS-CHEMO used the chair and nurse assignments for scheduling purposes, but due to the stochastic nature of patient arrivals and treatment duration at the clinic, it was unrealistic to rigidly apply these rules. Instead, the assigned nurse and assigned chair were used only to schedule the appointment times for the patient. However, those assignments were not necessarily kept during the actual appointment. If the scheduling algorithm determined a nurse or chair assignment, DEVS-CHEMO first tried to use that assignment if the resource was available. Otherwise, DEVS-CHEMO utilizes a reassignment policy that re-assigns the patient to the next available resource.

The reassignment policy was implemented because initial experiments showed that maintaining resource assignments resulted in low utilization of some resources, over-utilization for other resources, and unacceptable levels of clinic overtime. This occurs because of the stochastic nature of patient treatment duration. When a patient has a longer treatment duration than expected, they are likely still occupying their chair when the next patient arrives to the clinic. At times a second chair may be available for the instances where other patients had a shorter treatment duration than expected. However, strict adherence to chair and nurse assignments requires that the second chair remain empty. Instead the next patient must continue to wait for the first patient to finish treatment and for the assigned chair to become available. Under this rigid assignment policy, most subsequent appointments will continue to be delayed and the clinic will stay open overtime to accommodate all scheduled appointments, even though other resources may have been available for use.

There are six parameters that are stochastic in the simulation run: number of nurses working each day, arrival time, appointment duration, type I + type II delay, treatment start date recommendation, and acuity levels. The first four of these

stochastic parameters were analyzed from historical data. First, the number of nurses working each day follows a uniform distribution with values ranging between four to eight nurses. Historical data showed that 4,5,6,7, or 8 nurses were present on 13.1%, 27.3%, 39.4%, 18.2%, and 2% of the days, respectively,.

Second, the distribution for early or late arrivals for each patient was analyzed. Patients were late roughly 24% of the time and the best data fit was weibull while the remaining 76% of patients were early and best followed a gamma distribution fit. Third, the appointment duration for each specific drug was stochastic. If historical data on a specific drug had at least one hundred data points, then the distribution was determined; otherwise the appointment duration time was sampled from the existing pool of data values. Fourth, the type I + type II delay, or the time from arrival to the clinic until the IV is started, was also analyzed for each patient appointment in the historical data. In the simulation, this data value was stochastic and best follows a gamma distribution.

The remaining two stochastic parameters are used for scheduling purposes, but were not available in the historical data. Fifth, the treatment start date recommended by the oncologist was generated using a uniform distribution between one to seven days where each value had equal weight. Data on the start date recommendation was unavailable and the equally-weighted uniform distribution was chosen because it was assumed that the oncologist wants every patient to begin treatment within one week.

Sixth, the acuity level for each appointment was also generated via simulation. There are several ways to handle acuity levels in the literature [18, 24]. The acuity levels can be based on appointment duration, drugs, or patient characteristics. Since this is a new concept for the oncology clinic collaborating on this dissertation, expertise was unavailable on how to best implement acuity levels for this clinic. Thus,

we assumed that the patient has an acuity level value of one occurring 70% of the time, a value of two occurring 20% of the time, and a value of three occurring 10% of the time, where three is the maximum acuity level for each patient. These percentages are true under the assumption that 70% of patients have a mild reaction to the chemotherapy drugs, 20% have a moderate reaction, and 10% have a severe reaction. The maximum acuity a single registered nurse can have at one time was assumed to be five. This value was determined by taking the average acuity level of the patients (1*0.7+2*0.2+3*0.1 = 1.4) and multiplying by the average number of patients per nurse (17 patients divided by 5.6 nurses = 3.1), then rounding up.

The amount of time used to schedule and allocate time for each appointment comes from a Drug Infusion Time Sheet that the clinic uses for scheduling purposes. This sheet tells the scheduler how much time to allocate for each appointment, depending on the drug used. The simulation uses the time from the Drug Infusion Time Sheet to schedule patients, but the actual appointment duration was stochastic based on analysis results from the historical data. Each day is divided into fifteen minute time slots.

Each simulation day is an independent day in the system. In order to create a warm-up period, a number of patient appointment requests are simulated to fill the schedule on day zero, before the first simulation day begins for the clinic. The historical data provided the average number of patients seen in the clinic each day denoted by X. Since each patient has an average number of appointments, n, then $\frac{X}{n}$ patients finish chemotherapy treatment each day. The clinic informed us that they were scheduling patients D days into the future. Thus, $\frac{DX}{n}$ patients are already on the schedule. For the simulation $X = 23.5, n = 4.10, D = 30$, thus 172 patients, after rounding, were scheduled before the first simulation day to fill the schedule. The frequency of scheduling requests was also computed. To do this, the length of each

simulation day, T, in seconds is divided by the number of patients finishing treatment each day, $\frac{X}{n}$. Then patients were assumed to request appointment schedules every $\frac{Tn}{N}$ seconds. This simulation used $T = 690$ seconds each simulation day, thus patients requested treatment every 120 seconds. During the five-month simulation period, 811 new patients are scheduled.

The performance measures listed in Table 3.3 were used to analyze simulation results from the patient and management perspectives. The results for each scheduling algorithm or nurse comparison comes from 100 simulation replications where the clinic is simulated for a five-month period using a 300-day planning horizon. The average, STDEV, and 90% CI's for all performance measures were computed. The simulations were conducted on a Dell Precision T7500 with an Intel(R) Xeon(R) processor running at 2.4 GHz with 12.0 GB RAM.

Scheduling Algorithms

The first question asked was how patients should be scheduled? Four scheduling algorithms were developed and implemented: ASAP, Collective, Individual, and Nurse. Each algorithm varies by the type of resource used to make the scheduling decision and the constraints or limitations associated with those resources. These algorithms were designed to determine which resources were most important in scheduling chemotherapy patient appointments. Next is a description of how each algorithm makes decisions. Following the algorithm name, (C) indicates that a chair resource is assigned to each patient appointment, (N) indicates that a nurse resource is assigned to each patient appointment, and (CN) indicates that both a chair and nurse resource are assigned to each patient appointment.

Individual Algorithm (CN)

Patients are scheduled using the chair and nurse availability and both a chair and nurse are assigned for each patient appointment. The algorithm starts the recommended date of the first appointment and considers each chair resource one-at-a-time until a chair with an adequate number of time slots is found. Once a chair is selected, the algorithm uses a similar procedure to find a nurse who can start the appointment and handle the additional acuity level. The latter constraint requires that the sum of the acuity levels of all patients assigned to the nurse is less than or equal to the maximum acuity level. This algorithm is called "Individual" because the maximum acuity level constraint is only checked for one individual nurse at a time. If the constraint is satisfied, then the appointment schedule is kept; otherwise, the nurse search process is resumed or another time slot is selected based on chair availability.

The Individual algorithm is the most detailed algorithm and will prove to be the preferred scheduling method. For this reason, the Individual algorithm is fully stated using psuedocode. The remaining three algorithms are then described in reference to the Individual algorithm's code in Appendix A.2. All algorithms schedule one patient at a time and assume a long planning horizon such that a solution can be found within the planning horizon. Each algorithm knows the recommended start date ($startDate$) of the first appointment and that there are n appointments in the patient's treatment regimen. The spacing between each appointment in the planning horizon ($regimenDates[]$), the number of time slots required by each appointment ($numSlots[]$), and the acuity level for each appointment ($acuity[]$) are all known, where $regimenDates[], numSlots[]$, and $acuity[]$ are all data sets of size n. Additionally, each algorithm knows the number of chairs each day C, the number of time slots each day S, and the number of nurses N_d working on day d. The Individual

algorithm will schedule the treatment dates ($treatDays[]$), the starting time slots ($slots[]$), chairs ($chairs[]$), and nurses ($nurses[]$). The $treatDays[], slots[], chairs[]$, and $nurses[]$ are all data sets of size n. The five methods used in the Individual algorithm are described next.

- $setTreatDays(start, regimenDates[])$: returns the treatment dates that begin on start date $start$ based on treatment regimen $regimenDates[]$.
- $checkTreatDays(regimenDates[])$: increases every day in $regimenDates[]$ by one day until all are week days and returns those dates.
- $StartSlot(d, numSlots, j, s)$: Begins looking in slot s of chair j on day d for $numSlots$ consecutive available slots and returns the slot number if found. Else, if no space available, returns -1.
- $Acuity(n, s, d, acuity, numSlots)$: returns true if nurse n can handle the additional load of $acuity$ starting in slot s on day d for $numSlots$ slots, else returns false;
- $Start(n, s, d)$: returns true if nurse n is available to start a new patient during slot s on day d, else returns false;

The left arrow $\leftarrow$ is used to denote assignment, & denotes the "and" operator, ! denotes the "not" operator, and == denotes the "equality" operator. The Individual algorithm returns the char ($chairs[]$) and nurse ($nurses[]$) assignments. The specific steps of the Individual algorithm, $IndividualAlg()$, are listed next.

$IndividualAlg()$

01. $scheduled \leftarrow false; firstDate \leftarrow startDate;$

02. $treatDays[] \leftarrow setTreatDays(firstDate, regimenDates[])$;
03. $treatDays[] \leftarrow CheckTreatDays(treatDays[])$;
04. **while**(!$scheduled$)
05. **for**($i \leftarrow 0; i < n; i++$)
06. $d \leftarrow treatDays[i]$;
07. $chairFound \leftarrow false$;
08. **for**($j \leftarrow 0; j < C; j++$)
09. $s \leftarrow 1$;
10. **while**($s \leq S$)
11. $s \leftarrow StartSlot(d, numSlots[i], j, s)$;
12. **if**($s > 0$)
13. $nurseFound \leftarrow false$;
14. $nurse \leftarrow 1$;
15. **while**(!$nurseFound$ & $nurse < N_d$)
16. $fail \leftarrow 0$;
17. $startCheck \leftarrow Start(nurse, s, d)$;
18. **if**(!$startCheck$)
19. $fail \leftarrow fail + 1$;
20. $acuityCheck \leftarrow Acuity(nurse, s, d, acuity[i], numSlots[i])$;
21. **if**(!$acuityCheck$)
22. $fail \leftarrow fail + 1$;
23. **if**($fail == 0$)
24. $nurseFound \leftarrow true$;
25. **else**
26. $nurse \leftarrow nurse + 1$;
27. **if**($nurseFound$)

28. $slots[i] \leftarrow s; chairs[i] \leftarrow j; nurses[i] \leftarrow nurse;$

29. $chairFound \leftarrow true; s \leftarrow S; j \leftarrow C;$

30. **else**

31. $s \leftarrow s + 1;$

32. **else**

33. $s \leftarrow S$

34. **if**(!$chairFound$)

35. $i \leftarrow n;$

36. **if**($chairFound$)

37. $scheduled \leftarrow true;$

38. **else**

39. $firstDate \leftarrow treatDays[0];$

40. $treatDays[] \leftarrow setTreatDays(firstDate, regimenDates[]);$

41. $treatDays[] \leftarrow CheckTreatDays(treatDays[]);$

42. **return** $treatDays[], slots[], chairs[], nurses[];$

ASAP Algorithm (C)

In the ASAP algorithm, patients are scheduled using only the chair availability and a chair is assigned for each patient appointment. This algorithm was the current algorithm used in the oncology clinic at the time of this study. The ASAP algorithm ignores nurse resources. The algorithm starts the recommended date of the first appointment and considers each chair resource one-at-a-time until a chair with an adequate number of time slots is found. If the chairs are unavailable for the date, then all appointments are moved forward one day and the search process begins again. Appendix A.2.1 provides more details on the ASAP algorithm.

Collective Algorithm (C)

Patients are scheduled using the chair and nurse availability and a chair is assigned for each patient appointment. The algorithm uses the same search procedure as the ASAP to find an available chair. Once a chair is selected, the algorithm checks two constraints. In the first constraint, the number of scheduled new starts is less than or equal to the number of nurses on duty. In the second constraint, the sum of the acuity levels of all patients for each time slot is less than or equal to the maximum acuity level multiplied by the number of nurses on duty. This algorithm is called "Collective" because the maximum acuity level constraint includes all patients and nurses. If both constraints are satisfied, then the appointment schedule is kept; otherwise, the chair search process is resumed. Appendix A.2.2 provides more details on the Collective algorithm.

Nurse Algorithm (N)

Patients are scheduled using only the nurse availability and a nurse is assigned for each patient appointment. The Nurse algorithm ignores chair resources. The algorithm finds the recommended date of the appointment, considers each nurse resource one-at-a-time until a nurse is found that satisfies two constraints. In the first constraint, the number of scheduled new starts is less than or equal to the number of nurses on duty. In the second constraint, the sum of the acuity levels of all patients assigned to that nurse is less than or equal to the maximum acuity level. If both constraints are satisfied, then the appointment schedule is kept; otherwise, the nurse search process is resumed. If all nurses are unavailable for that date, then all appointments are moved forward one day and the search process begins again. Appendix A.2.3 provides more details on the Nurse algorithm.

Number of Nurses

The second question asked how the number of nurses impacted the system performance for a 20% increase in demand for oncology clinic services. Nurses are the most limited resource in the oncology clinic. The current average number of nurses in the clinic is 5.64 nurses. This set of experiments assumes that the same number of nurses are present each day. Now 967 patients are scheduled instead of 811 patients. The ASAP algorithm was implemented for six instances with one hundred replications each, where each simulation instance increases the number of nurses from 5 to 10.

Sensitivity Analysis

The third question was to determine how sensitive the performance results were to changes in the probability distributions of the input factors. This was accomplished by changing the probability distribution assumptions for appointment duration. Specifically, changes were made to the probability distribution for type II + III delay. Recall that type II + III delay is the time between the patient's arrival to the clinic and the time the infusion is started. In the data analysis for type II + III delay, the average time was 36.13 minutes and the standard deviation was 22.34 minutes. After performing a goodness-of-fit test, it was determined that the three-parameter gamma distribution, Gamma(a, d, p), and the Weibull distribution, Weibull(a,d), were a good fit. Here, a is the shape factor, d is the scale factor, and p is the threshold factor. In this set of experiments, the number of nurses was set to seven. The seven nurses were assumed to be present every day, as was done in the number of nurse experiments.

Table 3.5: Probability Distributions Used for Type II + III Delay

	Parameters			Statistics	
Name	a	d	p	AVG	STDEV
Gamma0	2.89	13.20	-2.07	36.13	22.34
Gamma1	7.00	5.16	-	36.13	13.65
Gamma2	5.00	5.10	-	25.50	11.40
Weibull1	1.69	40.53	-	36.13	22.34
Weibull2	1.69	28.56	-	25.50	11.10

Table 3.5 lists the five probability distributions used in the sensitivity analysis. The first three probability distributions utilize the gamma distribution. Gamma0 has an average of 36.13 minutes and a standard deviation of 22.34 minutes. Gamma1 has the same average value but the standard deviation was reduced to 13.65 minutes. This was done to see what would happen if the clinic improved operations to achieve more consistent waiting times for the patients. For Gamma2 the average was reduced to 25.50 minutes with a standard deviation of 11.40 minutes. Weibull1 has the same average and standard deviation as Gamma0. The purpose of the change was to examine the impact of using the Weibull distribution instead of the gamma distribution. Weibull2 has the same average as Gamma2 and a standard deviation of 11.10 minutes.

3.3.4 Simulation Results

Now the computational simulation results are presented. Discussion of the results are appear in the next section.

Table 3.6: Performance Results for Scheduling Algorithms (1 of 2)

Algorithm	Performance Measure (units)	AVG	STDEV	90% CI
ASAP	Total Throughput (appts.)	2629.8	65.6	(2619.1,2640.6)
	Daily Throughput (appts.)	23.7	0.6	(23.6,23.8)
	Chair Utilization (%)	49.58	1.33	(49.36,49.80)
	Nurse Utilization (%)	84.05	1.89	(83.74,84.36)
	Nurse Overtime^{+} (min.)	107.17	7.44	(105.94,108.39)
	Nurse Overtime^{+} Count	253.51	14.08	(251.19,255.83)
	Nurse Overtime (min.)	43.02	4.55	(42.27,43.76)
	Type I Delay (days)	1.30	0.04	(1.30,1.31)
	Type II Delay (min.)	21.41	2.71	(20.96,21.85)
	Type III Delay (min.)	32.07	0.38	(32.01,32.13)
	System Time (min.)	209.42	4.71	(208.65,210.20)
Collective	Total Throughput (appts.)	2610.9	73.9	(2598.8,2623.1)
	Daily Throughput (appts.)	23.5	0.7	(23.4,23.6)
	Chair Utilization (%)	49.21	1.33	(48.99,49.43)
	Nurse Utilization (%)	83.92	1.76	(83.63,84.21)
	Nurse Overtime^{+} (min.)	104.52	6.01	(103.53,105.51)
	Nurse Overtime^{+} Count	253.87	15.70	(251.29,256.45)
	Nurse Overtime (min.)	630.55	10.30	(628.86,632.24)
	Type I Delay (days)	1.33	0.05	(1.33,1.34)
	Type II Delay (min.)	15.26	1.47	(15.02,15.51)
	Type III Delay (min.)	31.96	0.43	(31.89,32.03)
	System Time (min.)	203.33	3.44	(202.77,203.90)

Nurse Overtime^{+} excludes zero entries

Table 3.7: Performance Results for Scheduling Algorithms (2 of 2)

Algorithm	Performance Measure (units)	AVG	STDEV	90% CI
Individual	Total Throughput (appts.)	2618.6	64.4	(2608.0,2629.2)
	Daily Throughput (appts.)	23.6	0.6	(23.5,23.7)
	Chair Utilization (%)	49.61	1.36	(49.38,49.83)
	Nurse Utilization (%)	84.45	2.01	(84.12,84.78)
	Nurse Overtime^{+} (min.)	103.26	5.25	(102.39,104.12)
	Nurse Overtime^{+} Count	256.94	15.59	(254.38,259.50)
	Nurse Overtime (min.)	42.02	3.71	(41.41,42.63)
	Type I Delay (days)	1.35	0.05	(1.35,1.36)
	Type II Delay (min.)	14.20	1.12	(14.02,14.38)
	Type III Delay (min.)	32.01	0.42	(31.94,32.07)
	System Time (min.)	203.24	4.01	(202.58,203.90)
Nurse	Total Throughput (appts.)	2612.91	64.14	(2602.36,2623.46)
	Daily Throughput (appts.)	23.54	0.58	(23.44,23.63)
	Chair Utilization (%)	49.28	1.28	(49.07,49.49)
	Nurse Utilization (%)	74.05	1.73	(73.76,74.33)
	Nurse Overtime^{+} (min.)	94.54	9.20	(93.02,96.05)
	Nurse Overtime^{+} Count	115.76	11.92	(113.80,117.72)
	Nurse Overtime (min.)	17.37	2.57	(16.95,17.79)
	Type I Delay (days)	1.49	0.11	(1.48,1.51)
	Type II Delay (min.)	46.69	2.58	(46.27,47.12)
	Type III Delay (min.)	32.24	0.41	(32.17,32.31)
	System Time (min.)	234.63	4.85	(233.83,235.43)

Nurse Overtime^{+} excludes zero entries

Scheduling Algorithms

The average run times of the ASAP, Collective, Individual, and Nurse scheduling algorithms were 4.99 seconds, 5.41 seconds, 6.12 seconds, and 5.02 seconds respectively. The results for the scheduling algorithm experiments are in Tables 3.6 and 3.7. Each algorithm has results reported for the performance measures specified in Section 3.2.4. The throughput is given as total throughput, or appointments (appts.), for the five-month period. The nurse overtime is reported in two different ways. The nurse overtime$^+$ count is the number of nurses that work overtime in the five-month period and nurse overtime$^+$ is the average of the overtime during these instances (zero entries are excluded). Nurse overtime is the average overtime among all nurses during the five-month period (zero entries included). The total throughput, type I delay, and some of the time-based performance measures (system time, type II delay, type III delay, nurse overtime$^+$, and nurse overtime) are depicted graphically in Figures 3.14, 3.15, and 3.16.

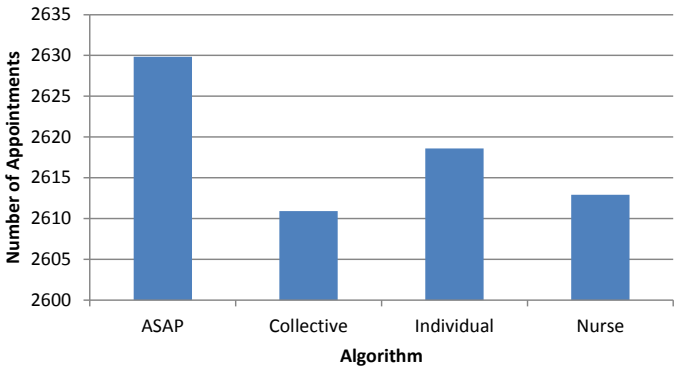


Figure 3.14: Results for Throughput for Scheduling Algorithms

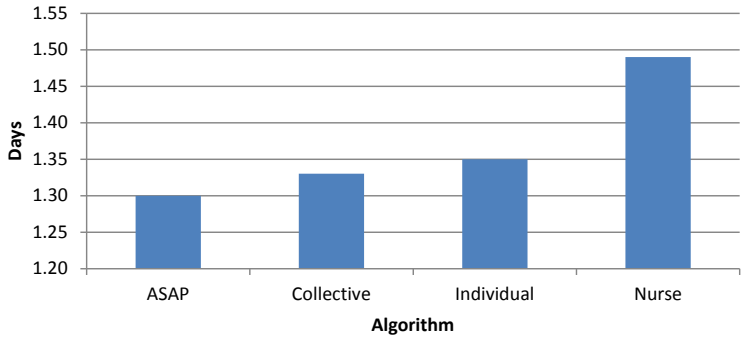


Figure 3.15: Results for Type I Delay for Scheduling Algorithms

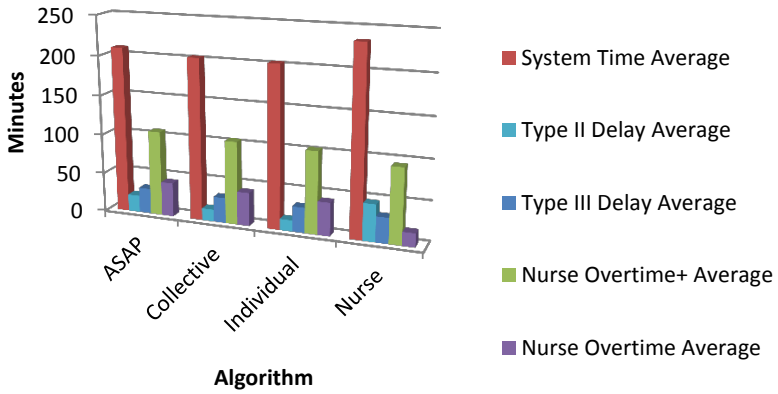


Figure 3.16: Results for Time-Based Performance Measure for Scheduling Algorithms

Number of Nurses

Table 3.8 shows the results of the experiments with the number of nurses. Only the averages are listed in Table 3.8, but the full results (with STDEV and CI's) are provided in Appendix A.3. The average for the system time is depicted graph-

ically in Figure 3.17 for each number of nurses used. Similarly, the type II delay, nurse overtime$^+$, and nurse overtime are depicted graphically in Figure 3.18 for each number of nurses used.

Table 3.8: Performance Results for DEVS-CHEMO Nurse Experiments for ASAP Algorithm

	Number of Nurses					
Performance Measures (units)	5	6	7	8	9	10
Total Throughput (appts.)	3092.9	3085.3	3090.2	3082.6	3098.7	3099.8
Daily Throughput (appts.)	27.9	27.8	27.8	27.8	27.9	27.9
Chair Utilization (%)	58.3	58.36	58.42	58.4	58.84	59.01
Nurse Utilization (%)	98.84	90.01	82.98	76.84	71.48	66.68
Nurse Overtime$^+$ (min.)	113.37	100.3	98.82	98.78	100	98.73
Nurse Overtime$^+$ Count	309.56	304.57	305.36	305.8	310.36	311.55
Nurse Overtime (min.)	63.26	45.9	38.87	34.04	31.09	27.72
Type I Delay (days)	1.31	1.31	1.31	1.31	1.31	1.32
Type II Delay (min.)	29.65	18.64	15.41	13.81	13.05	12.49
Type III Delay (min.)	31.73	32.01	32.24	32.6	32.97	33.23
System Time (min.)	217.65	207.37	204.06	202.84	202.5	202.41

Nurse Overtime$^+$ excludes zero entries

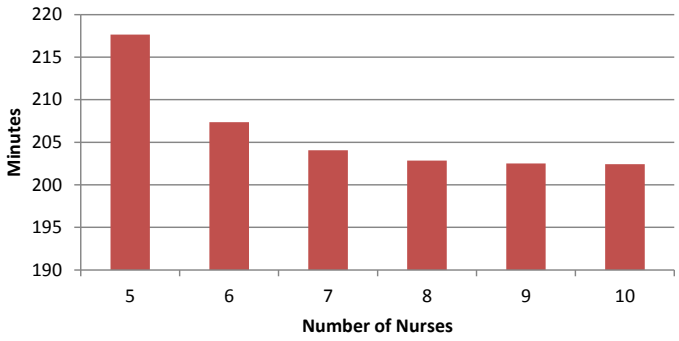


Figure 3.17: Results for System Time for Nurse Experiments

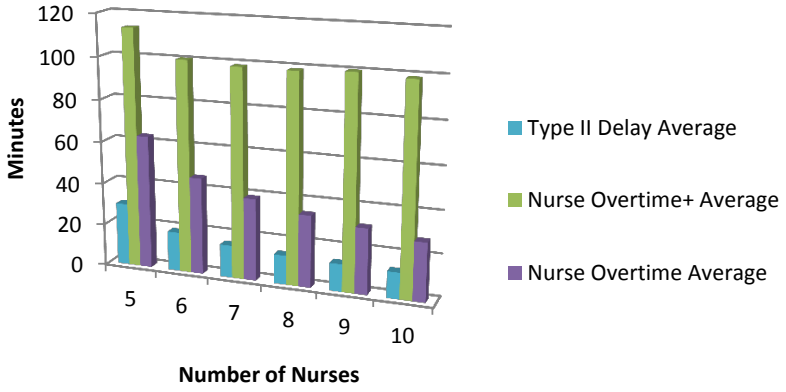


Figure 3.18: Results for Time-Based Performance Measures for Nurse Experiments

Sensitivity Analysis

The results for the sensitivity analysis experiments are given in Table 3.9. G0, G1, G2, W1, and W2 represent the Gamma0, Gamma1, Gamma2, Weibull1, and Weibull2 probability distributions, respectively.

