On the Performance of Metaheuristics for the Blood Platelet Production and Inventory Problem

UNIVERSITY OF
KWAZULU-NATAL

FAGBEMI SEUN OLAYEMI

(215040661)

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COLLEGE OF AGRICULTURE, ENGINEERING AND SCIENCE

DECLARATION

The research described in this thesis was performed at the University of KwaZulu-Natal under the supervision of Professor A.O. Adewumi and co-supervision of Dr. M. O. Olusanya. I hereby declare that all materials incorporated in this thesis are my own original work except where acknowledgement is made by name or in the form of a reference. The work contained herein has not been submitted in part or whole for a degree at any other university.

Signed:

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Fagbemi Seun Olayemi

Date: February, 2016

As the candidate's supervisor, I have approved/disapproved the dissertation for submission

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Professor A.O. Adewumi

Date: February, 2016

As the candidate's co-supervisor, I have approved/disapproved the dissertation for submission

____

Dr. M.O. Olusanya

Date: February, 2016

DECLARATION II - PLAGIARISM

I, Fagbemi Seun Olayemi, declare that

1. The research reported in this thesis, except where otherwise indicated, is my original research.
2. This thesis has not been submitted for any degree or examination at any other university.
3. This thesis does not contain other persons' data, pictures, graphs or other information, unless specifically acknowledged as being sourced from other persons.
4. This thesis does not contain other persons' writing, unless specifically acknowledged as being sourced from other researchers. Where other written sources have been quoted, then:
    a. Their words have been re-written but, the general information attributed to them has been referenced.
    b. Where their exact words have been used, their writing has been placed in italics and in quotation marks, and referenced.
5. This thesis does not contain text, graphics or tables which are copied and pasted from the internet, unless specifically acknowledged, and the source being detailed in the thesis and in References section.

Signed:

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Date: February, 2016

DEDICATION

This research work is dedicated to the Almighty God, who saw me through the thick and thin of this research, and to my precious daughter, Grace.

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My appreciation goes first to God, my Maker and the giver of all good things, for the successful completion of my Masters programme. My profound and sincere gratitude goes to my husband, Mr. Peter Olukanmi; I could not have done this without your support and love. Thank you for being there.

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LIST OF ABBREVIATIONS

ACO	Ant Colony Optimization
BA	Bat Algorithm
BPPIP	Blood Platelet Production and Inventory Problem
COP	Combinatorial Optimization Problem
DE	Differential Evolution
DP	Dynamic Programming
FIFO	First in First out
GRASP	Greedy Random Adaptive Search Procedure
OFAT	One Factor at a Time
PLT	Platelet
PSO	Particle Swarm Optimization
RBC	Red Blood Cell
RCL	Restricted Candidate List
SANBS	South African National Blood Service

ABSTRACT

The need for natural human blood and its derived components remains prevalent despite substantial developments in the area of artificial blood products. Being a critical component of modern therapies, the inventory management of blood platelets is of high importance in healthcare practice. Every blood component has a known shelf life after which the product can no longer be used. According to the South African National Blood Service (SANBS), platelets have the shortest shelf life of 5 -7 days and are the most expensive. This shortness of shelf life leads to huge challenges in production and inventory management. On one hand, production and operational costs are high, while on the other, shortage can result into higher costs of loss of lives. Large outdate rates are also thought to be a threat to the stability of the platelet supply chain because donor participation rates are typically low. The blood platelet production and inventory problem is therefore that of minimizing operational costs while ensuring low shortage and outdate rates.

Exact methods have been proposed to handle blood platelet production and inventory management. These methods can only handle small or moderate-sized problems due to the explosive growth in computational expense with the increase of problem size. Some of these methods have also been reported to be very difficult to implement in practice. Due to these limitations of exact solution methods, most studies in the area have focused on the use of either approximate models or heuristic techniques to produce usable solutions.

Having identified the advantages that metaheuristics have over many classical approaches, and how these advantages make them quite suitable for the problem, this research explores the utility of metaheuristics in solving this real world problem. Two different approaches are considered for

solving the blood platelet production and inventory problem: optimization of order-up-to policy and optimization of daily production amounts. The Greedy Random Adaptive Search Procedure (GRASP) is explored for the latter, while differential evolution and Bat Algorithm are explored for the former. For the optimization of the order-up-to policy, the operations of the blood platelet producer is modeled in two different ways (Model 1 and 2). The algorithms are chosen for