Table 3.9: Performance Results for DEVS-CHEMO Sensitivity Analysis Experiments

	Distribution				
Performance Measures (units)	G0	G1	G2	W1	W2
Total Throughput (appts.)	3090.2	3090.8	3083.4	3087.6	3086.2
Daily Throughput (appts.)	27.8	27.9	27.8	27.8	27.8
Chair Utilization (%)	58.42	57.26	54.38	56.82	53.47
Nurse Utilization (%)	82.98	81.75	77.05	80.74	75.67
Nurse Overtime$^+$ (min.)	98.82	100.45	99.21	100.19	99.29
Nurse Overtime$^+$ Count	305.36	286.38	254.8	290.82	258.15
Nurse Overtime (min.)	38.87	37.04	32.54	37.5	33.02
Type I Delay (days)	1.31	1.32	1.31	1.31	1.31
Type II Delay (min.)	15.41	14.24	10.91	13.89	10.69
Type III Delay (min.)	32.24	29.3	20.05	27.26	16.63
System Time (min.)	204.06	199.09	188.27	199.59	188.34

Nurse Overtime$^+$ excludes zero entries

3.3.5 Discussion

The results provided in Section 3.3.4 provide insight into the questions about how patients should be scheduled and how the number of nurses impacts system performance. First, consider Tables 3.6 and 3.7 for the scheduling algorithms. The ASAP algorithm had the highest total throughput of 2629 appointments (Figure 3.14) and daily throughput values. However, the STDEV for both performance measures was large enough that the average values of the Collective and Individual algorithms fall within the 90% confidence interval for the ASAP algorithm. Therefore, the ASAP algorithm was not necessarily an improvement over the Collective or Individual algorithm. The Collective, Individual, and Nurse algorithms had between 2613 appointments to 2619 appointments.

The chair utilization values for all four algorithms was between 49% and 50%. The nurse utilization values were 84% to 85% for the ASAP, Collective, and Individual algorithms, but the Nurse algorithm had a lower average nurse utilization of about

74%. This indicates that the nurse is the limiting resource because scheduling based strictly on nurse availability kept the nurse resources less busy during the normal working hours.

The Nurse algorithm had the lowest average nurse overtime$^+$ of around 95 minutes, 12% lower than the ASAP algorithm. The Collective and Individual algorithms were 2% and 4%, respectively, lower than the ASAP algorithm for the average nurse overtime$^+$. The Nurse algorithm had fewer instances of nurse overtime (lowest nurse overtime$^+$ count) with 116 instances. Overall, the nurse overtime was lowest with the Nurse algorithm with an average value of 17 minutes compared to the average values of 42 to 43 minutes with the other three algorithms.

From the patient's perspective, the ASAP algorithm had the lowest type I delay value of 1.30 days (Figure 3.15). The Collective and Individual algorithms had slightly higher values of 1.33 and 1.35 days, respectively. The Nurse algorithm had the largest type I delay average value of 1.49 days. The Individual algorithm had the best type II delay and system time average values (Figure 3.16). The Collective algorithm was within 1% of the Individual algorithm for type III delay and system time. However, the Nurse algorithm had a very high type II delay of around 47 minutes as compared to the 14 to 21 minutes with the other three algorithms. As a result, the system time for the Nurse algorithm was 25 to 32 minutes higher than the other algorithms as well. The Nurse algorithm does not adapt well to the stochastic nature of the appointment duration and the patients end up waiting a long time in the waiting room for their appointment to begin.

In summary of the scheduling algorithm experiment, the Collective and Individual algorithms have similar system performance results when compared to the ASAP and Nurse algorithms. The Individual algorithm is best for minimizing the patient perspective's performance measures of type II delay and system time. The ASAP

algorithm is best for minimizing type I delay and maximizing throughput. Although the Nurse algorithm best minimized the number of overtime instances and total average overtime, the patient's perspective performance measures were unacceptably worse for system time and type II delay. Therefore, the Nurse algorithm is not recommended for implementation in the real oncology clinic. The recommended scheduling algorithm would be the Individual algorithm because it is best for the most performance measures. Implementing the Individual algorithm over the ASAP will not significantly impact the throughput and will increase type I delay by 0.05 days. However, the Individual algorithm reduces system time for the patient by 6 minutes (3% improvement), reduces type II delay by 7 minutes (34% improvement), and reduces nurse overtime$^+$ by 4 minutes (4%) improvement.

Second, consider the results of the the number of nurses experiments in Table 3.8. The throughput does not show a consistent increasing or decreasing pattern as the number of nurses increases from five to ten. The STDEVs for the total throughput and daily throughput performance measures were large enough that the AVG values all fall within the 90% CI's and thus it can be concluded that the number of nurses does not impact the throughput with ASAP algorithm. This observation is expected because the nurses are ignored with the ASAP algorithm so modifying the number of nurses should not impact the scheduling decisions. Similarly, the type I delay, type III delay, and chair utilization appear to be independent of the number of nurses in the oncology clinic.

However, the type II delay, system time, nurse overtime$^+$, and nurse overtime all decreased (Figures 3.17 and 3.18) as the number of nurses in the clinic increased from five to ten nurses with the ASAP algorithm. The type II delay decreased because more nurses are available which allows the patient's infusion to start sooner. Since type II delay is a component of system time, the system time decreases as well.

More nurses are able to help start and monitor patient appointments so the nurse overtime decreases, too . Also, the nurse utilization decreased as the number of nurses increased because more nurses are handling similar work loads.

Considering Figures 3.17 and 3.18 again, observe that the concept of diminishing returns is present. Thus, the performance measures of type II delay, system time, nurse overtime^{+}, and nurse overtime all decrease by a smaller percentage each time. Although having more nurses improves each of these performance measures under the ASAP algorithm, the improvement is smaller with each additional nurse. After observing two steep drops from five to six nurses, then six to seven nurses for the four performance measures, seven is the recommended number of nurses to have on duty with the ASAP algorithm under a 20% increase in demand. The current average number of nurses is around 5 nurses, then for a 20% increase in demand, having 7 nurses will results in lower system time by 14 minutes (6%) for patients and lower nurse overtime by 24 minutes (39%).

Third, consider the results for the distribution experiments in Table 3.9. The results indicate a sensitivity in the type II and type III delay when changing the probability distribution and changing the parameters of the distribution. The throughput and type I delay did not change because the scheduling decisions were made using the planned times from the Drug Infusion Time Sheet. Using Gamma0 as a baseline, the results indicate that the type II delay was reduced by 8% when the standard deviation was reduced by roughly 50% for Gamma1 and by 10% when the distribution was changed to Weibull1. When both the standard deviation and average values were reduced for Gamma2 and Weibull2, the type II delay decreased by 29% and 31%, respectively. As a result, the system time was reduced by 2% (Gamma1 and Weibull1) and 8% (Gamma2 and Weibull2).

The type III delay was reduced by 9% and 15% for the Gamma1 and Weibull1

probability distributions. The type III delay was reduced by 38% and 48% for the Gamma2 and Weibull2 probability distributions. Similarly, the chair utilization and nurse utilization were reduced by 2% and 3% for the Gamma1 and Weibull1 probability distributions, and by 7% and 9% for the Gamma2 and Weibull2 probability distributions. Finally, the nurse overtime^{+} was reduced by 4% and 5% for the Gamma1 and Weibull1 probability distributions, and by 15% and 16% for the Gamma2 and Weibull2 probability distributions. In summary, reducing the average and standard deviation for the type II + III delay improved system performance by reducing type II delay (30%), type III delay (38%), resource utilization (8%), system time (8%), and nurse overtime (15%).

3.4 Summary

The DEVS-CHEMO simulation is a new tool that allows for the modeling and simulation of the scheduling process of oncology clinic resources (chairs and nurses) and chemotherapy patients; the arrival process of the patients to the clinic on the day of their appointment; and the patient chemotherapy treatment process. This discrete event simulation of oncology clinic operations provides managers with a tool for analyzing decision-making and operational policies within the oncology clinic.

The implementation of DEVS-CHEMO featured four performance measures from the patient's perspective (type I delay, type II delay, type III delay, and system time) and four performance measures from the management's perspective (throughput, chair utilization, nurse utilization, and nurse overtime). DEVS-CHEMO was developed using the DEVS formalism; it is a coupled model that consists of two smaller coupled models, EF and CHEMO. EF is the experimental frame, a coupled model containing four atomic models: PGENR, CGENR, TRANSD, and SCHED. CHEMO is the chemotherapy clinic, a coupled model containing five atomic models:

RECEPT, WAITROOM, PHARM, CHARGENURSE, and REGNURSE.

DEVS-CHEMO is a tool that oncology clinic managers can use to test decision and operational policies before implementation in the clinic. In one set of experiments, four scheduling algorithms were compared and it was determined that although the current scheduling algorithm, ASAP, at Scott & White's oncology clinic may provide the best throughput and type I delay, the Individual algorithm was best overall. Implementing the Individual algorithm over the current ASAP algorithm reduces system time for the patient by 3%, reduces type II delay by 34%, and reduces nurse overtime by nearly 4%. In the second set of experiments, the number of nurses was increased from five to ten nurses using the ASAP algorithm. The results showed that the type II delay, system time, nurse utilization, nurse overtime^{+}, and nurse overtime, all decrease as the number of nurses increases. Due to the concept of diminishing returns, it was determined that the ideal number of nurses for the Scott & White oncology clinic is seven nurses when the demand for oncology clinic services is increased by 20%. Using an average of seven nurses will lower system time by 6% and reduce overtime by 39%.

The system performance results for type II delay, type III delay, resource utilization, system time, and nurse overtime seem to be sensitive to changes in the type of the probability distribution and the parameters of the probability distribution. Therefore, data from a longer time period (e.g., 6-months to 1-year) would be necessary to make conclusive results regarding the results of the sensitivity analysis experiments.

4. MEAN-RISK STOCHASTIC INTEGER PROGRAMMING MODEL FOR CHEMOTHERAPY SCHEDULING

Scheduling oncology clinic appointments is challenging. The spacing between each chemotherapy appointment is crucial to the patient's health status and therefore each appointment needs to be scheduled as close to the start date recommended by the oncologist as possible. Clinic resources should be allocated to the patient for each appointment, but the nature of the nurse assignment is complicated because of new patient starts and acuity levels. The appointment scheduling problem for oncology clinics is stochastic in nature and deterministic models do not sufficiently capture the scheduling process. Patient requests for appointments, treatment duration, and resource availability are all examples of stochastic parameters in oncology clinic scheduling. In this chapter, several SIP models, termed SIP-CHEMO, are developed to address the complexities of the chemotherapy scheduling problem. The SIP-CHEMO models reflect the constraints and objectives of the decision problem and incorporate uncertainty into the decision problem. Some of the SIP-CHEMO models also include mean-risk measures in order to better reflect the inherent "risk" in the decision problem. This research develops the first optimization model for scheduling chemotherapy appointments that incorporates uncertainty in problem parameters and considers risk.

The rest of this chapter is organized as follows: Section 4.1 defines the chemotherapy scheduling decision problem and gives an overview of mean-risk SIP problems. The notation for the SIP-CHEMO models is given section 4.2. The risk-neutral chemotherapy scheduling problem is stated in section 4.3 while section 4.4 defines the risk-averse scheduling problem using two mean-risk measures. Real application

parameters are described in Section 4.5 along with computational experiments. Section 4.6 summarizes the chapter.

4.1 Introduction

4.1.1 Scheduling Chemotherapy Appointments

Information acquired through visits and communication with an outpatient oncology clinic provided valuable insight into the constraints and objectives that are important for the SIP-CHEMO models. Once a patient is diagnosed with cancer, an oncologist prescribes a unique *treatment regimen*, or series of chemotherapy appointments, to each cancer patient based on the patient's current state of health. A *treatment regimen* (Table 3.1) consists of a prescribed *start date* for the patient, frequency of appointments (treatment day), suggested duration (in minutes), acuity level, and chemotherapy drug name for each appointment. Treatment regimens depend on the patient's type of cancer, stage of cancer growth, and current health. Therefore treatment regimens are unique to each individual patient.

Recall the chemotherapy scheduling process in Figure 3.1. The *treatment regimen* prescribed by the oncologist is sent to a scheduler to determine the appointment schedule and to allocate clinic resources for each appointment in the treatment regimen. The scheduler must immediately schedule all appointments in the *treatment regimen* to guarantee the availability of the later appointments. To maximize treatment effectiveness, these appointments should be scheduled as close to the earliest state date recommended by the oncologist as possible. Delay from the prescribed treatment date is referred to as *type I delay*. The scheduler must make a *chemotherapy scheduling decision*, which allocates a specific date, time, and set of clinic resources (e.g., chair and nurse) to each appointment in the patient's treatment regimen. The chemotherapy scheduling decision problem determines when to

schedule all of the appointments in the chemotherapy patient's treatment regimen and to determine which resources to allocate to the patient at each appointment.

Chemotherapy chairs and nurses are both assigned to a patient for the entire duration of their chemotherapy treatment. It generally takes around 15 to 30 minutes to start the chemotherapy drug infusion for each patient. This process is called a *new start*. During a new start, the nurse is primarily dedicated to starting the drug infusion of that patient. As a result, each nurse is limited to one new start during each time period. After completing a new start with a patient, the nurse is free to continue monitoring all of their assigned patients.

Chemotherapy treatments are well-known for causing nausea and the cancer weakens the immune system, both of which can severely deteriorate a patient's state of health. The side-affects can occur suddenly during chemotherapy administration. Depending on the type and intensity of the treatment, the assigned nurse must pay close attention to the patient in order to monitor the patient's condition and reactions to these side-affects. However, it is possible for each nurse to simultaneously monitor the chemotherapy treatments of several patients at the same time. It is crucial that the nurses are not over-utilized since they must be available to assist patients experiencing adverse reactions to the chemotherapy drugs. To account for this, the concept of acuity levels is used. An *acuity level* is a relative measure of the nurse's attention required by a patient during an appointment. Acuity levels are assigned a value of one, two, or three, where an acuity level of three represents the maximum attention required by the patient from the nurse. Each nurse can monitor several patients at once provided that the sum of the acuity levels for all patients is less than or equal to a pre-determined maximum acuity level for that nurse. Refer to the example of acuity levels and new patient starts in Figure 3.3 of the previous chapter for details.

There are several stochastic parameters associated with the chemotherapy scheduling problem. The side-affects of chemotherapy drugs can influence both the treatment duration and acuity level during an appointment. If a patient is very sick, the patient may require more attention from the nurse and in some cases, treatment may be paused to allow the patient time to recover. This translates to a higher acuity level and a longer appointment duration. Additionally, some patients take longer to begin treatment because of small veins for the infusion needle or a clogged port-a-catheter, among other things. Due to these variations, the acuity level and treatment duration of an appointment are stochastic parameters.

The number of nurses on duty on a given day is also a stochastic parameter. This is because nurses are the limiting resource when scheduling patients at the oncology clinic collaborating on this research. When a nurse is unexpectedly unavailable on a particular day (e.g., when a nurse calls in sick to work), then an understaffed clinic will have difficulty adjusting. Therefore, nurse availability is assumed to be stochastic in the decision problem to account for the possibility that a nurse may not be able to complete their assigned responsibilities.

4.1.2 Mean-Risk Stochastic Integer Programming

SIP is used to formulate the chemotherapy scheduling problem because of stochastic parameters. In SIP-CHEMO each patient is scheduled based on their *treatment regimen* and the *start date* as prescribed by the oncologist. *Mean-Risk SIP models* represent risk using both the expected value and a mean-risk function in the objective function to more accurately reflect the inherent uncertainty in a problem. A mean-risk function has both a target value and a deviation measure from the target value.

The mean-risk SIP approach was chosen for this problem for two reasons. First,

mean-risk SIP allows for modeling different levels of risk using mean-risk measures such as *expected excess* (EE) and *absolute semideviation* (ASD). Risk in this problem is associated with delays in the treatment's start date. When appointments do not begin on the start date recommended by the oncologist, then the treatments become less effective and delays pose risk to the patient's health status. Second, scheduling decisions in this problem are *binary* and have to be made 'here-and-now' for each patient before observing future *uncertainty*. The second-stage decisions represent the "recourse" decisions made after uncertainty is realized.

A *mean-risk* two-stage SIP [34] can be stated as follows:

$$\begin{aligned} \text{SIP: Min } & \mathbb{E}[f(x,\tilde{\omega})] + \lambda \mathbb{D}[f(x,\tilde{\omega})], \\ \text{s.t. } & Ax \geq b \\ & x \in \mathbb{R}^{\bar{n_1}} \times \mathbb{Z}^{n'_1}, \end{aligned} \tag{4.1}$$

where x is the first-stage decision vector and $f(x,\tilde{\omega})) = c^\top x + Q(x,\tilde{\omega})$. The vector $c \in \mathbb{R}^{n_1}$ (where $n_1 = \bar{n_1} + n'_1$) is the first-stage cost vector, $b \in \mathbb{R}^{m_1}$ is the right-hand side, $A \in \mathbb{R}^{m_1 \times n_1}$ is the first-stage constraint matrix, and $\tilde{\omega}$ is a multi-variate discrete random variable with an outcome (scenario) $\omega \in \Omega$ with probability of occurrence p_ω. The random variable $\tilde{\omega}$ is defined on the probability space, $(\Omega, \mathcal{A}, \mathcal{P})$ where Ω is the set of all possible outcomes, $\mathcal{A}$ is the set of events, and $\mathcal{P}$ is the probability measure. $\mathbb{E} : \mathcal{F} \to \mathbb{R}$ denotes the expected value, where $\mathcal{F}$ is the space of all real random cost variables $f : \Omega \to \mathbb{R}$ satisfying $\mathbb{E}[|f(\tilde{\omega})|] < \infty$. Modeling problems using only the expectation in the objective makes the formulation risk-neutral. To introduce risk, a risk measure $\mathbb{D} : \mathcal{F} \mapsto \mathbb{R}$ is used resulting in the so-called *mean-risk* stochastic program, where $\lambda > 0$ is a suitable weight factor that quantifies the tradeoff between expected cost and risk. $\mathbb{D}$ measures the dispersion (variability) of

the random variable $f(x, \tilde{\omega})$. Common deviation measures in the literature include conditional value-at-risk (CVaR), EE, and ASD.

For any outcome (scenario) ω, the recourse function $Q(x, \omega)$ is given by the following standard second-stage subproblem:

$$\begin{aligned} Q(x,\omega) = &\text{Min } q(\omega)^\top y \\ &\text{s.t. } W(\omega)y \geq r(\omega) - T(\omega)x \\ &y \in \mathbb{R}^{\bar{n_2}} \times \mathbb{Z}^{n_2'}. \end{aligned}$$

The vector $q(\omega) \in \mathbb{R}^{n_2}$ is the second-stage cost vector, $W(\omega) \in \mathbb{R}^{m_2 \times n_2}$ (where $n_2 = \bar{n_2} + n_2'$) is the recourse matrix, $r(\omega) \in \mathbb{R}^{m_2}$ is the right-hand side, and $T(\omega) \in \mathbb{R}^{m_2 \times n_1}$ is the technology matrix. A scenario defines the realization of the stochastic problem data $\{q(\omega), r(\omega), W(\omega), T(\omega)\}$.

The SIP-CHEMO models developed in this section utilize the EE and ASD mean-risk measures. These two deviation measures are suitable for this problem because they minimize the risk of deviation from the recommended start date and minimize deviation from an acceptable level of scheduling conflicts. Next, the EE and ASD risk measures are defined.

Given a target $\eta \in \mathbb{R}$ and $\lambda > 0$, EE [26] is defined as

$$\phi_{EE_\eta}(x) = \mathbb{E}[\max\{f(x, \tilde{\omega}) - \eta, 0\}].$$

It is the expected value of the excess over the target $\eta \in \mathbb{R}$. Substituting $\mathbb{D} := \phi_{EE_\eta}$ in (4.1) results in SIP with EE as follows:

$$\text{Min }_{x \in X} \ \mathbb{E}[f(x, \tilde{\omega})] + \lambda \phi_{EE_\eta}(x). \tag{4.2}$$

Assuming a finite number of scenarios $\omega \in \Omega$, each with probability of occurrence $p(\omega)$, $\lambda \geq 0$, and a target level $\eta \in \mathbb{R}$, problem (4.2) is equivalent to the following formulation [26]:

$$\begin{aligned} \text{SIP-EE: Min} \quad & c^\top x + \sum_{\omega \in \Omega} p(\omega) q(\omega)^\top y(\omega) \ + \lambda \sum_{\omega \in \Omega} p(\omega) \nu(\omega) \\ \text{s.t.} \quad & T(\omega)x + W(\omega)y(\omega) \geq r(\omega), \ \forall \omega \in \Omega \\ & - c^\top x - q(\omega)^\top y(\omega) + \nu(\omega) \geq -\eta, \ \forall \omega \in \Omega \\ & x \in X, \ \ y(\omega) \in \mathbb{Z}_+^{\bar{n}_2} \times \mathbb{R}_+^{n_2'}, \ \nu(\omega) \in \mathbb{R}_+, \forall \omega \in \Omega. \end{aligned} \tag{4.3}$$

The ASD model is obtained by replacing the target value in EE with the expected (mean) value $\mathbb{E}[f(x, \tilde{\omega})]$ and is given as $\phi_{ASD}(x) = \mathbb{E}[\max\{f(x, \tilde{\omega}) - \mathbb{E}[f(x, \tilde{\omega})], 0\}]$. ASD reflects the expected value of the excess over the mean value. Setting $\mathbb{D} := \phi_{ASD}$ in (4.1), results in the following SIP with semideviation:

$$\text{Min}_{\ x \in X} \ \mathbb{E}[f(x, \tilde{\omega})] + \lambda \phi_{ASD}(x). \tag{4.4}$$

Similarly to the EE problem, note that

$$\phi_{ASD}(x) \equiv \mathbb{E}[\max\{f(x, \tilde{\omega}), \mathbb{E}[f(x, \tilde{\omega})]\}] \ - \ \mathbb{E}[f(x, \tilde{\omega})],$$

give the DEP formulation for ASD. Given $\lambda \in [0, 1]$, problem (4.4) is equivalent to

the following formulation [26] :

$$\begin{aligned}
\text{SIP-ASD: Min} \quad & (1-\lambda)c^\top x + (1-\lambda)\sum_{\omega\in\Omega} p(\omega)q(\omega)^\top y(\omega) \ + \lambda \sum_{\omega\in\Omega} p(\omega)\nu(\omega) \quad (4.5)\\
\text{s.t.} \quad & T(\omega)x + W(\omega)y(\omega) \geq r(\omega), \ \forall \omega \in \Omega \\
& -c^\top x - q(\omega)^\top y(\omega) + \nu(\omega) \geq 0, \ \forall \omega \in \Omega \\
& -c^\top x - \sum_{\omega\in\Omega} p(\omega)q(\omega)^\top y(\omega) + \nu(\omega) \geq 0, \ \forall \omega \in \Omega \\
& x \in X, \ \ y(\omega) \in \mathbb{Z}_+^{\bar{n}_2} \times \mathbb{R}_+^{n_2'}, \ \nu(\omega) \in \mathbb{R}, \forall \omega \in \Omega.
\end{aligned}$$

4.2 Problem Definition and Notation

This section defines the notation for the SIP-CHEMO models. Consider a new patient whose oncologist has recommended a unique treatment regimen and start date. The treatment regimen specifies the number of appointments, number of days to rest between each appointment, the duration, acuity level, and chemotherapy drugs for each appointment. The availability of chemotherapy chair and nurse resources as well as the current schedule of appointments are known. An appointment schedule for this new patient is needed. The schedule should specify the start date, time slot, chair assignment, and nurse assignment for each appointment of the treatment regimen.

The chemotherapy scheduling problem assumes a finite planning horizon. Let set D be the days in the planning horizon where $\bar{D}$ is the last day of the planning horizon. Chemotherapy nurses expected to be on duty on day d are in the set J^d and the chemotherapy chairs on day d are the set K^d. The number of nurses working on day d is $\bar{J}^d$. All chair and registered nurse resources within each set are assumed to have the same properties and are therefore interchangeable.

Each day in the planning horizon is divided into time slots of equal length and the same number of time slots exist each day, which are specified by the set S. The size of the set S is $\bar{S}$. The set S^d is the set of time slots available on day d while S^{dk} is the set of time slots available on day d for chair k. Note that $\bigcup_{k \in K^d} S^{dk} = S^d$, $S^{dk} \subseteq S^d$, $S^{dk} \subseteq S$, and $S^d \subseteq S$.

Table 4.1: Sets Used in the SIP-CHEMO Models

D:	Set of days in the planning horizon, indexed by d
J^d:	Set of nurses expected to work on day d, indexed by j
K^d:	Set of available chairs on day d, indexed by k
S:	Set of time slots for the clinic's operating hours, indexed by s
S^d:	Set of available time slots on day d, indexed by s
S^{dk}:	Set of available time slots on day d for chair k, indexed by s
T:	Set of days in the treatment regimen, indexed by t
U_1^d:	$\{\hat{u} \mid \hat{u} = \max(1, s - r_t + 1) ... \max(1, s), \hat{u} \in S^d\}$
Ω :	Set of scenarios, indexed by ω
$J^d(\omega)$:	Set of nurses working on day d for scenario ω, indexed by j
$U_1^{dk}(\omega)$:	$\{\hat{u} \mid \hat{u} = \max(1, s - r_t(\omega) + 1) ... \max(1, s), \hat{u} \in S^{dk}\}$
$U_2^{dk}(\omega)$:	$\{\hat{u} \mid \hat{u} = \max(1, \bar{S} - r_t(\omega) + 2) ... \bar{S}, \hat{u} \in S^{dk}\}$

Each patient has a unique treatment regimen denoted by the set T. The set T is unique to each patient and specifies which days the patient has an appointment. The size of set T, $|T| = n$, specifies the number of appointments in the patient's treatment regimen. Consider $T = \{t_1, t_2, t_3\} = \{1, 8, 15\}$ where the patient has three treatments specified by t_1, t_2, and t_3 respectively. Note that $t_2 - t_1 = 8 - 1 = 7$ indicates that the

second appointment should be seven days after the first appointment. Set T should be defined such that $t_1 = 1$ and t_n is the length of the treatment regimen. All sets used in the SIP-CHEMO models are defined in Table 4.1.

The expected acuity level for appointment t of the treatment regimen is given by a_t, but the actual acuity level may be different. Similarly, the number of time slots expected to be needed for appointment t of the treatment regimen is r_t, but the actual number of time slots used may be different. The treatment start date recommended by the oncologist is specified by d^{start}. This date must be part of the planning horizon such that $d^{start} \in D$. The objective is to schedule the first date of the treatment regimen as close to this recommended start date as possible. The penalty for each day (either early or late) is δ^{delay}.

Each patient appointment needs two resource assignments: a chemotherapy nurse and a chemotherapy chair. The patient must be assigned to the same chair for the duration of the appointment and no other patient should be assigned to that chair at the same time. Therefore, there is a one-to-one relationship between a patient and a chair for the duration of the appointment. The patient is also assigned to one nurse for the duration of the appointment. However, nurses can have multiple patients assigned to them during the same time slot. There are two constraints associated with the patient to nurse assignments. First, the nurse can only start one patient's appointment during a time slot. After starting the patient's appointment, nurses can have multiple patients for the remainder of the appointment slots provided that the sum of all their patient's acuity levels at that time is less than or equal to a predefined maximum acuity level, $a^{\max}$.

There are a number of existing patients whose appointments have already been scheduled. For those existing patients on the schedule, let b_{jds} be the acuity of the patient who has been assigned to nurse j during slot s on day d. The acuity across

all nurses on day d in slot s is $\sum_{j \in J^d} b_{jds} = q_{ds}$. If a nurse j is assigned to start a patient on day d in slot s, let $n_{jds} = 1$, otherwise $n_{jds} = 0$.

There are three types of uncertainty considered in this problem formulation. A scenario is the realization of an outcome for the number of nurses on duty, acuity level, and appointment duration for each appointment in the patient's treatment regimen. The set Ω represents a finite set of scenarios indexed by ω. First, the number of nurses on duty may decrease because a nurse may be unable to work that day. $J^d(\omega)$ is the set of nurses working on day d in scenario ω. The number of nurses available during the realization of any scenario ω is assumed to be less than or equal to the number of nurses originally scheduled to work, therefore $J^d(\omega) \subseteq J^d, \forall \omega \in \Omega$. Second, the acuity level can increase or decrease during the realization of a specific scenario, although acuity levels are still bounded between one and three. Recall that the expected acuity level for appointment t of the treatment regimen is a_t, but the actual acuity level given the realization of scenario ω is $a_t(\omega)$. Third, the length of the appointment can increase or decrease, e.g., more or fewer time slots are needed. Recall that the number of time slots expected to be needed for appointment t of the treatment regimen is r_t, but the actual number of time slots used for the realization of scenario ω is $r_t(\omega)$.

One constraint imposes an upperbound on the combined patients' acuity levels during a time slot. For time slot s on day d, the maximum acuity level across all patients that the $\bar{J}^d$ nurses can handle is $\bar{J}^d * a^{\max}$. However, $o_{ds}(\omega) = \bar{J}^d(\omega) * a^{\max}$ is an upperbound on the maximum acuity level that the nurses can handle on day d in slot s for scenario ω. All of the parameters used in the SIP-CHEMO models are in Table 4.2.

Table 4.2: Problem Parameters for the SIP-CHEMO Models

$\bar{D}$:	$= \max\{d \mid d \in D\}$ last day of the planning horizon
$\bar{S}$:	$= \max\{s \mid s \in S\}$ last time slot of the clinic's operating hours
$\bar{J}^d$:	$= \lvert J^d \rvert$ the number of nurses working on day d
$\bar{T}$:	$= \max\{t \mid t \in T\}$ the last day, or length, of treatment regimen cycle
a_t:	Acuity level on day t of the treatment regimen, $a_t \in \{1, 2, 3\}$
$a^{\max}$:	Maximum acuity level per nurse in one time slot
b_{jds}:	Acuity on day d of existing patients for nurse j in slot s
d^{start}:	Treatment start day recommended by the oncologist
r_t:	Number of time slots needed for appointment t of the treatment regimen
δ^{delay}:	Penalty for each day of treatment delay
δ_s^{slot}:	Penalty for time slot s
δ^{slot}:	Penalty for each additional time slot
δ^{α}:	Penalty for α overtime variable
δ^{β}:	Penalty for β excess acuity variable
δ^{γ}:	Penalty for γ new start variable
δ^{δ}:	Penalty for δ overlap variable
n_{jds}:	$= 1$ if nurse j is starting an existing patient on day d during time slot s, 0 otherwise
q_{ds}:	Sum of the acuity levels of existing patients on day d in slot s
$\bar{J}^d(\omega)$:	$= \lvert \bar{J}^d(\omega) \rvert$ number of nurses working on day d in scenario ω
$a_t(\omega)$:	Acuity level on day t of their treatment regimen in scenario ω
$r_t(\omega)$:	Number of time slots needed for appointment t in scenario ω
$o_{ds}(\omega)$:	$= \bar{J}^d(\omega) * a^{\max}$, the maximum acuity level load that the nurses can handle on day d in slot s in scenario ω

4.3 Risk-Neutral SIP-CHEMO Scheduling Problem

This section first defines the formulation of the risk-neutral (RN) SIP-CHEMO model. RN is defined first because it is the simplest of the SIP-CHEMO models. The remaining two SIP-CHEMO models are extensions of RN. The decision variables, objective, and constraints are described for the first- and second-stages of the RN SIP-CHEMO model. Then an algorithm is developed to improve solution performance.

4.3.1 First-Stage

There are three primary decisions that need to be made here-and-now and these are defined in Table 4.3. Let x_d be a binary decision variable that indicates if the first appointment in the treatment regimen begins on day d, also known as the start date. Let $y_{ks}^{d^t}$ be a binary decision variable that indicates if appointment t of the patient's treatment regimen is scheduled for day d in chair k during time slot s. Finally, let $\hat{v}_{js}^{d}$ be a binary decision variable that indicates if nurse j is assigned to start the patient during slot s on day d. The decision variable for the chair assignment is separated from the decision variable with the nurse assignment because they have different constraints for subsequent time slots.

Table 4.3: Risk-Neutral First-Stage Decision Variables

x_d:	$x_d = 1$ if the first treatment is on day d, $x_d = 0$ otherwise.
$y_{ks}^{d^t}$:	$y_{ks}^{d^t} = 1$ if the t^{th} treatment starts in chair k during slot s on day d, $y_{ks}^{d^t} = 0$ otherwise.
$\hat{v}_{js}^{d}$:	$\hat{v}_{js}^{d} = 1$ if nurse j is scheduled to start the patient during slot s on day d, $\hat{v}_{js}^{d} = 0$ otherwise.

The first-stage objective (4.6a) is to minimize the deviation from the desired start date of the first appointment and to minimize the penalties associated the each time slot. It is expected that $\delta^{delay} \geq \delta_s^{slot}\ \forall s$ because moving the appointment backwards or forwards one day has larger consequences than moving the appointment backward or forward one time slot. By defining δ_s^{slot} appropriately, one can encourage appointments to be scheduled early in the day, late in the day, or even consider patient preferences for certain times of the day.

Constraint (4.6b) links the x_d decision variable and the $y_{ks}^{d^t}$ decision variable by forcing agreement on the start date of the first treatment in the treatment regimen. Constraint (4.6c) is necessary to make sure that the rest periods between appointments is consistent with the recommendation the oncologist made for the patient's treatment regimen. Constraint (4.6d) creates the requirement that each appointment in the patient's treatment regimen is scheduled. If this constraint is not satisfied, then the problem is infeasible and the planning horizon should be extended. Constraint (4.6e) requires that the sum of the acuity levels of all nurses assigned to a nurse during any given time slot is less than or equal to $a^{\max}$. Constraint (4.6f) links the $y_{ks}^{d^t}$ decision variable to the $\hat{v}_{js}^{d}$ decision variable such that all patients scheduled to start must have a nurse assigned. Constraint (4.6g) limits the number of new patient starts for a nurse during a time slot to one or fewer. Constraints (4.6h)-(4.6j) are binary constraints.

$$\text{RN: Min } \sum_{d\in D}[\delta^{delay} * |d - d^{start}|x_d + \sum_{t\in\{t|t\in T, t\leq d\}} \sum_{k\in K^d} \sum_{s\in S^{dk}} \delta_s^{slot} * y_{ks}^{d^t}] + \mathbb{E}[f(x, y, \hat{v}, \tilde{\omega})] \tag{4.6a}$$

$$s.t.\ x_d - \sum_{k\in K^d} \sum_{s\in S^{dk}} y_{ks}^{d^1} = 0, \forall d \in D \tag{4.6b}$$

$$- x_d + \sum_{k\in K^d} \sum_{s\in S^{(d+t-1),k}} y_{ks}^{(d+t-1)^t} \geq 0, \forall d \in 1...(\bar{D} - \bar{T} + 1), \forall t \in T, d \geq t \tag{4.6c}$$

$$\sum_{d\in\{d|d\in D, d\geq t\}} \sum_{k\in K^d} \sum_{s\in S^{dk}} y_{ks}^{d^t} = 1, \forall t \in T \tag{4.6d}$$

$$- \sum_{u\in U_1^d} a_t * \hat{v}_{ju}^d \geq b_{jds} - a^{\max}, \forall d \in D, \forall j \in J^d, \forall s \in S \tag{4.6e}$$

$$\sum_{j\in J^d} \hat{v}_{js}^d - \sum_{t\in\{t|t\in T, t\leq d\}} \sum_{k\in\{k|k\in K^d, s\in S^{dk}\}} y_{ks}^{d^t} = 0, \forall d \in D, \forall s \in S^d \tag{4.6f}$$

$$- \hat{v}_{js}^d \geq n_{jds} - 1, \forall d \in D, \forall j \in J^d, \forall s \in S^d \tag{4.6g}$$

$$x_d \in \{0, 1\}, \forall d \in D \tag{4.6h}$$

$$y_{ks}^{d^t} \in \{0, 1\}, \forall d \in D, \forall k \in K^d, \forall s \in S^{dk}, \forall t \in T, d \geq t \tag{4.6i}$$

$$\hat{v}_{js}^d \in \{0, 1\}, \forall d \in D, \forall s \in S^d, \forall j \in J^d \tag{4.6j}$$

4.3.2 Second-Stage

The second-stage decision variables are the recourse decision variables. There are four types of scheduling conflicts that can occur from the realization of uncertainty: overtime, excess acuity, new starts, and appointment overlaps. Each scheduling conflict is modeled as a second-stage decision variable given in Table 4.4. First, an increase in the appointment duration can cause overtime for the clinic. Let $\alpha^d(\omega)$ be a continuous decision variable that indicates the number of overtime slots caused

by the realization of scenario ω on day d. Second, an increase in acuity level or a decrease in the number of nurses can cause the maximum acuity level for a time slot to be exceeded. Let $\beta_s^d(\omega)$ be a continuous decision variable that indicates the amount of excess acuity in time slot s on day d in scenario ω.

Third, a decrease in the number of nurses on duty can cause scheduling problems with the schedule for starting patient appointments if the nurse who does not come in to work was assigned to start a patient's appointment that day. Let $\gamma_{js}^d(\omega)$ be a continuous decision variable that indicates if an nurse j is not able to start the assigned patient during day d in slot s under scenario ω. Fourth, an increase in appointment duration can cause the appointment to overlap another appointment already scheduled. Let $\delta_{ks}^d(\omega)$ be a continuous decision variable that indicates if an appointment overlaps an existing appointment in chair k on day d in time slot s for scenario ω. Each of these four continuous decision variables has an associated penalty of $\delta^\alpha, \delta^\beta, \delta^\gamma, \delta^\delta$ respectively.

Table 4.4: Risk-Neutral Second-Stage Decision Variables

$\alpha^d(\omega)$:	(overtime variable) number of overtime slots for the clinic on day d in scenario ω
$\beta_s^d(\omega)$:	(excess acuity variable) excess acuity above the maximum for all nurses during slot s on day d in scenario ω
$\gamma_{js}^d(\omega)$:	(new start variable) indicates if nurse j is unable to start an assigned patient on day d in slot s in scenario ω
$\delta_{ks}^d(\omega)$:	(overlap variable) indicates if an appointment overlaps an existing appointment in chair k on day d in slot s in scenario ω

For each outcome (scenario) $\omega \in \Omega$ of $\tilde{\omega}$:

$$\text{Min } f(x, y, \hat{v}, \tilde{\omega}) = \sum_{d \in D} [\delta^{\alpha} * \alpha^{d}(\omega) + \delta^{\beta} \sum_{s \in S} \beta_{s}^{d}(\omega) + \delta^{\gamma} \sum_{s \in S^{d}} \sum_{j \in J^{d} \backslash J^{d}(\omega)} \gamma_{js}^{d}(\omega)$$

$$+ \delta^{\delta} \sum_{k \in K^{d}} \sum_{s \in S \backslash S^{dk}} \delta_{ks}^{d}(\omega)] \tag{4.7a}$$

$$s.t.\ \alpha^{d}(\omega) \geq \sum_{t \in \{t | t \in T, t \leq d\}} \sum_{k \in K} \sum_{s \in U_{2}^{dk}(\omega)} (\bar{S} - r_{t}(\omega) - s + 3) * y_{ks}^{d^{t}}, \forall d \in D \tag{4.7b}$$

$$\beta_{s}^{d}(\omega) \geq q_{ds} - o_{ds}(\omega) + \sum_{t \in \{t | t \in T, t \leq d\}} \sum_{k \in K} \sum_{u \in U_{1}^{dk}(\omega)} a_{t}(\omega) * y_{ku}^{d^{t}}, \forall d \in D, \forall s \in S \tag{4.7c}$$

$$\gamma_{js}^{d}(\omega) \geq \hat{v}_{js}^{d} + n_{jds}, \forall d \in D, \forall s \in S^{d}, \forall j \in J^{d} \backslash J^{d}(\omega) \tag{4.7d}$$

$$\delta_{ks}^{d}(\omega) \geq \sum_{t \in \{t | t \in T, t \leq d\}} \sum_{u \in U_{1}^{dk}(\omega)} y_{ku}^{d^{t}}, \forall d \in D, \forall k \in K^{d}, \forall s \in S \backslash S^{dk} \tag{4.7e}$$

$$\alpha^{d}(\omega) \geq 0, \forall d \in D \tag{4.7f}$$

$$\beta_{s}^{d}(\omega) \geq 0, \forall d \in D, \forall s \in S \tag{4.7g}$$

$$\gamma_{js}^{d}(\omega) \geq 0, \forall d \in D, \forall s \in S^{d}, \forall j \in J^{d} \backslash J^{d}(\omega) \tag{4.7h}$$

$$\delta_{ks}^{d}(\omega) \geq 0, \forall d \in D, \forall k \in K^{d}, \forall s \in S \backslash S^{dk} \tag{4.7i}$$

The second-stage formulation is stated in (4.7). The second-stage objective (4.7a) minimizes scheduling conflicts for overtime, excess acuity, new starts, and appointment overlaps by minimizing the sum of all second-stage decision variables with their respective penalties $\delta^{\alpha}, \delta^{\beta}, \delta^{\gamma}$, and δ^{δ}. Constraint (4.7b) determines the number of overtime slots for the clinic in scenario ω, which may occur if $r_{t}(\omega) > r_{t}$. In the second-stage, patients assigned to nurses that are unable to come to work need to be re-allocated to other nurses on duty. Because some nurses may be unavailable for some scenarios, the individual nurse acuity is no longer limited to $a^{\max}$. Instead, the

sum of acuity levels of all patients scheduled for each time slot is less than or equal to the collective maximum acuity $o_{ds}(\omega) = \bar{J}^d(\omega) * a^{\max}$ of all nurses on duty. The collective acuity requirement is used because the nurses that are available must work together to handle the patients who had been assigned to the absent nurse.

Constraint (4.7c) determines if any time slots have excess acuity for scenarios in which $a_t(\omega) > a_t$ and\or $\bar{J}^d(\omega) < \bar{J}^d$. Constraint (4.7d) determines if any nurses that are unable to work (e.g., scenarios in which $\bar{J}^d(\omega) < \bar{J}^d$) have been assigned to start a patient's appointment. Constraint (4.7e) determines if the new appointment overlaps any existing appointments, which can occur in scenarios where $r_t(\omega) > r_t$. Finally, constraints (4.7f) - (4.7i) define all second-stage variables to be non-negative.

4.3.3 Simplification of SIP-CHEMO formulation

When solving SIP-CHEMO, there are several ways to keep the problem tractable. Three of these approaches are: generating only necessary constraints, using a small number of scenarios, and branching using the x_d decision variable. The first approach is to only generate only necessary constraints in the second-stage formulation. Note that overtime and overlapping appointments can only be caused when $r_t(\omega) > r_t$. Therefore, only generate constraints (4.7b) and (4.7e) for such scenarios. Similarly, excess acuity can only exist when $a_t(\omega) > a_t$, therefore, only generate constraints (4.7c) for such scenarios.

The second approach to simplifying SIP-CHEMO involves using only a limited number of scenarios so that the set Ω is relatively small. SIP-CHEMO is suitable for this approach because all three stochastic parameters are limited to two or three scenarios. The acuity levels can only take three values and it is assumed that only one nurse will call in sick on any given day and thus $|J^d(\omega)| = 2$. The third stochastic parameter, treatment duration, is discrete and bounded between zero and $\bar{S}$. In the

realistic setting, if the size of each time slot s is reasonably large (e.g., 15 or 30 minutes), then the treatment regimen may only change by a few time slots and thus be limited to a few (e.g., three to five) scenarios as well.

The third and final approach is to separate the decision problem using the treatment regimen and set D. When a potential start date is selected from set D, then the spacing between appointments, as determined by the treatment regimen in set T (constraints (4.6c)), reduces the scope of days in set D to size $|T|$. This approach is similar to a branch-and-cut approach in which one chooses a start date d by setting $x_d = 1$. One can then determine the following appointment dates using set T and thereby reduce $|D| = |T|$. Observe then that there is a need to only create variables $y_{ks}^{d^t}$ for $d = d_i$ and $t = t_i$ when d_i and t_i correspond to element i in sets D and T respectively.

The objective increases as one selects d farther from d^{start}. Thus, there is an algorithm, $MinAlg()$, that first checks $x_d = d^{start}$, then searches values in the neighborhood (e.g., $d^{start} + 1, d^{start} - 1$, etc.) to find the start date d that results in the minimum objective value. Furthermore, this approach eliminates the need for constraint (4.6c). It should also be noted that each appointment $t \in T$ is a separable problem now, too, because the start time and resource assignments of each appointment is independent of the other appointment start times and resource assignments.

Next, pseudocode is used to describe the algorithm $MinAlg()$ that identifies the best solution x^*. The methods (functions) used in the solution search algorithm are first described and then the algorithm, $MinAlg()$, is stated. The methods used are:

- $inSetD(\hat{D})$: returns $true$ if for each $d \in \hat{D}$, then $d \in D$; returns $false$ otherwise.
- $getDHat(d)$: returns set D of size $|T|$ where $d_1 = d$.

- $solve(\hat{D})$: returns (x^*, obj^*) after solving an SIP-CHEMO problem instance (e.g., problem RN in (4.6)) using $D = \hat{D}$ where x^* is the solution and obj^* is the objective value.

This search method assumes there is a global minimum value for the SIP-CHEMO problem instance near d^{start}. The search method first finds the solution using $x_{d^{start}} = 1$. Afterwards, the algorithm searches above and then below that initial d^{start} value until finding $maxFail$ worse objective values in each direction. When the $maxFail$ worse objective values are found above (below) the d^{start} value, then $posStop$ ($negStop$) becomes true. For simplicity, assume there is a solution for each start date and corresponding set of dates $\hat{D}$ when the method $solve(\hat{D})$ is used. The left arrow $\leftarrow$ is used to denote assignment, & is the "and" operator, ! is the "not" operator, and == is the "equal to" operator. The steps of the $MinAlg()$ algorithm are stated next.

$MinAlg()$

01. $obj^* \leftarrow \infty, negStop \leftarrow false, posStop \leftarrow false, done \leftarrow false, fail \leftarrow 0;$
02. $d \leftarrow d^{start};$
03. $\hat{D} \leftarrow getDHat(d);$
04. **while** $(!done)$
05. **if**$(inSetD(\hat{D}))$
06. $(x, obj) \leftarrow solve(\hat{D});$
07. **if** $(obj < obj^*)$
08. $obj^* \leftarrow obj, x^* \leftarrow x;$
09. **else**
10. $fail \leftarrow fail + 1;$
11. **if** $(fail \geq maxFail \ \& \ posStop == false)$

12. $posStop \leftarrow true, fail \leftarrow 0, d \leftarrow d^{start}$;
13. **else if** $(fail \geq maxFail$ & $negStop == false)$
14. $negStop \leftarrow true$;
15. **else**
16. **if** (!$posStop$)
17. $d \leftarrow d + 1$;
18. **else if** (!$negStop$)
19. $d \leftarrow d - 1$;
20. **if** ($posStop$ & $negStop$)
21. $done \leftarrow true$;
22. **else**
23. $\hat{D} \leftarrow getDHat(d)$;
24. **return** x^*, obj^*

The $MingAlg()$ algorithm identifies the optimal solution x^* and optimal objective value obj^* to problem (4.6).

4.4 Risk-Averse SIP-CHEMO Scheduling Problem

This section develops two additional SIP-CHEMO models that utilize the EE and ASD mean-risk measures. These two deviation measures are suitable for this problem because they minimize the risk that comes from deviating from the recommended start date. Next, the RN SIP-CHEMO model is adapted to include the EE and ASD risk measures.

4.4.1 Expected Excess

The RN chemotherapy scheduling problem ((4.6) and (4.7)) was adapted to the deterministic equivalent formulation (4.3) for EE. The adapted model, EE, is:

$$\text{EE: Min } \sum_{d\in D}[\delta^{delay} * |d - d^{start}|x_d + \sum_{t\in\{t|t\in T, t\leq d\}} \sum_{k\in K^d} \sum_{s\in S^{dk}} \delta_s^{slot} * y_{ks}^{d^t}]$$
$$+ \sum_{\omega\in\Omega} p(\omega) * \sum_{d\in D}[\delta^{\alpha} * \alpha^d(\omega) + \sum_{s\in S} \delta^{\beta} * \beta_s^d(\omega) + \sum_{s\in S^d} \sum_{j\in J^d\setminus J^d(\omega)} \delta^{\gamma} * \gamma_{js}^d(\omega)$$
$$+ \sum_{k\in K^d} \sum_{s\in S\setminus S^{dk}} \delta^{\delta} * \delta_{ks}^d(\omega)] + \lambda * \sum_{\omega\in\Omega} p(\omega)\nu(\omega) \tag{4.8a}$$

$$s.t. \text{ Constraints (4.6b), (4.6d) } - \text{ (4.6j)} \tag{4.8b}$$

$$\text{Constraints (4.7b) } - \text{ (4.7i)} \tag{4.8c}$$

$$- \sum_{d\in D}[\delta^{delay} * |d - d^{start}|x_d + \sum_{t\in\{t|t\in T, t\leq d\}} \sum_{k\in K^d} \sum_{s\in S^{dk}} \delta_s^{slot} * y_{ks}^{d^t}]$$
$$- \sum_{d\in D}[\delta^{\alpha} * \alpha^d(\omega) + \delta^{\beta} \sum_{s\in S} \beta_s^d(\omega) + \delta^{\gamma} \sum_{s\in S^d} \sum_{j\in J^d\setminus J^d(\omega)} \gamma_{js}^d(\omega)$$
$$+ \delta^{\delta} \sum_{k\in K^d} \sum_{s\in S\setminus S^{dk}} \delta_{ks}^d(\omega)] + \nu(\omega) \geq -\eta, \forall\omega \in \Omega \tag{4.8d}$$

$$\nu(\omega) \geq 0, \forall\omega \in \Omega \tag{4.8e}$$

In problem (4.8), a new decision variable $\nu(\omega)$ was introduced. The objective is stated in (4.8a) which now has one additional summation for the expected value of the new decision variable multiplied by lambda. Several constraints were unmodified as indicated by (4.8b) and (4.8c). Two additional constraints were needed: the complicating constraint (4.8d) and the non-negative constraint (4.8e) for the new decision variable.

4.4.2 Absolute Semideviation

The RN chemotherapy scheduling problem ((4.6) and (4.7)) was adapted to the deterministic equivalent formulation (4.5) for ASD. The adapted model, ASD, is:

$$\text{ASD: Min } (1-\lambda)\sum_{d\in D}[\delta^{delay} * |d-d^{start}|x_d + \sum_{t\in\{t|t\in T, t\leq d\}}\sum_{k\in K^d}\sum_{s\in S^{dk}}\delta_s^{slot} * y_{ks}^{d^t}]$$

$$+ (1-\lambda) * \sum_{\omega\in\Omega} p(\omega)\sum_{d\in D}[\delta^{\alpha} * \alpha^d(\omega) + \delta^{\beta}\sum_{s\in S}\beta_s^d(\omega) \tag{4.9a}$$

$$+ \delta^{\gamma}\sum_{s\in S^d}\sum_{j\in J^d\setminus J^d(\omega)}\gamma_{js}^d(\omega) + \delta^{\delta}\sum_{k\in K^d}\sum_{s\in S\setminus S^{dk}}\delta_{ks}^d(\omega)] + \lambda * \sum_{\omega\in\Omega} p(\omega)\nu(\omega)$$

$$s.t. \text{ Constraints (4.6b), (4.6d)} - \text{(4.6j)} \tag{4.9b}$$

$$\text{Constraints (4.7b)} - \text{(4.7i)} \tag{4.9c}$$

$$-\sum_{d\in D}[\delta^{delay} * |d-d^{start}|x_d + \sum_{t\in\{t|t\in T, t\leq d\}}\sum_{k\in K^d}\sum_{s\in S^{dk}}\delta_s^{slot} * y_{ks}^{d^t}]$$

$$-\sum_{d\in D}[\delta^{\alpha} * \alpha^d(\omega) + \sum_{s\in S}\delta^{\beta} * \beta_s^d(\omega) + \sum_{s\in S^d}\sum_{j\in J^d\setminus J^d(\omega)}\delta^{\gamma} * \gamma_{js}^d(\omega)$$

$$+\sum_{k\in K^d}\sum_{s\in S\setminus S^{dk}}\delta^{\delta} * \delta_{ks}^d(\omega)] + \nu(\omega) \geq 0, \forall\omega\in\Omega \tag{4.9d}$$

$$-\sum_{d\in D}[\delta^{delay} * |d-d^{start}|x_d + \sum_{t\in\{t|t\in T, t\leq d\}}\sum_{k\in K^d}\sum_{s\in S^{dk}}\delta_s^{slot} * y_{ks}^{d^t}]$$

$$-\sum_{\omega\in\Omega} p(\omega)\sum_{d\in D}[\delta^{\alpha} * \alpha^d(\omega) + \sum_{s\in S}\delta^{\beta} * \beta_s^d(\omega) + \sum_{s\in S^d}\sum_{j\in J^d\setminus J^d(\omega)}\delta^{\gamma} * \gamma_{js}^d(\omega)$$

$$+\sum_{k\in K^d}\sum_{s\in S\setminus S^{dk}}\delta^{\delta} * \delta_{ks}^d(\omega)] + \nu(\omega) \geq 0, \forall\omega\in\Omega \tag{4.9e}$$

$$\nu(\omega) \text{ free}, \forall\omega\in\Omega \tag{4.9f}$$

In problem (4.9), a new decision variable $\nu(\omega)$ was also needed. The objective (4.9a) for ASD now has the original objective (4.6a) multiplied by $1-\lambda$ and one additional summation for the expected value of the new decision variable multiplied by lambda. Several constraints were unmodified as indicated by (4.9b) and (4.9c). Three additional constraints were needed: two complicating constraints (4.9d)and

(4.9e) and the unbounded, continuous constraint (4.9f) for the new decision variable.

4.5 Computational Experiments

The SIP-CHEMO models were analyzed using data from a real outpatient oncology clinic. This section first describes the real oncology clinic setting at Scott & White Hospital and then provides details on the setup for the computational experiments for SIP-CHEMO. The first set of experiments implemented five scheduling models and compared their performance. The second set of experiments examined the impact that the λ value had on scheduling performance for the EE and ASD SIP-CHEMO models. Finally, the third set of experiments analyzed how the target value of η impacted the EE SIP-CHEMO model. Results from the computational experiments are discussed at the end of this section.

4.5.1 Design of Experiments

The outpatient oncology clinic at Scott & White Hospital in Temple, Texas, USA operates five days a week for nine hours each day. The clinic typically has one charge nurse and four to eight registered nurses on duty at any given time. There are 17 chemotherapy chairs that are regularly used in the oncology clinic for scheduling purposes. The clinic treats an average of 23.5 patients each day. The DEVS-CHEMO simulation (Chapter 3) was used to evaluate each SIP-CHEMO model's performance.

Patients were sampled from a database of historical patient data from a five-month period at the Scott & White oncology clinic. The database contained 505 sample patients. On average there were around four appointments in each patient's treatment regimen, but actual values ranged from one appointment to 21 appointments . The maximum acuity a single registered nurse could have was assumed to be five ($a^{\max} = 5$). All experiments assumed a four-month planning horizon and simulated the clinic operations for one-month to collect information on the system

performance. For scheduling purposes, time slots were assumed to be 30 minutes each because the clinic currently uses time slots of this length. With nine operating hours, there were 18 time slots in each day.

Creating scenarios is an important part of the experimental design for the SIP-CHEMO models. For each scheduling problem solved, there were 12 scenarios. The 12 scenarios came from combining three outcomes of appointment duration, two outcomes of acuity levels, and two outcomes of number of nurses. An example of these outcomes is shown in Table 4.5. The three outcomes of stochastic appointment duration were created by generating a time for each appointment using historical data. The times depend on the drug(s) used in that appointment and each outcome is equally weighted. If historical data on a specific drug had at least one hundred data points in the historical database, then the distribution was determined and the appointment duration was generated using the distribution. Otherwise, the appointment duration was sampled from the existing pool of data values because there were not enough data values to determine the distribution. The number of time slots was then found by dividing the appointment duration by the time per slot and rounding to the nearest integer value.

Table 4.5: Example SIP-CHEMO Outcomes

Treatment No.	Outcome	Appointment Duration (slots)	Probability
1;8;10	1	4;3;4	0.33
	2	5;3;3	0.33
	3	3;4;5	0.33
Treatment No.	Outcome	Acuity	Probability
1;8;10	1	1;1;2	0.50
	2	1;3;1	0.50
Days	Outcome	No. of Nurses	Probability
	1	5;7;6	0.90
	2	4;6;5	0.10

For the two outcomes of acuity levels, the acuity level at each appointment was generated with a value of one occurring 70% of the time, a value of two occurring 20% of the time, and a value of three occurring 10% of the time. It was assumed that there was a 10% probability of an employee taking a vacation or sick day. This assumption came from the Bureau of Labor statistics by citing the average sick and vacation time for a ten-year employee. Finally, the original number of nurses was assumed to be available 90% of the time. However, the second outcome of the number of nurses assumed that one less nurse is available on each appointment day and this outcome occurred with 10% probability. There were 12 outcomes because 3 x 2 x 3 = 12 and combining the outcomes from Table 4.5 results in the 12 scenarios in Table 4.6 for a start date on day eight ($x_8 = 1$).

Table 4.6: Example SIP-CHEMO Scenarios with $x_8 = 1$

ω	Prob.	Days	Treatment No.	Appt. Dur.	Acuity	No. of Nurses
1	0.15	8;15;17	1;8;10	4;3;4	1;1;2	5;7;6
2	0.15	8;15;17	1;8;10	5;3;3	1;3;1	5;7;6
3	0.15	8;15;17	1;8;10	3;4;5	1;1;2	5;7;6
4	0.15	8;15;17	1;8;10	4;3;4	1;3;1	5;7;6
5	0.15	8;15;17	1;8;10	5;3;3	1;1;2	5;7;6
6	0.15	8;15;17	1;8;10	3;4;5	1;3;1	5;7;6
7	0.02	8;15;17	1;8;10	4;3;4	1;1;2	4;6;5
8	0.02	8;15;17	1;8;10	5;3;3	1;3;1	4;6;5
9	0.02	8;15;17	1;8;10	3;4;5	1;1;2	4;6;5
10	0.02	8;15;17	1;8;10	4;3;4	1;3;1	4;6;5
11	0.02	8;15;17	1;8;10	5;3;3	1;1;2	4;6;5
12	0.02	8;15;17	1;8;10	3;4;5	1;3;1	4;6;5

The penalties for the delta values in the SIP-CHEMO objective functions (4.6a), (4.8a), and (4.9a) were determined by converting the units of each variable into acuity. Recall that one time slot has a maximum acuity $a^{\max}$ and one day has $\bar{S}$ time slots. Therefore, 1 slot $= a^{\max}$ and 1 day $= \bar{S} * a^{\max}$. Then $\delta^{\beta} = 1$ because the β decision variable already represents acuity. Next $\delta^{\gamma} = a^{\max}$ and $\delta^{\delta} = a^{\max}$ because the γ and δ decision variables are both indicators for a time slot. The α decision variable also represents time slots and thus one could use $\delta^{\alpha} = a^{\max}$. However, early experiments revealed that this penalty was not large enough to impact the solution. Therefore, the penalty measure for α was set to $\delta^{\alpha} = 0.5 * a^{\max} * \bar{S}$. Since

the x decision variable represents one day, then $\delta^{delay} = \bar{S} * a^{\max}$. Note that the y decision variable represents a time slot. In the SIP-CHEMO models, later time slots were penalized more heavily and thus the model rewarded appointments that started early in the day. Since this is a penalty term used to avoid unnecessary gaps between appointments, one-tenth of the value was used and thus $\delta_s^{slot} = 0.1 * s * a^{\max}$.

The first research question for SIP-CHEMO requires a comparison of five scheduling methods. When patients call the scheduler to get an appointment schedule, patients provide their recommended treatment regimen and start date. In the real oncology clinic, the scheduler uses a scheduling algorithm called the *as-soon-as-possible* (ASAP) algorithm. The ASAP algorithm uses only the availability of the chemotherapy chairs to schedule the patient's appointments and ignores the availability of the registered nurses. Psuedocode for the ASAP algorithm is given in Appendix A.2. The Individual algorithm performed best in Chapter 3 and is included here for comparison as well. Details on the Individual algorithm are given in Appendix A.2. The first experiment compared the ASAP and Individual algorithms to three SIP-CHEMO models: RN, EE, and ASD. These models used $\lambda = 0.5$ in the first experiment and the EE model used a target value of two days with $\eta = 2 * \bar{S} * a^{\max}$. This value was chosen to indicate that moving more than two days from the recommended start date can cause risk to the patient's state of health.

The second research question examined how the value of λ in the EE and ASD scheduling models impacts the system performance. In this experiment, the EE and ASD SIP-CHEMO models were used to schedule patients while a value of 0.5 and 1.0 was used for λ for each model. The EE model used $\eta = 1 * \bar{S} * a^{\max}$. The labels of ASD_05 and ASD_10 were used to label the ASD mean-risk SIP-CHEMO model simulation runs with $\lambda = 0.5$ and $\lambda = 1.0$ respectively. Similarly, the names of EE_05 and EE_10 were used to label the EE mean-risk SIP-CHEMO model simulation runs.

Finally, the third research question focused on how the value of η impacts the system performance. Recall that η is the target value for the EE mean-risk SIP-CHEMO model. In all simulation runs, $\lambda = 0.5$ and the value of η changes with $\eta = 0.0$, $\eta = 1 * \bar{S} * a^{\max}$, and $\eta = 2 * \bar{S} * a^{\max}$ in the simulation runs labeled EE-Eta0, EE-Eta1, and EE-Eta2 respectively.

In all three experiments, the system performance was captured by simulating the clinic performance for one-month using DEVS-CHEMO. There were 170 patients initially scheduled to fill the schedule with five to six additional appointment requests each day until 276 patients were scheduled. DEVS-CHEMO gives system performance results on the type I delay, type II delay, type III delay, system time, throughput, chair utilization, nurse utilization, and nurse overtime.

The throughput results are reported as the total throughput, or appointments (appts.), for the month and the average daily throughput. The nurse overtime is reported in two different ways. The nurse overtime$^+$ count is the number of times that a nurse had to work overtime during the month and nurse overtime$^+$ is the average of the overtime on those occasions (zero entries are excluded). Nurse overtime is the average overtime among all nurses during the simulation period (zero entries included). The next subsection provides the average for each performance measure from DEVS-CHEMO in the 100 replications of each experiment. The experiments were all conducted on a Dell Precision T7500 with an Intel(R) Xeon(R) processor running at 2.4 GHz with 12.0 GB RAM.

4.5.2 Results and Discussion

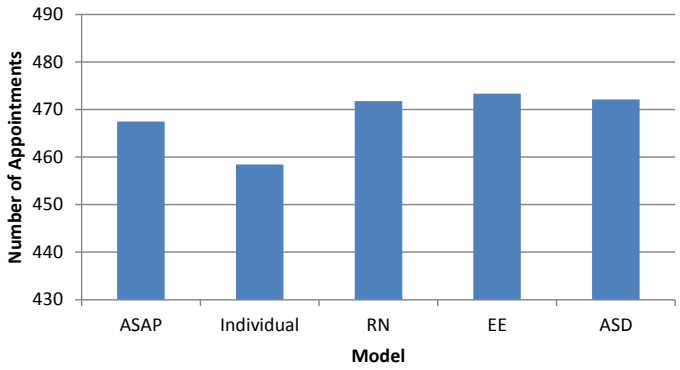


Figure 4.1: Results for Throughput for Scheduling Models

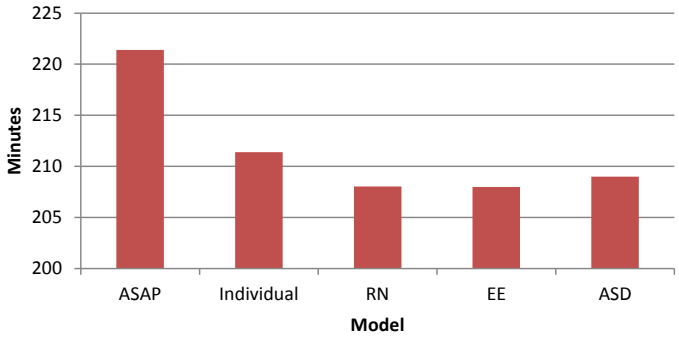


Figure 4.2: Results for System Time Performance Measures for Scheduling Models

The first set of experiments compared five scheduling algorithms (Table 4.7). All SIP-CHEMO models (RN, EE, and ASD) outperformed the ASAP and Individual algorithms for several performance measures such as total throughput (Figure 4.1),

system time (Figure 4.2), type II delay, nurse overtime^{+}, and nurse overtime (Figure 4.3). The EE model had the highest total throughput (473 appointments) and the lowest type II delay (16 minutes), type III delay (32 minutes), and system time (208 minutes). The RN model had the lowest nurse overtime^{+} (95 minutes) and nurse overtime (31 minutes).

Table 4.7: Performance Results for Scheduling Models

	Experiments				
Performance Measures (units)	ASAP	Individual	RN	EE	ASD
Total Throughput (appts.)	467.5	458.4	471.8	473.4	472.1
Daily Throughput (appts.)	23.4	22.9	23.6	23.7	23.6
Chair Utilization (%)	50.24	49.18	50.28	50.48	50.49
Nurse Utilization (%)	83.68	85.76	81.37	82.67	82.46
Nurse Overtime^{+} (min.)	116.96	108.71	94.96	98.33	99.64
Nurse Overtime^{+} Count	45.32	47.29	36.75	39.28	39.83
Nurse Overtime (min.)	46.91	45.19	30.64	34.17	34.97
Type I Delay (days)	1.36	1.63	1.55	1.54	1.54
Type II Delay (min.)	28.46	18.69	16.57	16.44	716.89
Type III Delay (min.)	32.26	32.20	32.26	32.23	32.28
System Time (min.)	221.39	211.39	208.02	207.97	209.00
Simulation Run Time (sec.)	1.46	1.32	67.78	86.00	102.84

ASAP has the lowest type I delay (1.4 days) because the algorithm schedules patients as quickly as possible and ignores the nurse resource. Aside from the ASAP

algorithm, the SIP-CHEMO models have the lowest type I delay (Figure 4.4) with 1.5 days. The SIP-CHEMO models take much longer to run than the two algorithms which took only 1 to 2 seconds each. The run times for the SIP-CHEMO models increase as the number of constraints increases in the RN, EE, and ASD models which took an average of 68, 86, and 103 seconds to run, respectively. EE is the preferred SIP-CHEMO model because it had the best performance measures for the most categories. The EE SIP-CHEMO model held type I delay within 0.2 days while making improvements in other performance measures such as throughput (increased 1%), overtime (reduced 27%), system time (reduced 6%), and type II delay (reduced 42%) when compared to the ASAP algorithm. Thus, it can be concluded that the SIP-CHEMO models supersede the decisions made using just the DEVS-CHEMO simulation model scheduling algorithms. The standard deviation and 90% confidence intervals for each performance measure for the five models is in Tables B.1, B.2, and B.3 in Appendix B.

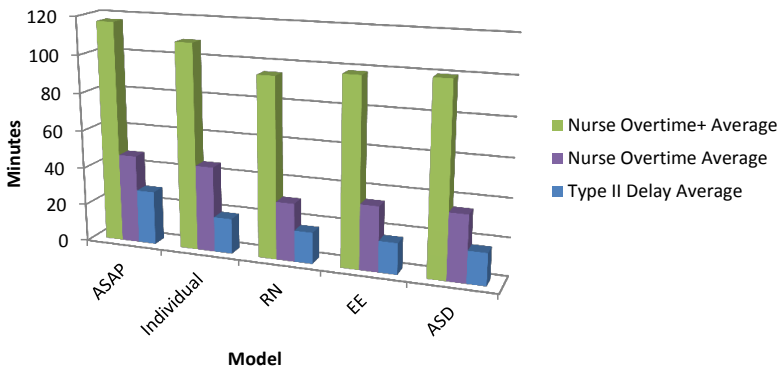


Figure 4.3: Results for Time-Based Performance Measures for Scheduling Models

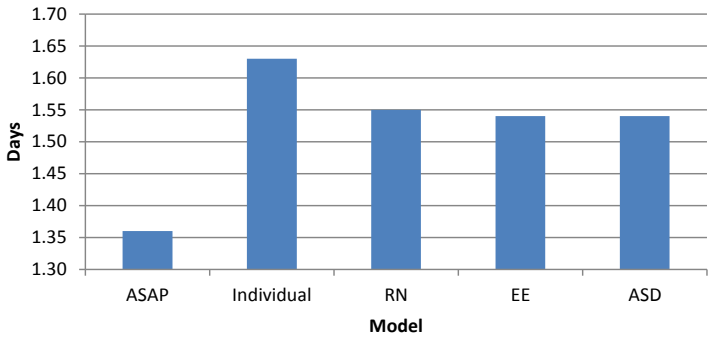


Figure 4.4: Results for Type I Delay for Scheduling Models

The second set of experiments investigated the impact of lambda on the system performance. Table 4.8 contains the averages for each performance measure from 100 replications of DEVS-CHEMO using the EE and ASD SIP-CHEMO models. The λ value was set to 0.5 in EE_05 and ASD_05 and was set to 1.0 for EE_10 and ASD_10. ASD_05 outperforms ASD_10 for total throughput by 37 appointments and type I delay by 1.9 days. ASD_05 had roughly 2 more appointments per day and improved type I delay by 40%. ASD_10 had lower nurse overtime$^+$ (by 19 minutes), nurse overtime$^+$ count (by 8 instances), nurse overtime (by 12 minutes), type II delay (by 5 minutes), type III delay (17 seconds), and system time (by 4 minutes) than ASD_05. Although ASD_10 is better then ASD_05 for more performance measures, these small improvements do not seem significant enough to justify two fewer patient appointments each day. Comparatively, for the EE model ($\eta = 1 * \bar{S} * a^{\max}$ was used) there was little difference in using $\lambda = 0.5$ or $\lambda = 1.0$ for the EE_05 and EE_10 experiments, respectively. The throughput only differed by 2 appointments (<1%) and type I delay by 0.01 days (1%).

Table 4.8: Performance Results for the λ Experiments

Performance Measures (units)	ASD_05	ASD_10	EE_05	EE_10
Total Throughput (appts.)	474.8	476.7	472.1	434.8
Daily Throughput (appts.)	23.7	23.8	23.6	21.7
Chair Utilization (%)	50.90	50.69	50.49	46.68
Nurse Utilization (%)	83.05	82.24	82.46	73.97
Nurse Overtime$^+$ (min.)	99.85	99.78	99.64	79.73
Nurse Overtime$^+$ Count	40.41	39.29	39.83	32.36
Nurse Overtime (min.)	35.61	34.31	34.97	22.74
Type I Delay (days)	1.54	1.55	1.54	2.57
Type II Delay (min.)	17.25	16.80	16.89	11.97
Type III Delay (min.)	32.44	32.43	32.28	31.99
System Time (min.)	209.77	207.77	209.00	204.85

The third set of experiments investigated the impact of eta on system performance for the EE SIP-CHEMO model (Table 4.9). The results indicate that there is very little difference in the system performance results based on η. The type I delay was around 1.5 days and daily throughput was about 24 appointments for all three experiments. The system time was between 208 and 210 minutes while the nurse overtime was 39 to 41 minutes. Although the target value eta impacted the scheduling decision, it did not substantially influence the system performance.

Table 4.9: Performance Results for the η Experiments

Performance Measures (units)	EE-Eta0	EE-Eta1	EE-Eta2
Total Throughput (appts.)	472.6	474.8	473.4
Daily Throughput (appts.)	23.6	23.7	23.7
Chair Utilization (%)	50.64	50.90	50.48
Nurse Utilization (%)	82.43	83.05	82.67
Nurse Overtime$^+$ (min.)	98.13	99.85	98.33
Nurse Overtime$^+$ Count	40.41	40.41	39.28
Nurse Overtime (min.)	34.82	35.61	34.17
Type I Delay (days)	1.54	1.54	1.54
Type II Delay (min.)	16.79	17.25	16.44
Type III Delay (min.)	32.27	32.44	32.23
System Time (min.)	209.23	209.77	207.97

4.6 Summary

The SIP-CHEMO optimization models are for the problem of scheduling chemotherapy patients, chairs, and nurses under uncertainty. SIP-CHEMO aims to determine an optimal appointment schedule for a new chemotherapy patient who has been prescribed a unique treatment regimen and recommended start date. The appointment duration, acuity levels, and nurse resource availability were assumed to be stochastic. A risk-neutral formulation for the chemotherapy decision problem was developed. The first-stage decisions determined an appointment time and resource assignment while minimizing the type I delay and appointment start times. The second-stage objective minimized clinic overtime, excess acuity assignments, conflicts with new

patient starts, and conflicts with overlapping appointment times.

The risk-neutral formulation was extended to include two mean-risk measures. EE aims to minimize expected value of the excess over a target value. ASD is similar but instead uses the mean value as the target and thus minimizes the expected value of the excess over the mean value. An algorithm was developed that branched on the start date to improve the solution speed of the model. Together, the RN, EE, and ASD models constitute the three SIP-CHEMO models.

Three sets of experiments were then designed and conducted to answer three questions. First, can any of the three SIP-CHEMO models outperform current algorithms for scheduling patients at a real outpatient oncology clinic? All three SIP-CHEMO models, RN, EE, and ASD, were found to outperform the algorithms for most performance measures. Using the SIP-CHEMO models, throughput increased by 1%, type II delay decreased by 41%, system time decreased by 6%, nurse overtime^{+} decreased by more than 15%, and nurse overtime decreased by more than 25% over the current scheduling methods. The EE model had the highest total throughput, lowest type II delay, type III delay, and system time. Second, how does the value of lambda impact system performance when using the EE and ASD mean-risk SIP-CHEMO models? There was little different for the EE mean-risk SIP CHEMO model, but the ASD model performed best with lower risk values. Third, does the value of eta for the EE mean-risk SIP-CHEMO model impact the system performance? No, there was little variation depending on the value of η used in the experiments.

5. INTEGRATED SIMULATION AND OPTIMIZATION FOR ONCOLOGY CLINIC OPERATIONS

5.1 Introduction

In real complex systems, data uncertainties often evolve over time. DMs are sometimes required to make important system decisions prior to observing uncertain events. Uncertainty can occur in a number of important problem parameters such as task duration or demand. Often the decisions epochs occur during discrete times periods and influence future decisions. The time between each decision epoch may be unknown. Stochastic optimization is useful in determining a combination of stochastic conditions that would result in best system performance. Yet, even with stochastic optimization, decision-making is *not* trivial. Often, it is still impossible to model the system using an explicit mathematical formulation. In such case, simulation of the system performance under a combination of conditions becomes necessary in order to model uncertain events and evaluate possible decision options. Information obtained from the simulation can also be used to improve the stochastic optimization model in order to find a set of decisions that perform well under the realization of uncertain events.

Stochastic optimization has evolved into a viable approach for decision-making under uncertainty. However, much of the progress has been made under simplifying assumptions such as, closed-form objective functions, precise knowledge of a static underlying probability distribution, and decisions do not influence the future decisions. In many practical applications, however, these simplifying assumptions are not appropriate. Scheduling decisions made in one time period impact future decisions. Therefore, simulation of the underlying system is necessary in order to make any

data-driven decisions. Consequently, SIP alone is *not* always adequate for optimal decision-making.

Discrete event simulation has been shown to be a useful tool for evaluating complex systems under a given combination of conditions. However, simulation models are traditionally designed without knowledge of mathematical decision models. Therefore, simulation alone is generally not sufficient when it comes to making optimal decisions under uncertainty. A new framework for combining stochastic optimization with simulation is needed, whereby the stochastic optimization and system simulation models interact and exchange information leading to solutions that adapt to changes in system data. This chapter first defines a new framework for integrated DEVS and mean-risk SIP, termed DEVS-SIP.

DEVS-SIP can be applied to a variety of applications with challenging decision problems. Scheduling chemotherapy patient appointments is a challenging decision problem that aims to determine a date, time, chair, and nurse for each appointment in a patient's treatment regimen that yields optimal system performance. Requests for new chemotherapy patient appointments arrive over time and the scheduling decision must be made right away. This type of scheduling is called *online scheduling*. In online scheduling, decisions are made one-at-a-time where the current state of the system and past decisions are known but knowledge of future events, including future decision requests, are not known. Online scheduling is challenging because the uncertainty in the problem makes it difficult to find an optimal solution. Future requests for appointments also compete for the limited clinic resources, thus the current decision impacts the future scheduling decision options. In chemotherapy appointment scheduling, the scheduling problem is even more challenging because of other uncertain parameters such as appointment duration, acuity levels, and resource availability. Furthermore, the uncertainty as well as the interaction between clinic

resources and patients makes it difficult to evaluate the scheduling decisions.

This chapter also implements the DEVS-SIP framework for oncology clinic operations. This dissertation work is the first to address uncertainty in oncology clinic operations and scheduling by using an integrated simulation and optimization approach. The DEVS-SIP framework is developed and used as a template for combining the DEVS-CHEMO simulation from Chapter 3 and the SIP-CHEMO models from Chapter 4. The new model, called DEVS-SIP-CHEMO, is an integrated simulation and optimization approach that improves the chemotherapy appointment scheduling decisions in order to obtain better system performance.

This dissertation chapter provides details for developing and implementing DEVS-SIP-CHEMO. Computational experiments evaluate the effectiveness of DEVS-SIP-CHEMO. The objective of the experiments for DEVS-SIP-CHEMO is to determine a) if using the integrated DEVS-SIP-CHEMO model to schedule patient appointments has better system performance than using SIP-CHEMO and DEVS-CHEMO models alone; b) if yes, then how much improvement on system performance is observed for each stopping criterion; c) how the results vary between the EE and ASD versions of the SIP-CHEMO models.

The rest of this chapter is organized as follows: the DEVS-SIP framework is described in section 5.2. Details for implementing DEVS-SIP-CHEMO, including how to select stopping criteria, are provided in section 5.3. Computational experiments were conducted and the results are discussed in section 5.4. Finally section 5.5 contains a summary of the chapter.

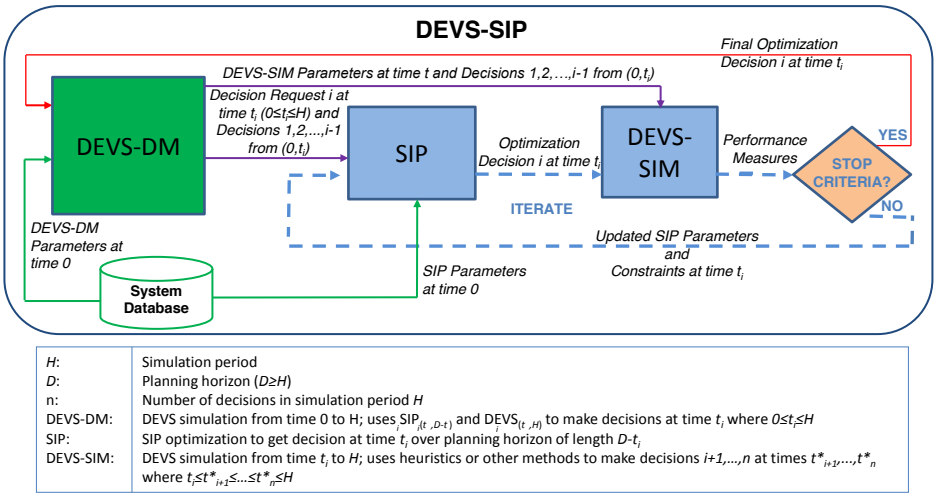
5.2 DEVS-SIP Framework

To integrate simulation and optimization, the literature shows that either the optimization model is used to optimize the simulation model's parameters or the

simulation model is used solely to generate predictions (scenarios) for the optimization model. A simulation and optimization framework was designed to have a strong coupling between the simulation (DEVS) and optimization (SIP) models. The coupling is strong because it is defined using the DEVS formalism and the two models rely on one another for input. The real system of interest, which is subject to data uncertainties, is first abstracted and modeled using both DEVS and SIP. The SIP model captures the decision-making aspects of the system at a high level in terms of time, while the DEVS model captures the system dynamics at a finer scale in terms of time and space.

5.2.1 DEVS-SIP Model

The current specification of DEVS models developed by [51] is extended to realize the DEVS-SIP paradigm. The DEVS-SIP framework described in Figure 1.1, depicts a real system with a DM who needs to make and implement decisions for the real system over time. Each decision arises at unknown time periods, influences future decisions, and is subject to uncertain problem parameters. The DEVS-SIP framework depicted in Figure 5.1 has a simulation model in place of the DM. In order to model the real system and the DM, the DEVS simulation is needed to generate each decision epoch, implement the decision, mimic the clinic operations, and capture the system performance. This simulation, DEVS-DM, runs from time 0 to H where H defines the length of time required for analysis, known as the simulation period. A system database initializes DEVS-DM at time 0. This initialization step defines important system parameters from the real system and defines stochastic distributions for sampling uncertain outcomes. Known parameters such as the number of resources are defined during initialization. The distributions of uncertain parameters, such as task duration or demand, are defined during initialization as well.



H:	Simulation period
D:	Planning horizon (*D*≥*H*)
n:	Number of decisions in simulation period *H*
DEVS-DM:	DEVS simulation from time 0 to H; uses $SIP_{(t_i, D-t_i)}$ and $DEVS_{(t_i, H)}$ to make decisions at time t_i where $0 \le t_i \le H$
SIP:	SIP optimization to get decision at time t_i over planning horizon of length $D-t_i$
DEVS-SIM:	DEVS simulation from time t_i to *H*; uses heuristics or other methods to make decisions *i+1,...,n* at times $t^*_{i+1},...,t^*_n$ where $t_i \le t^*_{i+1} \le ... \le t^*_n \le H$

Figure 5.1: The DEVS-SIP Framework for Decision-Making Under Uncertainty

DEVS-DM also portrays the role of the DM and generates a decision request i at time t_i where $0 \le t_i \le H$. The decision request i is modeled by the SIP model. The SIP model has some parameters initialized from the system database, while other details are defined by the decision request i. The SIP model, termed SIP, makes a decision at time t_i over a planning horizon of length $D - t_i$, where D is the length of the original planning horizon of interest. It is assumed that $D > H$. DEVS-DM also provides SIP with information on previous decisions 1,2,...,i-1 that were made during earlier decision periods.

Once the SIP model is formulated and solved, the optimization decision i is implemented in a second simulation model, DEVS-SIM. DEVS-SIM is intended to represent DEVS-DM beginning at time t_i. Therefore DEVS-SIM is initialized using the current simulation parameters from DEVS-DM at time t_i. Decisions 1,2,...,i-1 are also included in the initialization of the DEVS-SIM simulation. DEVS-SIM simulates the real system from time t_i to time H, and uses an algorithm to predict

decisions $i+1, i+2, ..., n$ at times $t_i^*, t_{i+1}^*, ..., t_n^*$ where $t_i \leq t_i^* \leq t_{i+1}^* \leq ... \leq t_n^* \leq H$ and n is the number of decision periods in the simulation period H. DEVS-SIM is necessary in order to simulate future decision requests, predict future decisions, realize uncertain events, and analyze the impact of the decisions in time period H.

The DEVS-SIM simulation computes performance measures which are then compared to a set of stopping criteria. The stopping criteria are based on pre-established thresholds for the performance measures that are set by the DM or their supervisor. The stopping criteria may also be time-based in order to find a decision in an acceptable time period. If the performance measures do not satisfy the stopping criteria, then the performance measures are used to update the SIP model's constraints and parameters. The SIP is re-solved and the decision search process continues until a decision satisfies the stopping criteria. By including the time-based stopping criteria, such as a limit on the number of iterations spent searching for an acceptable solution, then the time-based stopping criteria is guaranteed to stop the decision search process. Once the stopping criteria is satisfied, the final optimization decision i from SIP is sent to DEVS-DM for implementation. DEVS-DM simulation continues until the end of the simulation period H.

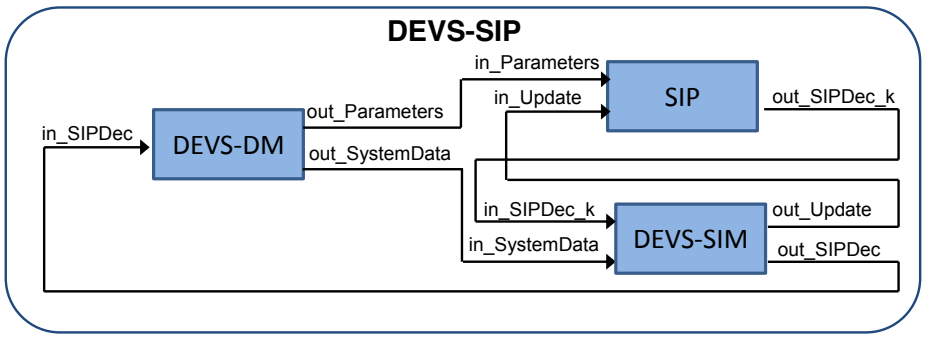


Figure 5.2: DEVS-SIP Block Diagram

The notation from [28] is adopted to give a detailed mathematical definition of DEVS-SIP. The DEVS-SIP framework couples two DEVS simulation models (also coupled models) to the SIP optimization model as shown in Figure 5.2. DEVS-SIP has five internal couplings. First, DEVS-DM's "out_Parameters" output port is coupled to SIP's "in_Parameters" input port while DEVS-DM's "out_SystemData" output port is coupled to DEVS-SIM's "in_SystemData" input port. Then, SIP's "out_SIPDec_k" output port is coupled to DEVS-SIM's "in_SIPDec_k" input port. Finally, DEVS-SIM's "out_Update" output port is coupled to SIP's "in_Update" input port and DEVS-SIM's "out_SIPDec" output port is coupled to DEVS-DM's "in_SIPDec" input port.

DEVS-SIP Coupled Model.

DEVS-SIP = $(X_M, Y_M, D, \{M_d | d \in D\}, EIC, EOC, IC)$ where,

$X_M = \emptyset$ is the set of input ports and values;

$Y_M = \emptyset$ is the set of output ports and values;

D = {DEVS-DM, SIP, DEVS-SIM};

$M_{\text{DEVS-DM}}, M_{SIP}, M_{\text{DEVS-SIM}}$ are DEVS models;

$EIC = \emptyset$ is the external input couplings;

IC = {((DEVS-DM, "$out\_Parameters$"), (SIP, "$in\_Parameters$")),
((DEVS-DM, "$out\_SystemData$"), (DEVS-SIM, "$in\_SystemData$")),
((SIP, "out_SIPDec_k"), (DEVS-SIM, "in_SIPDec_k")),
((DEVS-SIM, "out_Update"), (SIP, "in_Update")),
((DEVS-SIM, "out_SIPDec"), (DEVS-DM, "in_SIPDec")), } is the internal couplings;

$EOC = \emptyset$ is the external output couplings.

Each input port or output port passes a message. The class message is derived from class bag and holds instances of class content, with slots for port, p, and value, val. The latter carries an *entity* instance transmitted from sender to receiver. An entity is characterized as the base class for all classes of objects to be put into containers. The value val can be an instance of any derived class of entity, whether defined by the system or user. The entity passed along the internal coupling between DEVS-DM and SIP using their respective "$in\_SystemData$" input ports is called the SystemData entity. All entities are named after their ports such that entity X is passed from the out_X output port to the in_X input port. A brief description of the purpose of the SystemData entity and other entities in DEVS-SIP are given in Table 5.1. The entities are containers that transmit data between DEVS models. Specific attributes and methods for each entity are dependent on the problem and application. The attributes are next described in relation to their purpose in DEVS-SIP and to the mean-risk SIP parameters and decision variables.

Table 5.1: Description of DEVS-SIP Entities

Entity	**Brief Description**
Parameters	Contains parameters from the DEVS-DM simulation that are used in the formulation of the SIP model.
SystemData	Contains important parameters from the DEVS-DM simulation that initialize the DEVS-SIM simulation, including the start time of the DEVS-SIM simulation and any previous decisions before time t_i.
SIPDecision_k	Contains the decision from the SIP model that is implemented and evaluated by the DEVS-SIM simulation.
Update	Contains revised parameters for the SIP model based on evaluation in the DEVS-SIM simulation model.
SIPDecision	Contains the decision that meets the stopping criteria in the DEVS-SIM simulation that is implemented in the DEVS-DM simulation.

The Parameters entity contains parameters for the decision from the DEVS-DM simulation that is used in the formulation of the SIP model. The Paraemters entity defines $A, b, c, W(\omega), T(\omega), q(\omega)$, and $r(\omega)$ for each $\omega \in \Omega$. The SystemData entity contains parameters from the DEVS-DM simulation that initialize the DEVS-SIM simulation. These parameters include the start time of the DEVS-SIM simulation and all decisions 1,2,...,i-1 made prior to time t_i. The purpose of the SystemData entity is to provide information that allows DEVS-SIM to replicate DEVS-DM at time t_i. Entity SIPDecision_k contains the information for the decision from the SIP model made at time t_i that is implemented and evaluated by the DEVS-SIM simula-

tion. This information is the decision variables x and y. The Update entity contains information that revises the parameters for the SIP model based on evaluation in the DEVS-SIM simulation model. This information includes revised parameters for $A, b, c, W(\omega), T(\omega), q(\omega)$, and $r(\omega)$ for each $\omega \in \Omega$. Finally, the SIPDecision entity is the decision, x and y, that met the stopping criteria in the DEVS-SIM simulation and is then implemented in the DEVS-DM simulation.

This section detailed a new paradigm for decision-making under uncertainty in complex problem settings. DEVS-SIP formally defines an integrated simulation and optimization framework for use in a variety of applications. DEVS-SIP is suitable for decision problems that cannot be formulated using a closed-form mathematical expression and involve dynamic changes to the problem data over time. This kind of decision-making framework is necessary in many practical applications that require decisions over time in a rolling horizon manner.

Implementation of the DEVS-SIP framework requires coordination between the two model types: DEVS simulation and SIP optimization. DEVSJAVA is suitable for implementation of the DEVS model and CPLEX Concert Technology is suitable for the SIP model. By using DEVSJAVA and CPLEX Concert Technology, DEVS-SIP can be implemented using the Java programming language in the integrated environment of Eclipse to allow for easy communication between the DEVS and SIP models. The following two questions related to the iterative DEVS-SIP process are investigated in this chapter

1. What is a suitable stopping criteria for the DEVS-SIP model?

2. What type of modifications should be made to the SIP model at each iteration?

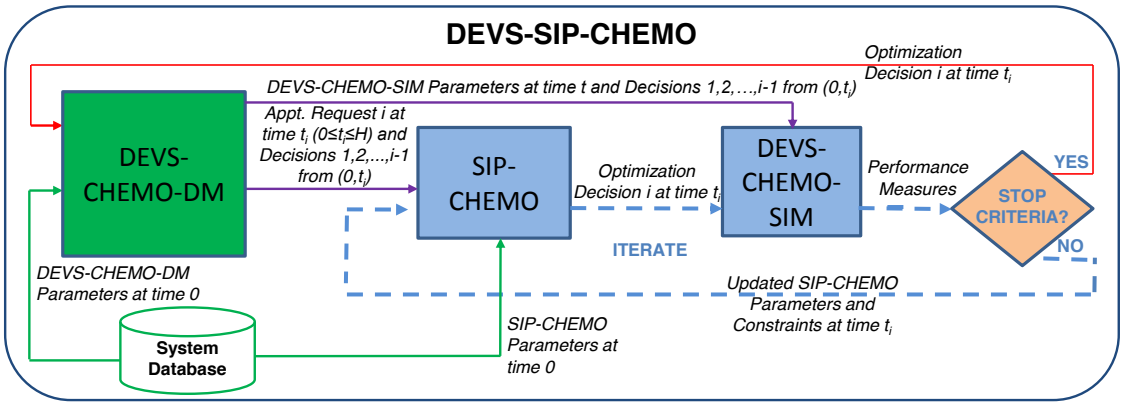
The answers to these two questions are unique as they rely on the type of performance measures used for the application. However, the following sections provide

insight on how the stopping criteria and SIP modifications can be chosen.

5.3 DEVS-SIP-CHEMO Model

5.3.1 Overview

The DEVS-SIP framework from section 5.2 was adapted to the chemotherapy scheduling problem at an outpatient oncology clinic. Let DEVS-CHEMO-DM be the simulation model of the oncology clinic that serves in the role of the DM. Let SIP-CHEMO be the optimization model that solves the chemotherapy appointment scheduling problem using mean-risk SIP. Finally, let DEVS-CHEMO-SIM also be a simulation model of the oncology clinic that tests decisions from SIP-CHEMO before implementation. DEVS-CHEMO-DM and DEVS-CHEMO-SIM are both implementations of the DEVS-CHEMO model from Chapter 3.



H: Simulation period
D: Planning horizon ($D \ge H$)
n: Number of decisions in simulation period *H*
DEVS-CHEMO-DM: DEVS simulation from time 0 to H; uses SIP-CHEMO and DEVS-CHEMO-2 to make decisions at time t_i where $0 \le t_i \le H$
SIP-CHEMO: SIP optimization to get decision at time t_i over planning horizon of length D-t_i
DEVS-CHEMO-SIM: DEVS simulation from time t_i to *H*; uses heuristics or other methods to make decisions $i+1,\ldots,n$ at times $t^*_{i+1},\ldots,t^*_n$ where $t_i \le t^*_{i+1} \le \ldots \le t^*_n \le H$

Figure 5.3: DEVS-SIP-CHEMO for Oncology Clinic Operations

The details of the DEVS-SIP-CHEMO model are in Figure 5.3. DEVS-CHEMO-DM is the primary simulation program, evaluated from time period 0 to H, that mimics the the oncology clinic operations. When DEVS-CHEMO-DM generates appointment request i at time t_i, the scheduler (SCHED atomic model) within DEVS-CHEMO-DM utilizes SIP-CHEMO to make decision i. The SIP-CHEMO model formulates the problem with deterministic and stochastic parameters to determine a schedule for all of the patient's chemotherapy appointments from appointment request i that fall within decision period D.

Once the schedule is determined, DEVS-CHEMO-SIM implements the scheduling decision i as well as past scheduling decisions 1,2,...,i-1 that have already been made. Possible future decisions $i+1, i+2, ..., n$ are also generated and implemented in DEVS-CHEMO-SIM at times $t_i^*, t_{i+1}^*, ..., t_n^*$ where n is the last decision in simulation period H. DEVS-CHEMO-SIM simulates oncology clinic operations from time t_i until H. The system performance from DEVS-CHEMO-SIM is evaluated and used to modify SIP-CHEMO. This process continues until the stopping criteria are met. Suggestions for determining the stopping criteria are discussed later in this section. Once decision i from the SIP-CHEMO model leads to performance measures from the DEVS-CHEMO-SIM simulation model that satisfy the stopping criteria, then decision i is implemented in DEVS-CHEMO-DM. This process continues until the end of time period H.

5.3.2 Chemotherapy Scheduling Problem and the DEVS-SIP Framework

The nature of the chemotherapy appointment scheduling problem makes the problem suitable for the DEVS-SIP framework which combines simulation and optimization for improved decision-making. Table 5.2 shows how the DEVS-SIP framework addresses each challenging attribute of the chemotherapy scheduling problem.

Table 5.2: Attributes of the Chemotherapy Scheduling Problem and the DEVS-SIP Framework

Attributes	**DEVS-SIP Approach**
Decision epochs	DEVS-CHEMO-DM generates appointment requests one-at-a-time.
Uncertain parameters	SIP-CHEMO is a SIP model of the chemotherapy appointment scheduling decision.
Unknown future appointment requests	DEVS-CHEMO-SIM generates future appointment requests and uses an algorithm to make and subsequently implement possible future scheduling decisions.
Realization of uncertainty	DEVS-CHEMO-DM and DEVS-CHEMO-SIM each implement realizations of different scenarios (e.g., appointment duration, acuity levels, etc.).
Impact of decision on future decisions	Decisions made by SIP-CHEMO are implemented in DEVS-CHEMO-SIM along with possible future appointment requests and their possible scheduling decisions.
Complex resource interactions	DEVS-CHEMO-DM and DEVS-CHEMO-SIM are simulations that models the complex behavior of each resource (receptionist, pharmacists, nurses, chairs).
Risk	Risk is modeled using mean-risk SIP-CHEMO.

Patient requests for appointment schedules are scheduling decisions that arise over time. The first simulation model, DEVS-CHEMO-DM, simulates the appointment requests. The uncertain problem parameters such as acuity levels, appointment duration, and resource availability motivate the need to use the SIP-CHEMO models

to determine the patient's appointment schedule. Additionally, the mean-risk SIP-CHEMO models allow the DM to make risk-averse decisions in order to keep the waiting time, system time, and overtime low. Because the decisions have to be made online with only current knowledge of the system, an integrated simulation and optimization approach is needed.

After SIP-CHEMO makes an appointment schedule for the patient, DEVS-CHEMO-SIM implements the decision, along with previous decisions, and simulates future appointment requests and uses an algorithm to predict those decisions. The realization of uncertain parameters as well as the complexity of patient and resource interactions are also handled by the DEVS-CHEMO-SIM simulation model. The results of the DEVS-CHEMO-SIM simulation model are used to update SIP-CHEMO and this process continues until an acceptable level of system performance is met. DEVS-SIP-CHEMO allows the scheduler to make a set of decisions and revise those decisions once they have been evaluated through simulation. Once the decisions have met the one of the stopping criteria set by the scheduler, the decisions are implemented in the DEVS-CHEMO-DM simulation model. Similar to the DEVS-CHEMO-SIM simulation, this model also incorporates the realization of uncertainty and simulates clinic resources and patients.

5.3.3 Block Diagram and Entities

The DEVS-SIP-CHEMO entities that are sent and received through the input and output ports (Figure 5.4) are listed in Table 5.3. The Parameters entity defines $A, b, c, W(\omega), T(\omega), q(\omega)$, and $r(\omega)$ for each $\omega \in \Omega$ for the SIP-CHEMO model. The Parameters entity is created in the DEVS-CHEMO-DM simulation model when an appointment request is generated. Tables 4.1 and 4.2 list specific attributes for the Parameters entity.

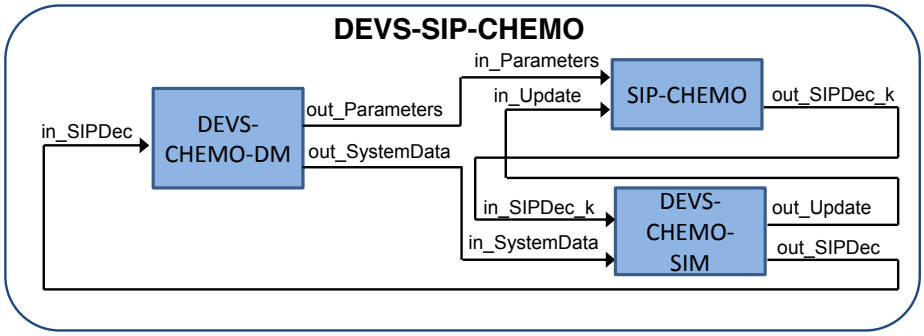


Figure 5.4: DEVS-SIP-CHEMO Block Diagram

The SystemData entity contains important parameters from the DEVS-CHEMO-DM simulation that initialize the DEVS-CHEMO-SIM simulation at time t_i. The attributes of the SystemData entity include the start time t_i and the previous decisions 1,2,...,i-1 before time t_i for the chair, nurse, and patient appointment schedules. Information about about oncology clinic setting such as the number of resources, service time distributions, etc. are also included. The purpose of the SystemData entity is to provide information that allows DEVS-CHEMO-SIM to be a duplicate of DEVS-CHEMO-DM at time t_i.

Entity SIPDecision_k contains the information for the decision from the SIP-CHEMO model made at time t_i that is implemented and evaluated by the DEVS-CHEMO-SIM simulation. This information is the decision variables x, $y(\omega)$, and $\nu(\omega)$. The Update entity includes updated parameters for $A, b, c, W(\omega), T(\omega), q(\omega)$, and $r(\omega)$ for each $\omega \in \Omega$ that is used to revise the parameters for the SIP-CHEMO model based on evaluation in the DEVS-CHEMO-SIM simulation model. Finally, the SIPDecision entity is the decision, x, $y(\omega)$, and $\nu(\omega)$, that met the stopping criterion in the DEVS-CHEMO-SIM simulation; it is the decision that is to be implemented in the DEVS-CHEMO-DM simulation.

Table 5.3: Description of DEVS-SIP-CHEMO Entities

Entity	**Brief Description**
Parameters	A, b, c and $W(\omega), T(\omega), q(\omega)$, and $r(\omega)$ for each $\omega \in \Omega$.
SystemData	Start time t_i of the DEVS-CHEMO-SIM simulation and previous decisions 1,2,...,i-1 before time t_i for the chair, nurse, and patient appointment schedules. Information about about oncology clinic setting such as the number of resources, service time distributions, etc. are also included.
SIPDecision_k	Decisions x, $y(\omega)$, and $\nu(\omega)$ from the SIP-CHEMO model which specify the start date and time for each appointment as well as the chair and nurse resource assignments.
Update	Contains revised parameters for the SIP-CHEMO model based on evaluation from the DEVS-CHEMO-SIM simulation model. The update entity has revisions for the A, b, c and $W(\omega), T(\omega), q(\omega)$, and $r(\omega)$ for each $\omega \in \Omega$ parameters.
SIPDecision	Contains the decision, x, $y(\omega)$, and $\nu(\omega)$, that met the stopping criterion in the DEVS-CHEMO-SIM simulation and is to be implemented in the DEVS-CHEMO-DM simulation.

5.3.4 Stopping Criteria

The stopping criteria for each application is determined by the DM or their supervisor. In oncology clinic operations, the scheduler is the DM. Stopping criteria should be based on the performance measures. In the case of chemotherapy appointment scheduling, performance measures are collected from both the patient and manage-

ment's perspective. The patient's perspective performance measures are type I delay, type II delay, type III delay, and system time. Type I delay is the difference between the prescribed start date and the actual start date of the first appointment. Type II delay is the time elapsed between the patient's arrival to the clinic and the time the patient is called by the registered nurse. The delay patient's experience after being called for treatment but before the chemotherapy drug infusion begins is called the type III delay. System time is the total time that the patient is in the oncology clinic, from arrival to discharge. From the management's perspective, the throughput, resource utilization, and nurse overtime are important performance measures. Throughput is the total number of patient appointments the clinic has during a defined time period. Resource utilization measures the percent of time that a resource is used during a day. Nurse overtime is the amount of time that nurses stay beyond the clinic closing time to finish assisting patients receiving treatment.

The DM should analyze each performance measure and identify which measures are suitable stopping criteria. A starting point is to select stopping criteria with high variation in order to set thresholds so that the iteration between the simulation and optimization models drive the performance measure toward a targeted threshold value. Additionally, the measures chosen should be related to the new patient that was most recently scheduled at time t_i by SIP-CHEMO because this schedule is the only one that can be modified on the next iteration between SIP-CHEMO and DEVS-CHEMO-SIM. This patient's schedule relates to appointment (or decision) request i, so this patient will now be referred to as patient i.

In the DEVS-CHEMO-SIM simulation, the type I delay is already known because the decision of when to start the appointment for patient i has already been determined. Thus, type I delay can be measured without simulation for patient i. The results from the simulations in Chapters 3 and 4 showed small changes across

decision models for the type III delay values, thus there is little to be gained by targeting this performance measure. Therefore, the focus on stopping criteria from the patient perspective is on the system time and the type II delay. Since the system time is dependent on the patient's treatment regimen, this performance measure is modified to be the time beyond the expected system time, which will be referred to as the *system time*$^+$.

From the management's perspective, the throughput, resource utilization, and nurse overtime performance measures can be evaluated with DEVS-CHEMO-SIM. Patient i's schedule does impact throughput, but it can be difficult to determine whether this is a positive or negative impact and how to adjust the scheduling decision to obtain improvement. Resource utilization is similar to type II delay in that there was little variation in previous computational experiments. Nurse overtime was identified as an important measure for the clinic collaborating on this study. Because of this and the high variation in overtime results in the previous experiments, nurse overtime is a strong candidate for the stopping criteria from the management's perspective. However, the stopping criteria should relate to patient i. Note that nurses stay overtime if a patient stays overtime. Therefore, *patient overtime*, or the amount of time that patient i stays beyond clinic operating hours, is used to estimate nurse overtime.

As previously mentioned, some of the stopping criteria may also be time-based in order to find a decision in a timely manner. The scheduler can consider setting a maximum time (e.g., 30 seconds) on the total time it takes to iterate between SIP-CHEMO and DEVS-CHEMO-SIM models or set a maximum number of iterations. It was determined through preliminary computational experiments that the latter, setting a maximum number of iterations works well for the chemotherapy appointment scheduling problem.

Table 5.4: Stopping Criteria for DEVS-SIP-CHEMO

Stopping Criteria	**Performance Measure**	**Suggested Threshold Values**
(A)	Patient Overtime	0 minutes
(B)	Type II Delay	15 minutes
(C)	System Time^{+}	15 minutes
(D)	Max Number Iterations	10 iterations

A threshold value is required for each performance measure that serves as a stopping criterion. The threshold values represent a target value for each performance measure. Table 5.4 shows each performance measure selected as a stopping criterion in DEVS-SIP-CHEMO as well as suggested threshold values. In order to drive nurse overtime down to 0 minutes, the patient overtime threshold is 0 minutes. Therefore, when stopping criterion (A) (patient overtime) is invoked, if the DEVS-CHEMO-SIM simulation runs indicate patient i stayed overtime (> 0 minutes) for an appointment, then the SIP-CHEMO model will reschedule patient i's appointments on the next iteration. A suggested threshold value of 15 minutes is used for the type II delay and system time^{+} performance measures. If patient i's type II delay exceeds 15 minutes when stopping criterion (B) is invoked or if patient i stays longer than 15 minute past their expected appointment time when stopping criterion (C) is invoked, then the patient's appointments are rescheduled on the next iteration between the simulation and optimization model.

The fourth stopping criterion is important because it specifies a maximum number of iterations between the SIP-CHEMO and DEVS-CHEMO-SIM models for each patient scheduled. When stopping criterion (D) is invoked, then at most 10 iterations occur between the simulation and optimization models to determine patient

i's schedule. This achieves two things: 1) limits the time spent searching for an improved solution to 10 attempts total, 2) guarantees that a solution will be found and the search process will not enter an infinite loop.

5.3.5 Modifications

Now that performance measures have been selected, it is important for the scheduler to also determine *how* the results can update the SIP-CHEMO model. This can be achieved a number of ways. For example, the objective can be modified, parameters can be changed, or constraints can be added. The important concept is that the modifications should be built off the the performance measure that caused the adjustment. For example, if the performance measures indicate a high level of patient overtime, then the penalty for overtime could be increased in the SIP-CHEMO objective. Several modifications based on stopping criteria A, B, and C were investigated. The most effective modifications found for DEVS-SIP-CHEMO are summarized in Table 5.5. Two types of modifications are shown for the patient overtime (A) stopping criterion and one modification each is shown for the type II delay (B) stopping criterion and the system time$^+$ (C) stopping criterion. Next is a description of these modifications.

Table 5.5: SIP-CHEMO Modifications in the DEVS-SIP-CHEMO Model

Modification	**Stopping Criterion**	**Modification**
(1)	(A) Patient Overtime	Add constraint: block start date in future schedules
(2)	(A) Patient Overtime	Change parameter: increase appointment duration by one time slot
(3)	(B) Type II Delay	Add constraint: block appointment's starting time slot
(4)	(C) System Time^{+}	Add constraint: block appointment's starting time slot

Modification (1): Blocking a Start Date

One objective of the SIP-CHEMO model is to start patients as early in the day as possible in order to avoid unnecessary gaps in the schedule. This objective was achieved by setting penalties for each time slot via the δ_s^{slot} penalty parameter. Once a possible scheduling decision for patient i is suggested by SIP-CHEMO and implemented in DEVS-CHEMO-SIM, the simulation capture's the patient overtime for every appointment t that occurs during the simulation horizon H. If any of the patient overtime values for these appointments exceeds the threshold for stopping criterion (A), then modification (1) can be invoked on the next iteration in SIP-CHEMO. If appointment $\hat{t}_{\bar{a}_i}$ caused patient i's overtime on iteration $\bar{a}_i$, then the scheduler presumes that the appointment was already scheduled to start at one of the earliest time slots on that day as possible. Therefore, selecting an alternative time slot, chair assignment, or nurse assignment, on the same day for appointment

$\hat{t}_{\bar{a}_i}$ is unlikely to show improvement in patient i's overtime. Because the spacing in the patient's treatment regimen is strict, then appointment $\hat{t}_{\bar{a}_i}$'s date is dependent on the start date for patient i which is referred to as start date $\hat{d}_{\bar{a}_i}$. This motivates the use of modification (1), which adds a constraint to block the start date $\hat{d}_{\bar{a}_i}$ from patient i's future schedules. Using the notation for SIP-CHEMO that was introduced in Chapter 4, then the following constraint can be added to the SIP-CHEMO model:

$$x_{\hat{d}_{\bar{a}_i}} = 0 \qquad\qquad \forall \bar{a}_i \in \bar{A}_i$$

where $\bar{A}_i$ is the set of iterations in which stopping criterion (A) was violated for patient i. If modification (1) is being used, then the constraint remains in effect for each iteration $\bar{a}_i$ of SIP-CHEMO for patient i so that the start date $\hat{d}_{\bar{a}_i}$ is not selected again.

Modification (2): Increasing Appointment Duration

Once a possible scheduling decision for patient i is suggested by SIP-CHEMO and implemented in DEVS-CHEMO-SIM, the simulation capture's the patient overtime for every appointment t that occurs during the simulation horizon H. If any of the patient overtime values for these appointments exceeds the threshold for stopping criterion (A), then modification (2) can be invoked on the next iteration in SIP-CHEMO. If appointment $\hat{t}_{\bar{a}_i}$ caused patient i's overtime on iteration $\bar{a}_i$, then one solution is to increase the expected duration of appointment $\hat{t}_{\bar{a}_i}$. By doing so, one of two things can occur. On the next iteration, the appointment may occur on the same day, but start earlier or receive a different chair or nurse assignment. Otherwise,

because the appointment is expected to last longer, it may be best to change the appointment date. This modification allows the model to determine whether it is best to modify the start date and thus impact the type I delay or to simply chose another assignment on this same day. Using the notation for SIP-CHEMO that was introduced in Chapter 3, then modification (2) forces the following parameter changes:

Original Value	Modified Value
$r_{\hat{t}_{\bar{a}_i}}$	$r_{\hat{t}_{\bar{a}_i}} + \lvert\bar{A}_i\rvert$
$r_{\hat{t}_{\bar{a}_i}}(\omega)$	$r_{\hat{t}_{\bar{a}_i}}(\omega) + \lvert\bar{A}_i\rvert$

where $\bar{A}_i$ is the set of iterations in which stopping criterion (A) was violated for patient i. If modification (2) is being used, then the number of time slots increases by one for each time that the stopping criterion was violated until the scheduled appointment time is early enough to avoid overtime for patient i.

Modification (3): Block Appointment Time Slot for Type II Delay

DEVS-CHEMO-SIM also captures the type II delay for every appointment t for patient i that occurs during simulation horizon H. If any of the type II delay values for these appointments exceeds the threshold for stopping criterion (B), then modification (3) is invoked on the next iteration in SIP-CHEMO. If appointment $\hat{t}_{\bar{b}_i}$ caused patient i's type II delay on iteration $\bar{b}_i$ to exceed the threshold on day $\hat{d}_{\bar{b}_i}$, then one solution is to block the time slot, $\hat{s}_{\bar{b}_i}$, that was scheduled for appointment $\hat{t}_{\bar{b}_i}$ on

day $\hat{d}_{\bar{b}_i}$. This modification was chosen on the basis that a number of other patients are scheduled at the same time and the combination of all appointments, acuity levels, etc. caused a delay for patient i's appointment $\hat{t}_{\bar{b}_i}$ on day $\hat{d}_{\bar{b}_i}$. Modification (3) moves this appointment to another time slot on either the same or a different day. The additional constraint also blocks all possible chair assignments at this time, too. Using the notation for SIP-CHEMO that was introduced in Chapter 4, then the following constraint can be added to the SIP-CHEMO model:

$$\sum_{k \in K^{\hat{d}_{\bar{b}_i}}} y_{k\hat{s}_{\bar{b}_i}}^{\hat{d}_{\bar{b}_i}^{\hat{t}_{\bar{b}_i}}} = 0 \qquad \forall \bar{b}_i \in \bar{B}_i$$

where $\bar{B}_i$ is the set of iterations in which stopping criterion (B) was violated for patient i. If modification (3) is used, then the constraint remains in effect for each iteration $\bar{b}_i$ in SIP-CHEMO for patient i so that the start slot $\hat{s}_{\bar{b}_i}$ on day $\hat{d}_{\bar{b}_i}$ for appointment $\hat{t}_{\bar{b}_i}$ is not used again.

Modification (4): Block Appointment Time Slot for System Time

Modification (4) is the same as modification (3) except that it is invoked for when stopping criterion (C) based on system time$^+$ exceeds the threshold value. If appointment $\hat{t}_{\bar{c}_i}$ caused patient i's system time$^+$ on iteration $\bar{c}_i$ to exceed the threshold on day $\hat{d}_{\bar{c}_i}$, then one solution is to block the time slot, $\hat{s}_{\bar{c}_i}$, that was scheduled for appointment $\hat{t}_{\bar{c}_i}$ on day $\hat{d}_{\bar{c}_i}$. This modification was chosen on the basis that a number of other patients are scheduled at the same time and the combination of all appointments, acuity levels, etc. caused a delay for patient i's appointment $\hat{t}_{\bar{c}_i}$ on day $\hat{d}_{\bar{c}_i}$. Modification (4) is as follows:

$$\sum_{k \in K^{\hat{d}_{\bar{c}_i}}} y_{k\hat{s}_{\bar{c}_i}}^{\hat{d}_{\bar{c}_i}^{\hat{t}_{\bar{c}_i}}} = 0 \qquad \forall \bar{c}_i \in \bar{C}_i$$

where $\bar{C}_i$ is the set of iterations in which stopping criterion (C) was violated for patient i. If modification (4) is used, then the constraint remains in effect for each iteration $\bar{c}_i$ in SIP-CHEMO for patient i so that the start slot $\hat{s}_{\bar{c}_i}$ on day $\hat{d}_{\bar{c}_i}$ for appointment $\hat{t}_{\bar{c}_i}$ is not used again.

5.4 Computational Experiments

The DEVS-SIP-CHEMO model was analyzed using data from a real outpatient oncology clinic. The design of experiments for DEVS-SIP-CHEMO is described in the first subsection. The second subsection gives experiment results and discusses their implications.

5.4.1 Design of Experiments

The objective of the design of experiments for DEVS-SIP-CHEMO is to determine: a) if using the integrated DEVS-SIP-CHEMO model to schedule patient appointments has better system performance than using SIP-CHEMO and DEVS-CHEMO models alone; b) if yes, then how much improvement on system performance is observed for each stopping criterion; c) how the results vary between the EE and ASD versions of the SIP-CHEMO models.

To test the DEVS-SIP-CHEMO model, the DEVS-CHEMO simulation and the SIP-CHEMO models from the previous two chapters were used. The experiments utilized data from the outpatient oncology clinic at Scott & White Hospital in Temple, Texas. The clinic was open five days a week for nine hours each day. There were between four to eight registered nurses and seventeen chemotherapy chairs available

each day. The patients were sampled from a database of historical patient data from a five-month period at the Scott & White oncology clinic. The database contained five-hundred and five model patients. There were an average of four appointments per treatment regimen. The maximum acuity a single registered nurse can have at one time was assumed to be five.

All experiments assumed a four-month planning horizon H and a one-month simulation period D. Time slots were assumed to be thirty minutes each, thus there are eighteen time slots in each day. Creating scenarios was an important part of the experimental design for the SIP-CHEMO models. The twelve scenarios developed in Table 4.6 were used in the DEVS-SIP-CHEMO experiments and the penalty values are kept the same for the SIP-CHEMO models. All DEVS-CHEMO variables from the experiments in Chapter 3 were used again, unless otherwise specified. The DEVS-CHEMO-SIM simulation model used the ASAP algorithm from Chapter 3 to predict the schedules of future patients $i+1, i+2, ...n$. The SIP-CHEMO model uses either the EE or ASD models for risk-averse decision-making. In both models, λ value is 0.5 and EE uses $\eta = 1 * \bar{S} * a^{\max}$.

To test the DEVS-SIP-CHEMO design of experiments objectives, a combination of stopping criteria, modifications, and threshold values was developed in a total of fourteen experiments, which are listed in Table 5.6. The ASD and EE experiments use only SIP-CHEMO to schedule patients and the "-" value for the three columns indicates that none of the stopping criteria or modifications were used. Next, the modifications (1)-(4) were implemented for the EE and ASD algorithms as EE_1-EE_4 and ASD_1- ASD_4 respectively. The fifth (EE_5 and ASD_5) and sixth (EE_6 and ASD_6) experiments combined modifications (1) and (3) and then (2) and (4) respectively to determine if multiple improvements in performance measures can be achieved at the same time. All experiments using stopping criteria have the

stopping criterion (D) time-based performance measure which limits the total number of iterations to ten. As mentioned earlier, this is useful for reducing speed and guaranteeing that a solution can be found.

Table 5.6: DEVS-SIP-CHEMO Experiments

Name	Stopping Criterion	Modification	Threshold Values
EE	-	-	-
EE_1	(A),(D)	(1)	0 minutes, 10 iterations
EE_2	(A),(D)	(2)	0 minutes, 10 iterations
EE_3	(B),(D)	(3)	15 minutes, 10 iterations
EE_4	(C),(D)	(4)	15 minutes, 10 iterations
EE_5	(A),(B),(D)	(1),(3)	0 minutes, 15 minutes, 10 iterations
EE_6	(A),(C),(D)	(2),(4)	0 minutes, 15 minutes, 10 iterations
ASD	-	-	-
ASD_1	(A),(D)	(1)	0 minute, 10 iterations
ASD_2	(A),(D)	(2)	0 minutes, 10 iterations
ASD_3	(B),(D)	(3)	15 minutes, 10 iterations
ASD_4	(C),(D)	(4)	15 minutes, 10 iterations
ASD_5	(A),(B),(D)	(1),(3)	0 minutes, 15 minutes, 10 iterations
ASD_6	(A),(C),(D)	(2),(4)	0 minutes, 15 minutes, 10 iterations

Preliminary experiments were conducted to determine the threshold values for each stopping criterion. These values were eluded to earlier in Table 5.4. The Scott & White oncology clinic wishes to eliminate nurse overtime. Thus the lowest possible

threshold value of 0 minutes was selected for the patient overtime stopping criteria. Preliminary results showed that a target value of 0 minutes helped drive the nurse overtime towards 0 minutes and still allowed the solution search process to end quickly. Therefore, 0 minutes was used as the threshold value for patient overtime.

For the system overtime$^+$ and type II delay performance measures, it was assumed that patients would be willing to wait between 0 to 15 minutes for their appointment to begin. Therefore, 15 minutes was implemented for a threshold value for both performance measures. Again, this value lent itself toward quick and meaningful solution results. Preliminary testing also experimented with reducing the threshold value to 5 or 10 minutes for type II delay and system overtime$^+$, but results showed that little or no improvement could be made and only slowed down the search process. The maximum number of iterations was also used as a stopping criterion and this value was set to ten iterations. In the experiments, patient schedule iterations in DEVS-SIP-CHEMO had an average of 2-3 iterations. In most experiments, between eight to fifteen patient schedules (2-6%) required the upperbound of ten iterations to find a solution.

In all DEVS-SIP-CHEMO experiments listed in Table 5.6, the system performance was captured by simulating the clinic performance for one-month. There were 172 patients initially used to fill the schedule with 5 to 6 additional patients generated each day. During the one-month simulation period, DEVS-SIP-CHEMO schedules 276 patients. DEVS-SIP-CHEMO provides system performance results on the type I delay, type II delay, type III delay, system time, throughput, chair utilization, nurse utilization, and nurse overtime. The total throughput is a measure of how many appointments occurred during the simulation period. Average run times in seconds for each experiment variation are also stated in the results section.

The throughput results are reported as the total throughput, or appointments

(appts.), for the month and the average daily throughput. The nurse overtime is reported in two different ways. The nurse overtime$^+$ count is the number of nurses that had to work overtime in the five-month period and nurse overtime$^+$ is the average of the overtime required during these instances (zero entries are excluded). Nurse overtime is the average overtime among all nurses during the one-month simulation period (zero entries included). The next subsection provides the average for the each of these performance measures over the ten replications for each experiment. Ten replications were sufficient for obtaining observable improvement over the previous scheduling algorithms and models. The simulations were conducted on a Dell Precision T7500 with an Intel(R) Xeon(R) processor running at 2.4 GHz with 12.0 GB RAM.

5.4.2 Results and Discussion

This subsection first compares the DEVS-CHEMO, SIP-CHEMO, and DEVS-SIP-CHEMO models. Results for DEVS-SIP-CHEMO are then discussed for the EE and ASD models separately under different combinations of stopping criteria and modifications. General observations are also made about stopping criteria used in DEVS-SIP-CHEMO.

Comparison of the Three Models: DEVS-CHEMO, SIP-CHEMO, and DEVS-SIP-CHEMO

The DEVS-CHEMO (simulation), SIP-CHEMO (optimization), and DEVS-SIP-CHEMO (simulation and optimization) models were tested under the same conditions and the results are depicted in Table 5.7. The ASAP algorithm was used to represent the DEVS-CHEMO model. The EE model with $\lambda = 0.5$ and $\eta = 1 * \bar{S} * a^{\max}$ was

used for SIP-CHEMO and DEVS-SIP-CHEMO. Additionally, the constraints from EE_5 were used for the DEVS-SIP-CHEMO model. In the results, DEVS-CHEMO had the lowest type I delay of 1.35 days. The SIP-CHEMO model had the highest throughput of 474 appointments. The DEVS-SIP-CHEMO model, which targeted patient overtime and type II delay, had the lowest nurse overtime of 1 minute (reduced more than 90%), lowest nurse overtime^{+} of 19 minutes (reduced 67%), lowest type II delay of 11 minutes (reduced 36% to 61%), and lowest system time of 199 minutes (reduced by 4% and 9%).

DEVS-SIP-CHEMO holds throughput within 1% when compared to both DEVS-CHEMO and SIP-CHEMO. Type I delay for DEVS-SIP-CHEMO is within 1% of SIP-CHEMO and only 0.31 days longer (23% increase) when compared to DEVS-CHEMO. Additionally, the average run times increase from 1 second with DEVS-CHEMO, to 94 seconds with SIP-CHEMO, to 541 seconds with DEVS-SIP-CHEMO. The scheduler can improve patient satisfaction with lower type II delay, type III delay, and system time and reduce nurse overtime by 90% using DEVS-SIP-CHEMO without sacrificing much on throughput and type I delay. Thus, DEVS-SIP-CHEMO supersedes the performance of using simulation or optimization alone.

Table 5.7: Performance Results for Scheduling Models

	Models		
Performance Measures (units)	DEVS-CHEMO	SIP-CHEMO	DEVS-SIP-CHEMO
Total Throughput (appts.)	466.0	474.3	467.7
Daily Throughput (appts.)	23.3	23.7	23.4
Chair Utilization (%)	49.40	50.06	48.86
Nurse Utilization (%)	75.04	74.76	71.36
Nurse Overtime^{+} (min.)	58.00	57.26	19.15
Nurse Overtime^{+} Count	46.61	28.90	8.90
Nurse Overtime (min.)	22.19	13.94	1.36
Type I Delay (days)	1.35	1.64	1.66
Type II Delay (min.)	28.11	17.07	10.87
Type III Delay (min.)	32.26	32.65	31.85
System Time (min.)	218.40	206.51	198.51
Simulation Run Time (sec.)	1.59	93.85	540.68

Results for EE

The results for DEVS-SIP-CHEMO using the EE model are listed in Table 5.8. EE (SIP-CHEMO) has one of the highest throughput values (474 appointments) and lowest type I delay (1.64 days), but the model performs poorly for other performance measures with the highest nurse overtime, nurse overtime^{+}, type II delay, and system time. DEVS-SIP-CHEMO holds the throughput and type I delay values to an acceptable level and makes improvements on the other performance measures. Con-

sider the total throughput in Figure 5.5 and the type I delay (details in Table 5.8). Most of the experiments EE_1 - EE_6 which use DEVS-SIP-CHEMO have lower total throughput than EE by 3 to 8 appointments; EE_4 is the one exception. This is because patient appointments may have to be spread out over more days (thus lower daily throughput) in order to achieve acceptable levels of overtime, system time, etc. The lowest throughput (466 appointments) was observed for EE_2 in which roughly eight fewer appointments during the one-month simulation period. The highest type I delay was observed for EE_1 (1.76 days) but the value is still less than 2 days for type I delay and is only a 7% change from EE. The results for the type III delay and resource utilization did not yield any interesting patterns for the DEVS-SIP-CHEMO analysis and are not discussed, though the values for these performance measures are in Table 5.8.

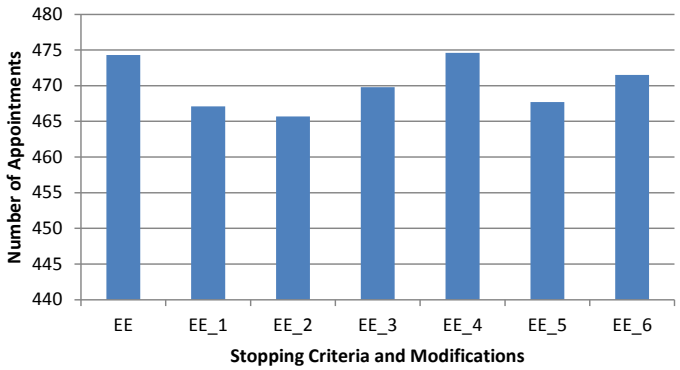


Figure 5.5: Results for Throughput for EE

Next, refer to Figure 5.6 which shows results for the nurse overtime$^+$, nurse overtime, and type II delay. When looking at the two measures for nurse overtime, the results show that EE_1, EE_2, EE_5, and EE_6 were successful in driving the

Table 5.8: Performance Results the EE

	Experiments						
Performance Measures (units)	EE	EE_1	EE_2	EE_3	EE_4	EE_5	EE_6
Total Throughput (appts.)	474.3	467.1	465.7	469.8	474.6	467.7	471.5
Daily Throughput (appts.)	23.7	23.4	23.3	23.5	23.7	23.4	23.6
Chair Utilization (%)	50.06	49.26	48.80	49.38	49.46	48.86	49.23
Nurse Utilization (%)	74.76	72.43	71.89	75.29	73.95	71.36	72.27
Nurse Overtime^{+} (min.)	50.06	49.26	48.80	49.38	49.46	48.86	49.23
Nurse Overtime^{+} Count	28.90	11.10	12.30	29.30	31.50	8.90	9.90
Nurse Overtime (min.)	13.94	3.40	3.54	11.48	11.08	1.36	2.02
Type I Delay (days)	1.64	1.76	1.74	1.68	1.54	1.66	1.72
Type II Delay (min.)	17.07	15.12	17.42	10.57	11.59	10.87	12.19
Type III Delay (min.)	32.65	32.48	32.01	32.58	31.98	31.85	32.63
System Time (min.)	206.51	204.37	205.59	199.25	198.72	198.51	199.62
Simulation Run Time (sec.)	93.85	414.84	432.13	598.86	396.58	540.68	584.54

patient overtime, and subsequently the nurse overtime$^+$ and nurse overtime, towards zero. All four of these experiments have lower nurse overtime$^+$ values than the other three experiments (EE, EE_3, and EE_4) by 18% (10 minutes) to 66% (38 minutes) and lower nurse overtime by 18% (2 minutes) to 90% (12 minutes). In fact, when reducing patient overtime (A) is combined with reducing type II delay (B) and system time (C) in experiments EE_5 and EE_6 respectively, the lowest values were observed with 19 to 25 minutes for nurse overtime$^+$ and 1 to 2 minutes for nurse overtime. Additionally, refer to Figure 5.7 which shows the average man-hours of overtime for the clinic. When patient overtime (A) is not targeted by DEVS-SIP-CHEMO (EE, EE_3, EE_4), then over 22 man-hours of overtime are required by the oncology clinic nurses during the one-month period. However, when patient overtime (A) is targeted in EE_1 and EE_2 then this value is reduced to six or seven hours. Nurse overtime$^+$ man-hours were further reduced to two to four hours a month when other performance measures (B) or (C) are also targeted by DEVS-SIP-CHEMO in EE_5 and EE_6.

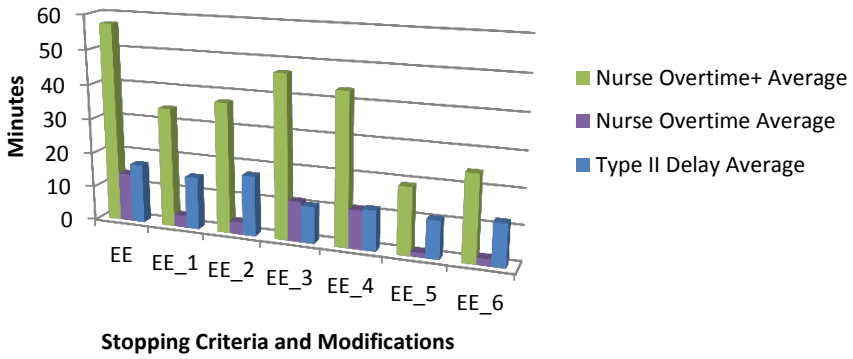


Figure 5.6: Results for Time-Based Performance Measures for EE

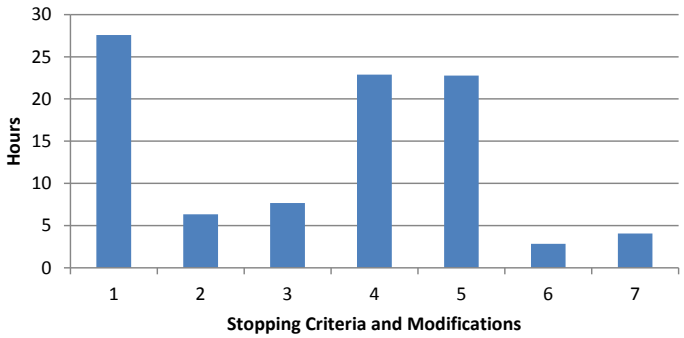


Figure 5.7: Results for Nurse Overtime^{+} Man-Hours for EE

Also depicted in Figure 5.6 is the type II delay for all EE DEVS-SIP-CHEMO experiments. The type II delay was highest at 17 minutes for EE and EE_2, in which the type II delay was not targeted. However, for experiments EE_3 and EE_5 where type II delay was targeted, then the type II delay was reduced to 10 minutes, roughly a 40% reduction. Figure 5.8 graphically depicts the system time average for the seven EE DEVS-SIP-CHEMO experiments. Like the type II delay, the system time was highest for EE with 207 minutes. In the EE_3, EE_4, EE_5, and EE_6 experiments, the system time is lower at 198 to 199 minutes. Interestingly, the lowest system time occurs in EE_5 when the type II delay was targeted because type II delay is a component of system time. For the case of EE_5, the total improvement was an 8 minute reduction in system time over the EE experiment without DEVS-SIP-CHEMO. The average (AVG), standard deviation (STDEV), and 90% confidence interval (CI) for the EE_5 experiments are listed in Appendix C.1 in Table C.1. Data for the other EE DEVS-SIP-CHEMO experiments was intentionally omitted for conciseness.

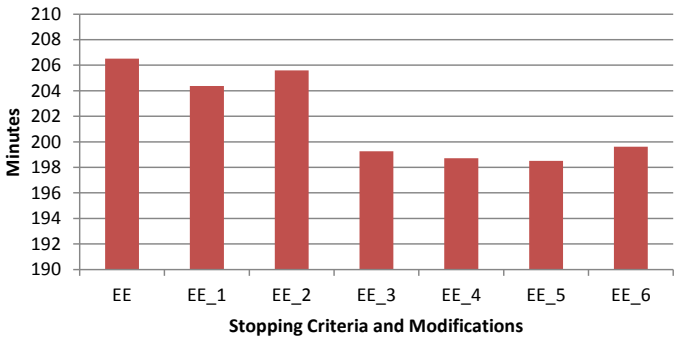


Figure 5.8: Results for System Time for EE

Results for ASD

The results for the ASD DEVS-SIP-CHEMO results are listed in Table 5.9. ASD (SIP-CHEMO) has one of the highest throughput values (474 appointments) and the lowest type I delay (1.54 days), but the model has the highest nurse overtime^{+}, nurse overtime, type II delay, and system time. DEVS-SIP-CHEMO holds the throughput and type I delay values to an acceptable level and makes improvements upon the other performance measures. Consider the total throughput in Figure 5.9 and the type I delay (details in Table 5.9). Most of the experiments ASD_1 - ASD_6 which use DEVS-SIP-CHEMO have lower throughput than ASD. The exception to this is ASD_3 which has higher total throughput of 476 appointments. The lowest throughput (452 appointments) occurred for ASD_5 which also has the lowest average type II delay of 10 minutes. ASD, ASD_1, and ASD_2 have the highest type II delay of 14 to 15 minutes. The results for the type III delay and resource utilization did not yield any interesting patterns for the DEVS-SIP-CHEMO analysis and are not discussed, though the values for these performance measures are in Table 5.9.

Table 5.9: Performance Results for ASD

	Experiments						
Performance Measures (units)	ASD	ASD_1	ASD_2	ASD_3	ASD_4	ASD_5	ASD_6
Total Throughput (appts.)	473.9	465.8	473.2	475.9	470.2	452.3	466.8
Daily Throughput (appts.)	23.7	23.3	23.7	23.8	23.5	22.6	23.3
Chair Utilization (%)	50.21	48.89	49.68	50.16	49.06	47.42	48.96
Nurse Utilization (%)	73.51	72.20	72.03	73.51	73.86	70.44	72.06
Nurse Overtime$^+$ (min.)	52.76	34.11	34.27	46.05	45.71	25.86	27.36
Nurse Overtime$^+$ Count	31.60	9.30	10.50	30.80	30.90	8.60	8.50
Nurse Overtime (min.)	13.61	2.90	2.98	11.86	11.67	1.79	1.76
Type I Delay (days)	1.54	1.78	1.65	1.66	1.58	1.79	1.76
Type II Delay (min.)	14.02	14.37	15.15	11.71	12.60	10.07	11.65
Type III Delay (min.)	32.22	32.60	32.24	32.65	32.46	31.83	32.39
System Time (min.)	204.28	202.72	203.51	200.89	199.82	198.40	199.96
Simulation Run Time (sec.)	103.54	391.16	394.78	656.48	480.33	565.67	592.76

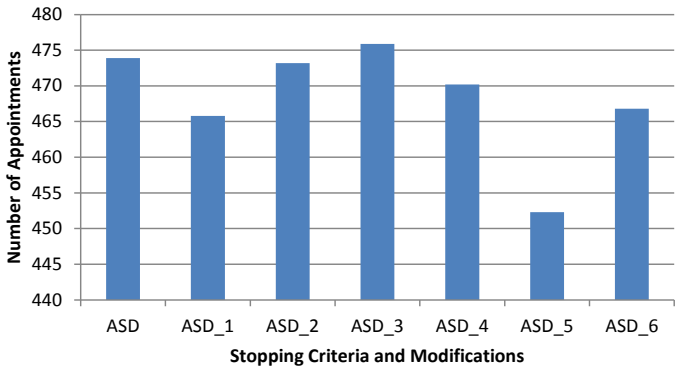


Figure 5.9: Results for Throughput for ASD

Next, refer to Figure 5.10 which shows results for the nurse overtime^{+}, nurse overtime, and type II delay. When looking at the two measures for nurse overtime, the results show that ASD_1, ASD_2, ASD_5, ASD_6 all drive the patient overtime, and subsequently the nurse overtime^{+} and nurse overtime, towards zero. All four of these experiments have lower nurse overtime^{+} values. In fact, when reducing patient overtime (A) is combined with reducing type II delay (B) and system time (C) in experiments EE_5 and EE_6 respectively, then the results are best for overtime. Additionally, refer to Figure 5.11 which shows the average man-hours of overtime for the clinic. When patient overtime (A) is not targeted by DEVS-SIP-CHEMO, then over 23 man-hours of overtime are required by the oncology clinic nurses during the one-month period. However, when patient overtime (A) is targeted alone then this value is reduced to 5 or 6 hours and reduced to 3 or 4 hours a month when other performance measures (B) or (C) are also targeted by DEVS-SIP-CHEMO in ASD_5 and ASD_6.

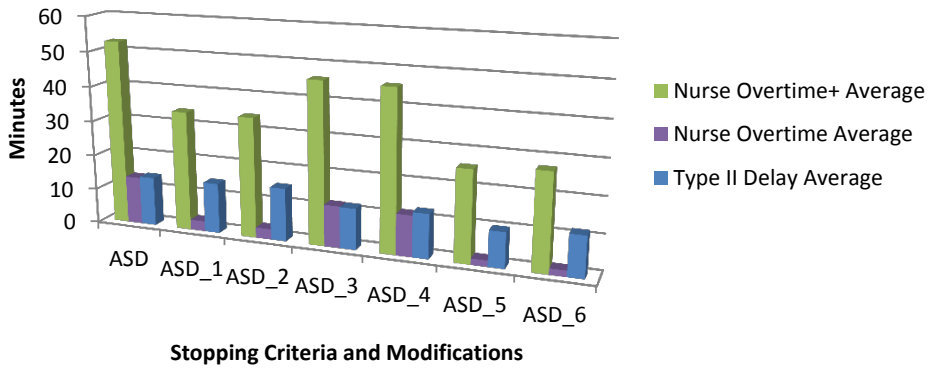


Figure 5.10: Results for Time-Based Performance Measures for ASD

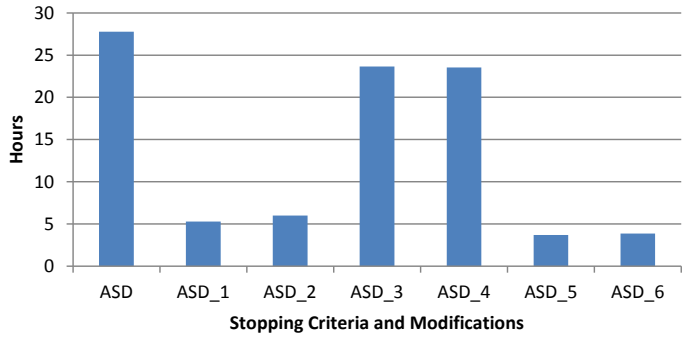


Figure 5.11: Results for Nurse Overtime^{+} Man-Hour for ASD

Also depicted in Figure 5.10 is the type II delay for all seven ASD DEVS-SIP-CHEMO experiments. The type II delay was highest at 14 to 15 minutes for ASD, ASD_1, and ASD_2, in which the type II delay was not targeted. However, for experiments ASD_3 and ASD_5 where type II delay was targeted, then the type II delay was reduced to 10 or 11 minutes, roughly a 30% reduction. Figure 5.12 graphically depicts the system time average for the seven ASD DEVS-SIP-CHEMO

experiments. Like the type II delay, the system time was highest for ASD with around 204 minutes. In the ASD_4, ASD_5, and ASD_6 experiments, the system time is less than 200 minutes. The lowest system time value occurs in ASD_5 when the type II delay was targeted. For the case of ASD_5, the total improvement was a six minute reduction in system time from the ASD experiment without DEVS-SIP-CHEMO. The AVG, STDEV, and 90% CI for the ASD_6 experiments are listed in Appendix C.1 in Table C.2. The same data for the other ASD DEVS-SIP-CHEMO experiments was intentionally omitted for conciseness.

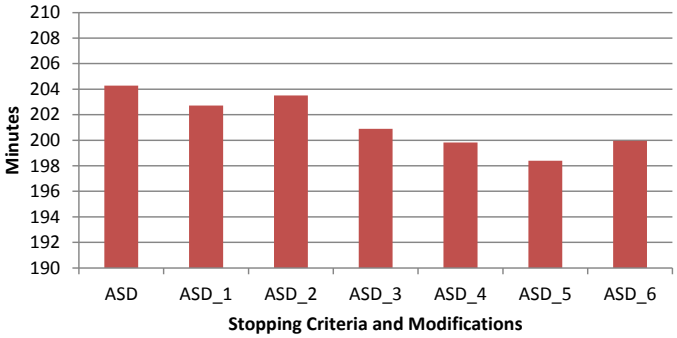


Figure 5.12: Results for System Time for ASD

General Observations

It is apparent in the results that it is difficult to simultaneously optimize all performance measures at once. Typically, a model with a high throughput value also has low type I delay but the system time, overtime, etc. are all higher. If the primary objective of the clinic is to achieve a high throughput and low type I delay, then DEVS-SIP-CHEMO is not valuable. However, if the clinic prefers

to keep throughput and type I delay at acceptable levels, but to make noticeable improvements in other performance measure, then DEVS-SIP-CHEMO is suitable for such a task.

DEVS-SIP-CHEMO does work improve targeted performance measures. Because type II delay is a component of system time, then results show that targeting either one of these values also yields improvement in the other. In general, targeting multiple performance measures yielded better results than targeting each performance measure individually. In the EE DEVS-SIP-CHEMO experiments, EE_5, which uses stopping criteria for patient overtime (A) and type II delay (B) and modifications (1) and (3), yielded the best results all around. This decision is based on the fact that EE_5 has high total throughput and low type I delay and system time (within 1% to 3%), but also yields improvements in nurse overtime (90%), nurse overtime$^+$ (67%), and type II delay (36%) over using SIP-CHEMO alone.

In the ASD DEVS-SIP-CHEMO experiments, ASD_6, which uses stopping criteria for patient overtime (A) and system time (C) and modifications (2) and (4), yielded the best results all around. This decision is based on the fact that ASD_6 has acceptably high total throughput but also yields low values for nurse overtime (4 minutes), type II delay (12 minutes), and system time (200 minutes). EE_5 is preferred to ASD_6 because it has slightly higher total throughput (by 1 patient), smaller type I delay (by 0.1 days), type II delay (by 1 minute), nurse overtime$^+$ (by 8 minutes), nurse overtime (by <1 minute), and system time (by 1 minute).

5.4.3 Feasibiliy of Implementation in a Real Oncology Clinic

An important point that has yet to be discussed, is how practical would it be to utilize DEVS-SIP-CHEMO in a real oncology clinic? To answer this question, consider Figure 5.13. A scheduler would request a schedule using SIP-CHEMO

and the iterations would proceed using DEVS-CHEMO-SIM. Observe that DEVS-CHEMO-DM is omitted from the diagram because its purpose was to generate the requests and analyze the results over the simulation period. However, in a real setting, actual patients generate requests through the scheduler and the system is analyzed in real time using real data. Once DEVS-CHEMO-SIM identifies a solution that has satisfied the stopping criteria, then the solution is reported to the scheduler who can then implement the decision in the real oncology clinic. In the results section, DEVS-SIP-CHEMO took roughly nine minutes to run. However, it takes only a few seconds to actually schedule one patient. In fact, for the preferred experiment that implemented three stopping criteria, EE_5, the average time to schedule a patient was 3.95 seconds. Therefore, DEVS-SIP-CHEMO is possible to implement in a real setting and achieve results in a timely manner.

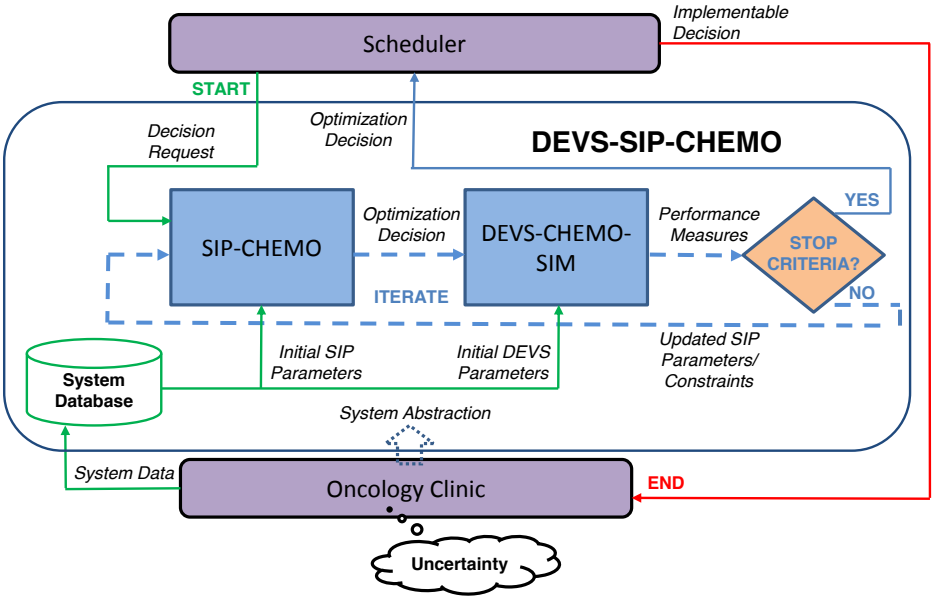


Figure 5.13: The Concept of the DEVS-SIP-CHEMO Framework for Oncology Clinic Operations

5.5 Summary

DEVS-SIP-CHEMO is a viable solution approach for the problem of scheduling chemotherapy appointments at an outpatient oncology clinic. The integrated simulation and optimization methodology is a novel approach that addresses the challenging problem aspects of online scheduling, uncertainty in problem parameters, risk-averse decision-making, and system performance evaluation. DEVS-SIP-CHEMO is the first model to consider risk-aversion and uncertain problem parameters for oncology clinic operations.

One simulation model, DEVS-CHEMO-DM, simulates the oncology clinic operations for a predefined simulation period. Each time an appointment request occurs from a new patient, the scheduling decision is determined by a mean-risk SIP-CHEMO optimization model. The SIP-CHEMO model then implements and evaluates the decision in a second simulation model, DEVS-CHEMO-SIM. DEVS-CHEMO-SIM simulates all current decisions and predicts future decisions using a scheduling algorithm. If the system performance satisfies stopping criteria set by the scheduler, or DM for the oncology clinic, then the most recent solution is implemented in DEVS-CHEMO-DM. Otherwise, the SIP-CHEMO model is revised and the search process for an implementable decisions continues until one or more stopping criteria are satisfied. DEVS-CHEMO-DM continues throughput the end of the simulation period and reports system performance results to the DM.

In order to determine if DEVS-SIP-CHEMO did out-perform the SIP-CHEMO optimization models alone, four stopping criteria were utilized based on patient overtime, type II delay, system time^{+}, and a maximum number of iterations. The latter was used to guarantee convergence to a solution in a reasonable time frame. Four types of modifications were used to either add constraints or modify parameters in

the SIP-CHEMO model. Computational experiments used six variations of stopping criteria and modifications within DEVS-SIP-CHEMO and were each applied using the EE and ASD mean-risk measures.

Computational results showed that DEVS-SIP-CHEMO did improve the chemotherapy appointment scheduling decisions by obtaining better system performance. Although it is difficult to simultaneously optimize all performance measures at once, DEVS-SIP-CHEMO performs well if the clinic prefers to keep throughput and type I delay at acceptable levels while making noticeable improvements in overtime, type II delay, and system time. Targeting multiple performance measures was better than targeting performance measures individually. EE_5, which uses stopping criteria for patient overtime and type II delay, yielded the best results. EE_5 has acceptably high total throughput and low type I delay (within 1 to 3%), but also yields improvements in nurse overtime (90%), nurse overtime^{+} (67%), system time (4%), and type II delay (36%) over using SIP-CHEMO alone.

DEVS-SIP-CHEMO is possible to implement in a real setting and achieve results in a timely manner. Although the full version of DEVS-SIP-CHEMO takes around nine minutes to simulate a one-month period and schedule 276 patients, only part of the model is required in a real implementation setting. The iterations between the SIP-CHEMO and DEVS-CHEMO-SIM models are the only components required to schedule a new patient in a real setting. For the preferred model using EE, it only took an average of 3.95 seconds to schedule one new patient, thus DEVS-SIP-CHEMO would be practical to implement in a real oncology clinic.

6. CONCLUSIONS AND FUTURE RESEARCH

6.1 Conclusions

This dissertation advances the state-of-the-art in stochastic programming with simulation by contributing new concepts, models, and algorithms for a variety of applications. DEVS and SIP have been extended to a new level beyond some of the traditional impractical assumptions. The extensions include the development of a formal coupling between DEVS and SIP, incorporating a decision component within a simulation model, development of non-static probability distributions for SIP (generated via DEVS), and non-closed-form objective functions for SIP (modeled, evaluated, and revised via DEVS). An important feature of DEVS-SIP is that it allows for automated online (or real-time) system data update for both DEVS and SIP models, thus enabling decision-making over time adapting to dynamic changes in the problem data. This kind of decision-making framework is necessary in many practical applications such as oncology operations management where a decisions have to be made at discrete time periods over a rolling horizon.

One contribution of this work is DEVS-CHEMO (Chapter 3), which is a discrete event simulation model of oncology clinic operations designed using the DEVS formalism. DEVS-CHEMO provides results for performance measures from the patient's perspective and from the management's perspective. DEVS-CHEMO was implemented using DEVSJAVA and is a tool that oncology clinic managers use to test decisions and operational policies before implementation in the clinic. Four algorithms were derived and implemented and results indicate that scheduling constraints for both nurse and chair resources led to the best overall system performance. It was found that assigning patients to both chairs and nurses improved system per-

formance by reducing appointment duration 3%, reducing type II delay by 34%, and reducing nurse overtime^{+} by 4% when compared to the current scheduling algorithm. A sensitivity analysis on the number of nurse resources in the clinic also demonstrated how to use DEVS-CHEMO to determine ideal staffing levels. The DEVS-CHEMO chapter was important because it developed a simulation model of oncology clinic operations and provides a tool for analyzing decision-making and operational policies within the oncology clinic. Although other simulation models have been developed, DEVS-CHEMO allowed for easy integration with the SIP-CHEMO optimization model.

A second contribution of this work is SIP-CHEMO (Chapter 4), which is an optimization model for scheduling chemotherapy appointments. The SIP-CHEMO optimization models are the first optimization models for the chemotherapy decision problem of scheduling chemotherapy patients, chairs, and nurses that consider uncertain problem parameters and risk. A risk neutral (RN) model was first developed and then risk-averse SIP-CHEMO models for expected excess (EE) and absolute semideviation (ASD) were developed to allow DMs to consider risk preferences in their scheduling decisions. SIP-CHEMO determines an optimal appointment schedule for a new chemotherapy patient who has been prescribed a unique treatment regimen and suggested appointment start date. The appointment duration, acuity level, and nurse resource availability were assumed to be stochastic. Computational experiments for SIP-CHEMO showed that all three SIP-CHEMO models, RN, EE, and ASD, outperformed the algorithms that were developed with DEVS-CHEMO. The chapter on SIP-CHEMO is important because a risk-averse optimization model was developed that outperforms the original scheduling algorithms to achieve better overall system performance. Using the SIP-CHEMO models, the throughput increased by 2%, waiting time decreased by 35%, system time decreased by 4%, and nurse

overtime decreased by 24% when compared to the current scheduling algorithm.

Another contribution of this work is the DEVS-SIP framework (Chapter 5), a new paradigm for decision-making under uncertainty. DEVS-SIP formally defines an integrated simulation and optimization framework for use in a variety of applications. DEVS-SIP is suitable for decision problems that cannot be formulated using a closed-form mathematical expression and involve dynamic changes to the problem data over time. This kind of decision-making framework is necessary in many practical applications that require decisions under uncertainty over time in a rolling horizon manner.

Combining DEVS-CHEMO and SIP-CHEMO using the DEVS-SIP framework led to the development of the fourth and final contribution, DEVS-SIP-CHEMO, an integrated simulation and optimization model for scheduling chemotherapy patient appointments. DEVS-SIP-CHEMO enables data-driven decision-making for both strategic and operational planning in outpatient oncology clinics. The integrated simulation and optimization methodology is a novel approach that addresses the challenging problem aspects of online scheduling, uncertainty in problem parameters, risk-averse decision-making, and the problem of being unable to model a closed-form objective for the decision problem. Four stopping criteria were utilized based on system performance measures as well as four modifications to the SIP-CHEMO model. Computational results showed that DEVS-SIP-CHEMO does improve the chemotherapy appointment scheduling decisions by obtaining better system performance. Additionally, DEVS-SIP-CHEMO can handle complex decision problems in a timely manner.

The chapter on DEVS-SIP-CHEMO is important because it showed that combining simulation and optimization can yield better system performance than either method alone. DEVS-SIP-CHEMO kept throughput and waiting time for the first

appointment within 1% but improved nurse overtime by 90%, nurse overtime$^+$ by 67%, and type II delay by 36% when compared to SIP-CHEMO. However, caution should be taken when considering the results for all models because the results are dependent on the treatment regimens and appointment duration observed from the limited five-month data set available at the time of this study. As shown in Chapter 3, the system performance results seem to be sensitive to changes in the probability distribution assumptions for the type II + type III delay.

DEVS-SIP has the potential to address challenging aspects of many important decision problems in a variety of applications. For the case of oncology clinic appointment scheduling, optimal decisions under uncertainty provide an improved patient-centered experience and reduce clinic overtime. Other potential applications include resource scheduling for large-scale wildfires or the military land move problem.

6.2 Future Research

The work presented in this dissertation is a step forward in addressing oncology clinic scheduling problems, but there are a few remaining aspects to the problem which serve as motivation for future research. The scope of the work in this dissertation for oncology clinic scheduling was limited to the drug infusion appointment. One extension would be to consider patient appointments for blood work and visits with the oncologist as well. Scheduling the blood exams, oncologist visit, and infusion appointment sequentially would pose new challenges to the scheduler. Furthermore, rescheduling is an important component of the chemotherapy scheduling problem. As future work, rescheduling of appointments can be incorporated in the models by assuming a certain percentage of appointments are rescheduled or modified due to poor blood test results. The DEVS-CHEMO and SIP-CHEMO models would then release the chair and nurse resources for the rescheduled appointments and the

new appointments would then be considered a new treatment regimen, which can be formulated as a decision problem in SIP-CHEMO. Incorporating the rescheduling feature will more accurately reflect the challenges faced by the scheduler in the oncology clinic.

The current implementation assumes stochastic appointment duration based on drug infusion times in the historical data. In reality, how and when the appointment duration changes is also patient-dependent. This is because the patient may have adverse reactions to the drug or take a long time to begin treatment because the nurse has difficulty setting up the patient's IV, which can also be captured with acuity levels. In light of this, another extension would be to model the patient as an atomic model in DEVS-CHEMO such that the patient's health status impacts appointment duration and acuity levels.

In the optimization model, the current formulation determines appointment dates and start times. The scheduler determines how much time to allocate for the appointment, which has been assumed to be the planned time provided by the oncology clinic. An extension for the SIP-CHEMO model would be to reformulate the problem to also determine the amount of time to allocate to each appointment. The EE and ASD mean-risk measures implemented in SIP-CHEMO are deviation measures. Another extension would be to model the problem using other mean-risk measures such as quantile deviation (QDEV). Also, the SIP-CHEMO models take significantly longer to solve with CPLEX than with algorithms. Although steps have been taken to simplify these models, current implementations still solve the deterministic equivalent formulation. One future direction would be to implement a decomposition method to further improve the solution speed for the SIP-CHEMO models.

Finally, there are improvements that can be made to DEVS-SIP-CHEMO regarding the stopping criteria and modifications. Although a few other ideas were explored,

a more detailed analysis on other stopping criteria and modifications would help gain further insight on whether more substantial improvements can be made. Improving the solution speed of SIP-CHEMO would also help complete this analysis quickly. Additionally, a more detailed guide for how to select stopping criteria and choose modifications for DEVS-SIP would help users in other application areas determine how to adapt their application to the DEVS-SIP framework to obtain improvements in system performance.

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APPENDIX A

DEVS-CHEMO MODEL

A.1 DEVS-CHEMO Atomic Model Mathematical Definitions

This appendix section uses the standard parallel DEVS [50] notation and adopts the notation from [28] to give detailed mathematical expressions of some of the DEVS-CHEMO atomic models. Additionally, $\wedge$ represents the "and" operator, == is the assignment operator, || is the "or" operator.

SCHED Atomic Model.

$$DEVS_{SCHED} = (X_M, Y_M, S, \delta_{ext}, \delta_{int}, \delta_{con}, \lambda, ta) \tag{A.1}$$

where,

$X_M = \{(p, v) | p \in IPorts, v \in X_p\}$ is the set of input ports and values, $IPorts = \{$"in_ApptRequest"$\}$, and $X_{\text{in\_ApptRequest}} = V_1$ is an arbitrary set of values;

$Y_M = \{(p, v) | p \in OPorts, v \in Y_p\}$ is the set of output ports and values, $OPorts = \{$"out_ApptTimes", "out_Wait1Time"$\}$, and $Y_{\text{out\_ApptTimes}}$ and $Y_{\text{out\_Wait1Time}}$ are arbitrary set of values;

$S = \{$"Idle", "Schedule"$\} \times \mathcal{R}_{+,0} \times V_1$ is the set of sequential states.

***External Transition Function*:**

$\delta_{ext}((phase, \sigma, ApptRequest), e, (p, v))$

$=$ ("Scheduling", t_s, $ApptRequest$), if $phase ==$ "Idle" $\wedge$ $p ==$ "in_ApptRequest",

$newSchedule = Algorithm(ApptRequest)$;

$= (phase, \sigma - e, ApptRequest)$, otherwise.

***Internal Transition Function*:**

$=$ ("Idle", ∞, $ApptRequest$), if $phase ==$ "Scheduling" $\wedge$ $schedQueue.isEmpty() == true$.

***Confluence Function*:**

$\delta_{con}((s, ta(s), x) = \delta_{ext}(\delta(s), 0, x)$.

***Output Function*:**

$\lambda(phase, \sigma, ApptRequest)$

= ("out_ApptTimes, $ApptTimes$), if $phase$ ==="Scheduling", where $ApptTimes$ is the message sent to PGENR;

= ("out_Wait1Time, $Wait1Time$), if $phase$ ==="Scheduling", where $Wait1Time$ is the message sent to TRANSD.

***Time Advance Function*:**

$ta(phase, \sigma, ApptRequest) = \sigma$.

CHARGENURSE Atomic Model.

$$DEVS_{CHARGENURSE} = (X_M, Y_M, S, \delta_{ext}, \delta_{int}, \delta_{con}, \lambda, ta) \tag{A.2}$$

where,

$X_M = \{(p, v) | p \in IPorts, v \in X_p\}$ is the set of input ports and values, $IPorts = \{$"in_PatientAppt", "in_NurseTask"$\}$, and $X_{\text{in\_PatientAppt}} = V_1$, and $X_{\text{in\_NurseTask}} = V_2$ are arbitrary sets of values;

$Y_M = \{(p, v) | p \in OPorts, v \in Y_p\}$ is the set of output ports and values, $OPorts = \{$"out_PatientAppt1", "out_PatientAppt2", ..., "out_PatientAppt$n$"$\}$, and $Y_{\text{out\_PatientAppt1}}$,

$Y_{\text{out\_PatientAppt2}}$, ..., $Y_{\text{out\_PatientAppt}n}$ are arbitrary sets of values;

$S = \{$"Available", "ProcessingPatient", "ChairAvailable"$\} \times \mathcal{R}_{+,0} \times V_1 \times V_2$ is the set of sequential states.

***External Transition Function*:**

$\delta_{ext}((phase, \sigma, msg), e, (p, v))$

= ("ProcessingPatient", $processingTime, msg$), if $phase$ == "Available" $\wedge$ p == "in_NurseTask;

= ("ChairAvailable", $processingTime, msg$), if $phase$ == "Available" $\wedge$ p == "in_PatientAppt";

= $(phase, \sigma - e, msg)$, otherwise.

***Internal Transition Function*:**

$= (\text{“ChairAvailable”}, processingTime, msg)$, if $phase == \text{“ProcessingPatient”} \wedge NTQueue.isEmpty() == false$;

$= (\text{“ProcessingPatient”}, processingTime, msg)$, if $phase == \text{“ChairAvailable”} \wedge CNQueue.isEmpty() == false$;

$= (\text{“Available”}, \infty, msg)$, if $phase == \text{“ProcessingPatient”} \wedge CNQueue.isEmpty() == true$;

$= (\text{“Available”}, \infty, msg)$, if $phase == \text{“ChairAvailable”} \wedge NTQueue.isEmpty() == true$.

***Confluence Function*:**

$\delta_{con}((s, ta(s), x) = \delta_{ext}(\delta(s), 0, x)$.

***Output Function*:**

$\lambda(phase, \sigma, msg)$

$= (\text{“out\_PatientAppt}i, PatientAppt)$, if $phase == \text{“ProcessingPatient”} \wedge outputType == 1$, where $PatientAppt$ is the message sent to REGNURSEi.

REGNURSE Atomic Model.

$$DEVS_{REGNURSE} = (X_M, Y_M, S, \delta_{ext}, \delta_{int}, \delta_{con}, \lambda, ta) \tag{A.3}$$

where,

$X_M = \{(p, v) | p \in IPorts, v \in X_p\}$ is the set of input ports and values, $IPorts = \{$“in_PatientAppt”, “in_DrugOrder”$\}$, and $X_{\text{in\_PatientAppt}} = V_1$, and $X_{\text{in\_DrugOrder}} = V_2$ are arbitrary sets of values;

$Y_M = \{(p, v) | p \in OPorts, v \in Y_p\}$ is the set of output ports and values, $OPorts = \{$“out_DrugOrder”, “out_NurseTime”, “out_Wait3Time”, “out_PatientChair”, “out_NurseTask”$\}$, and $Y_{\text{out\_DrugOrder}}$, $Y_{\text{out\_NurseTime}}$, $Y_{\text{out\_Wait3Time}}$, $Y_{\text{out\_PatientChair}}$, and $Y_{\text{out\_NurseTask}}$ are arbitrary sets of values;

$S = \{$“Available”, “CheckingWaitList”, “GettingPatient”, “SeatingPatient”, “OrderingDrug”, “CheckingVitals”, “WaitingOnDrug”, “StartingInfusion”, “MonitoringPatients”, “StoppingInfusion”, “UpdateTRANSD”, and “Home”$\} \times \mathcal{R}_{+,0} \times V_1 \times V_2$ is the set of sequential states.

***External Transition Function*:**

$\delta_{ext}((phase, \sigma, msg), e, (p, v))$

= (“CheckingWaitList”, $checkTime, RN$), if $phase ==$ “MonitoringPatients”$\wedge$ $p ==$ “in_PatientApppt”;

= (“CheckingWaitList”, $checkTime, RN$), if $phase ==$ “Available”$\wedge$ $p ==$ “in_PatientAppt”;

= (“StartingInfusion”, $infStartTime, RN$), if $phase ==$ “WaitingOnDrug”$\wedge$ $p ==$ “in_DrugOrder”;

= $(phase, \sigma - e, RN)$, otherwise.

***Internal Transition Function*:**

= (“Available”, $openTime, RN$), if $phase ==$ “Home”, where $openTime$ is the remaining time the clinic is open for the day;

= (“GettingPatient”, $gettingTime, RN$), if $phase ==$ “CheckingWaitList”$\wedge$ $WaitList.isEmpty() == false \wedge inadTimeCap() == false$;

= (“SeatingPatient”, $seatingTime, RN$), if $phase ==$ “GettingPatient”;

= (“OrderingDrug”, $orderTime, RN$), if $phase ==$ “SeatingPatient”;

= (“CheckingVitals”, $vitalTime, RN$), if $phase ==$ “OrderingDrug”;

= (“WaitingOnDrug”, ∞, RN), if $phase ==$ “CheckingVitals”$\wedge$ $vitalsTimeElapsed() \wedge DrugReadyList.isEmpty() == true$;

= (“StartingInfusion”, $infStartTime, RN$), if $phase ==$ “CheckingVitals”$\wedge$ $vitalsTimeElapsed() \wedge DrugReadyList.isEmpty() == false$;

= (“CheckingWaitList”, $checkTime, RN$), if $phase ==$ “StartingInfusion”;

= (“MonitoringPatients”, $nextTime, RN$), if $phase ==$ “CheckingWaitList”$\wedge$ $numPatients > 0 \wedge$ $(WaitList.isEmpty() == true || (WaitList.isEmpty() == false \wedge inadTimeCap() == true))$;

= (“StoppingInfusion”, $infStopTime, RN$), if $phase ==$ “MonitoringPatients”;

= (“CheckingWaitList”, $checkTime, RN$), if $phase ==$ “StoppingInfusion”;

= (“UpdateTRANSD”, $updateTime, RN$), if $phase ==$ “CheckingWaitList”$\wedge$ $WaitList.-$

$isEmpty() == true \wedge\ numPatients == 0 \wedge\ stopInf == true$;

= ("Available", $openTime, RN$), if $phase ==$ "UpdateTRANSD" $\wedge\ openTime > 0$;

= ("Home", $homeTime, RN$), if $phase ==$ "UpdateTRANSD" $\wedge\ openTime <= 0$ where $homeTime$ is the time until the clinic opens on the next business day;

= ("Home", $homeTime, RN$), if $phase ==$ "Available".

***Confluence Function*:**

$\delta_{con}((s, ta(s), x) = \delta_{ext}(\delta(s), 0, x)$.

***Output Function*:**

$\lambda(phase, \sigma, RN)$

= ("out_NurseTask, $NurseTask$), if $phase ==$ "StoppingInfusion", where $NurseTask$ is the message sent to CHARGENURSE;

= ("out_PatientDepart, $PatientChair$), if $phase ==$ "StoppingInfusion", where $PatientChair$ is the message sent to TRANSD;

= ("out_PatientSeated, $PatientChair$), if $phase ==$ "GettingPatient", where $PatientChair$ is the message sent to WAITROOM;

= ("out_DrugOrder, $DrugOrder$), if $phase ==$ "OrderingDrug", where $DrugOrder$ is the message sent to PHARM;

= ("out_NurseTime, $NurseTime$), if $phase ==$ "UpdateTRANSD", where $NurseTime$ is the message sent to TRANSD;

= ("out_Wait3Time, $Wait3Time$), if $phase ==$ "StartingInfusion", where $Wait3Time$ is the message sent to TRANSD.

A.2 DEVS-CHEMO Scheduling Algorithms

This appendix section specifies the steps for three scheduling algorithms: ASAP, Collective, and Nurse. All three algorithms build upon the Individual algorithm stated in section 3.3.3. The left arrow $\leftarrow$ is used to denote assignment, & denotes the "and" operator, ! denotes the "not" operator, and == denotes the "equality" operator.

A.2.1 ASAP Algorithm

The ASAP algorithm only schedules chairs. The code for the Individual algorithm is modified by removing lines (10), (13)-(27), and (30)-(33). Then the following lines are modified as follows:

28. $slots[i] \leftarrow s; chairs[i] \leftarrow j;$
29. $chairFound \leftarrow true; j \leftarrow C;$
42. **return** $treatDays[], slots[], chairs[];$

A.2.2 Collective Algorithm

The Collective algorithm only schedules chairs, but the nurse assignment is checked among all nurses. The code for the Individual algorithm is modified by removing lines (13)-(15) and (23)-(26). The following two methods are introduced:

- $TotalStart(N_d, s, d)$: returns true if there is a nurse available among the N_d nurses on duty who can start a new patient during slot s on day d, else returns false;
- $TotalAcuity(N_d, s, d, acuity, numSlots)$: returns true if all nurses on duty N_d can handle the additional load of $acuity$ starting in slot s on day d for $numSlots$ slots, else returns false.

Then the following lines are modified as follows:

17. $startCheck \leftarrow TotalStart(N_d, s, d);$
20. $acuityCheck \leftarrow TotalAcuity(N_d, s, d, acuity[i], numSlots[i]);$
27. **if**$(fail == 0)$
28. $slots[i] \leftarrow s; chairs[i] \leftarrow j;$
29. $chairFound \leftarrow true; j \leftarrow C;$

42. **return** $treatDays[], slots[], chairs[];$

A.2.3 Nurse Algorithm

The Nurse algorithm only schedules nurses. The code for the Individual algorithm is modified by removing lines (07)-(09), (11)-(12), (14), (25)-(26), (30)-(33). Then the following lines are modified as follows:

10. **for**$(s \leftarrow 1; s \leq S - numSlots[i] + 1; s++)$
15. **for**$(nurse \leftarrow 1; nurse \leq N_d; nurse++)$
28. $slots[i] \leftarrow s; nurses[i] \leftarrow nurse;$
29. $s \leftarrow S, nurse \leftarrow N_d;$
34. **if**$(!nurseFound)$
36. **if**$(nurseFound)$
42. **return** $treatDays[], slots[], nurses[];$

A.3 DEVS-CHEMO Experiment Results

Table A.1: Performance Results for Nurse Experiments (1 of 3)

No. of Nurses	Performance Measure (units)	AVG	STDEV	90% CI
5	Total Throughput (appts.)	3092.9	68.8	(3081.6,3104.3)
	Chair Utilization (%)	58.30	1.66	(58.02,58.57)
	Nurse Utilization (%)	98.84	1.71	(98.56,99.12)
	Nurse Overtime^{+} (min.)	113.37	5.27	(112.50,114.23)
	Nurse Overtime^{+} Count	309.56	14.64	(307.15,311.97)
	Nurse Overtime (min.)	63.26	4.58	(62.51,64.01)
	Type I Delay (days)	1.31	0.04	(1.31,1.32)
	Type II Delay (min.)	29.65	2.14	(29.30,30.00)
	Type III Delay (min.)	31.73	0.39	(31.67,31.79)
	System Time (min.)	217.65	4.07	(216.98,218.33)
6	Total Throughput (appts.)	3085.3	84.5	(3071.4,3099.2)
	Chair Utilization (%)	58.36	1.61	(58.10,58.63)
	Nurse Utilization (%)	90.01	1.64	(89.74,90.28)
	Nurse Overtime^{+} (min.)	100.30	5.32	(99.42,101.17)
	Nurse Overtime^{+} Count	304.57	16.20	(301.91,307.23)
	Nurse Overtime (min.)	45.90	3.93	(45.26,46.55)
	Type I Delay (days)	1.31	0.04	(1.30,1.31)
	Type II Delay (min.)	18.64	0.97	(18.48,18.80)
	Type III Delay (min.)	32.01	0.38	(31.95,32.07)
	System Time (min.)	207.37	3.92	(206.73,208.02)

Nurse Overtime^{+} excludes zero entries

Table A.2: Performance Results for Nurse Experiments (2 of 3)

No. of Nurses	Performance Measure (units)	AVG	STDEV	90% CI
7	Total Throughput (appts.)	3090.2	87.9	(3075.7,3104.6)
	Chair Utilization (%)	58.42	1.74	(58.14,58.71)
	Nurse Utilization (%)	82.98	1.74	(82.69,83.26)
	Nurse Overtime^{+} (min.)	98.82	4.85	(98.03,99.62)
	Nurse Overtime^{+} Count	305.36	17.53	(302.48,308.24)
	Nurse Overtime (min.)	38.87	3.29	(38.32,39.41)
	Type I Delay (days)	1.31	0.04	(1.30,1.31)
	Type II Delay (min.)	15.41	0.66	(15.30,15.52)
	Type III Delay (min.)	32.24	0.37	(32.18,32.31)
	System Time (min.)	204.06	3.68	(203.46,204.67)
8	Total Throughput (appts.)	3082.6	78.1	(3069.8,3095.4)
	Chair Utilization (%)	58.40	1.62	(58.14,58.67)
	Nurse Utilization (%)	76.84	1.62	(76.58,77.11)
	Nurse Overtime^{+} (min.)	98.78	5.21	(97.93,99.64)
	Nurse Overtime^{+} Count	305.80	19.34	(302.62,308.98)
	Nurse Overtime (min.)	34.04	3.06	(33.54,34.54)
	Type I Delay (days)	1.31	0.04	(1.30,1.31)
	Type II Delay (min.)	13.81	0.50	(13.73,13.90)
	Type III Delay (min.)	32.60	0.35	(32.54,32.66)
	System Time (min.)	202.84	3.36	(202.29,203.39)

Nurse Overtime^{+} excludes zero entries

Table A.3: Performance Results for Nurse Experiments (3 of 3)

No. of Nurses	Performance Measure (units)	AVG	STDEV	90% CI
9	Total Throughput (appts.)	3098.7	73.6	(3086.6,3110.8)
	Chair Utilization (%)	58.84	1.49	(58.60,59.09)
	Nurse Utilization (%)	71.48	1.45	(71.24,71.72)
	Nurse Overtime^{+} (min.)	100.00	5.58	(99.08,100.92)
	Nurse Overtime^{+} Count	310.36	16.22	(307.69,313.03)
	Nurse Overtime (min.)	31.09	2.67	(30.65,31.53)
	Type I Delay (days)	1.31	0.04	(1.31,1.32)
	Type II Delay (min.)	13.05	0.51	(12.96,13.13)
	Type III Delay (min.)	32.97	0.42	(32.90,33.04)
	System Time (min.)	202.50	3.20	(201.98,203.03)
10	Total Throughput (appts.)	3099.77	78.41	(3086.87,3112.67)
	Chair Utilization (%)	59.01	1.73	(58.72,59.29)
	Nurse Utilization (%)	66.68	1.64	(66.41,66.95)
	Nurse Overtime^{+} (min.)	98.73	5.57	(97.81,99.64)
	Nurse Overtime^{+} Count	311.55	18.51	(308.50,314.60)
	Nurse Overtime (min.)	27.72	2.42	(27.33,28.12)
	Type I Delay (days)	1.32	0.04	(1.31,1.32)
	Type II Delay (min.)	12.49	0.48	(12.41,12.57)
	Type III Delay (min.)	33.23	0.38	(33.17,33.29)
	System Time (min.)	202.41	3.46	(201.84,202.98)

Nurse Overtime^{+} excludes zero entries

APPENDIX B

SIP-CHEMO MODEL

B.1 SIP-CHEMO Experiment Results

Table B.1: Performance Results for Scheduling Algorithms(1 of 3)

Algorithm	Performance Measure (units)	AVG	STDEV	90% CI
ASAP	Total Throughput (appts.)	467.5	16.4	(464.8,470.2)
	Daily Throughput (appts.)	23.4	0.8	(23.2,23.5)
	Chair Utilization (%)	50.24	2.16	(49.88,50.59)
	Nurse Utilization (%)	83.68	3.77	(83.06,84.30)
	Nurse Overtime^{+} (min.)	116.96	16.36	(114.27,119.65)
	Nurse Overtime^{+} Count	45.32	4.41	(44.59,46.05)
	Nurse Overtime (min.)	46.91	8.45	(45.52,48.30)
	Type I Delay (days)	1.36	0.08	(1.34,1.37)
	Type II Delay (min.)	28.46	7.81	(27.17,29.74)
	Type III Delay (min.)	332.26	0.78	(32.14,32.39)
	System Time (min.)	221.39	10.16	(219.71,223.06)

Nurse Overtime^{+} excludes zero entries

Table B.2: Performance Results for Scheduling Algorithms (2 of 3)

Algorithm	Performance Measure (units)	AVG	STDEV	90% CI
Individual	Total Throughput (appts.)	458.4	14.5	(456.1,460.8)
	Daily Throughput (appts.)	22.9	0.7	(22.8,23.0)
	Chair Utilization (%)	49.18	1.95	(48.86,49.50)
	Nurse Utilization (%)	85.76	3.42	(85.20,86.32)
	Nurse Overtime^{+} (min.)	108.71	11.88	(106.75,110.66)
	Nurse Overtime^{+} Count	47.29	5.06	(46.46,48.12)
	Nurse Overtime (min.)	45.19	7.42	(43.97,46.41)
	Type I Delay (days)	1.63	0.16	(1.61,1.66)
	Type II Delay (min.)	18.69	4.73	(17.91,19.47)
	Type III Delay (min.)	32.20	0.75	(32.08,32.33)
	System Time (min.)	211.39	8.21	(210.04,212.74)
RN	Total Throughput (appts.)	471.8	20.5	(468.4,475.1)
	Daily Throughput (appts.)	23.6	1.0	(23.4,23.8)
	Chair Utilization (%)	50.28	2.16	(49.92,50.64)
	Nurse Utilization (%)	81.37	3.16	(80.85,81.89)
	Nurse Overtime^{+} (min.)	94.96	12.21	(92.95,96.96)
	Nurse Overtime^{+} Count	36.75	4.59	(35.99,37.51)
	Nurse Overtime (min.)	30.64	5.83	(29.68,31.60)
	Type I Delay (days)	1.55	0.10	(1.53,1.56)
	Type II Delay (min.)	16.57	3.87	(15.93,17.21)
	Type III Delay (min.)	32.26	0.86	(32.12,32.40)
	System Time (min.)	208.02	7.09	(206.85,209.19)

Nurse Overtime^{+} excludes zero entries

Table B.3: Performance Results for Scheduling Algorithms (3 of 3)

Algorithm	Performance Measure (units)	AVG	STDEV	90% CI
EE	Total Throughput (appts.)	473.4	18.8	(470.3,476.4)
	Daily Throughput (appts.)	23.7	0.9	(23.5,23.8)
	Chair Utilization (%)	50.48	2.27	(50.10,50.85)
	Nurse Utilization (%)	82.67	3.63	(82.07,83.27)
	Nurse Overtime$^+$ (min.)	98.33	13.55	(96.10,100.56)
	Nurse Overtime$^+$ Count	39.28	5.50	(38.38,40.18)
	Nurse Overtime (min.)	34.17	7.47	(32.94,35.40)
	Type I Delay (days)	1.54	0.11	(1.52,1.55)
	Type II Delay (min.)	16.44	4.28	(15.73,17.14)
	Type III Delay (min.)	32.23	0.85	(32.09,32.37)
	System Time (min.)	207.97	7.70	(206.71,209.24)
ASD	Total Throughput (appts.)	472.1	18.1	(469.2,475.1)
	Daily Throughput (appts.)	23.6	0.9	(23.5,23.8)
	Chair Utilization (%)	50.49	1.97	(50.17,50.82)
	Nurse Utilization (%)	82.46	3.00	(81.97,82.96)
	Nurse Overtime$^+$ (min.)	99.64	14.69	(97.22,102.05)
	Nurse Overtime$^+$ Count	39.83	5.59	(38.91,40.75)
	Nurse Overtime (min.)	34.97	7.04	(33.81,36.12)
	Type I Delay (days)	1.54	0.12	(1.52,1.56)
	Type II Delay (min.)	16.89	5.31	(16.02,17.77)
	Type III Delay (min.)	32.28	0.91	(32.13,32.43)
	System Time (min.)	209.00	8.05	(207.68,210.32)

Nurse Overtime$^+$ excludes zero entries

APPENDIX C

DEVS-SIP-CHEMO MODEL

C.1 DEVS-SIP-CHEMO Experiment Results

Table C.1: Performance Results for EE_5

Experiments	Performance Measure (units)	AVG	STDEV	90% CI
EE_5	Total Throughput (appts.)	467.70	21.02	(456.76,478.64)
	Daily Throughput (appts.)	23.38	1.05	(22.84,23.93)
	Chair Utilization (%)	48.86	1.94	(47.85,49.87)
	Nurse Utilization (%)	71.36	2.56	(70.03,72.69)
	Nurse Overtime^{+} (min.)	19.15	7.19	(15.41,22.89)
	Nurse Overtime^{+} Count	8.90	2.30	(7.70,10.10)
	Nurse Overtime (min.)	1.36	0.54	(1.08,1.64)
	Type I Delay (days)	1.66	0.09	(1.61,1.71)
	Type II Delay (min.)	10.87	1.03	(10.33,11.40)
	Type III Delay (min.)	31.85	0.79	(31.44,32.26)
	System Time (min.)	198.51	5.62	(195.59,201.44)
	Simulation Run Time (sec.)	540.68	47.34	(516.05,565.30)

Nurse Overtime^{+} excludes zero entries

Table C.2: Performance Results for ASD_6

Experiments	Performance Measure (units)	AVG	STDEV	90% CI
ASD_6	Total Throughput (appts.)	466.8	17.2	(457.9,475.7)
	Daily Throughput (appts.)	23.3	0.9	(22.9,23.8)
	Chair Utilization (%)	48.96	1.70	(48.07,49.85)
	Nurse Utilization (%)	72.06	2.25	(70.89,73.22)
	Nurse Overtime^{+} (min.)	27.36	8.98	(22.69,32.03)
	Nurse Overtime^{+} Count	8.50	3.35	(6.76,10.24)
	Nurse Overtime (min.)	1.76	0.66	(1.42,2.11)
	Type I Delay (days)	1.76	0.17	(1.67,1.84)
	Type II Delay (min.)	11.65	2.31	(10.45,12.85)
	Type III Delay (min.)	32.39	0.56	(32.10,32.68)
	System Time (min.)	199.96	3.89	(197.93,201.98)
	Simulation Run Time (sec.)	592.76	108.56	(536.29,649.24)

Nurse Overtime^{+} excludes zero entries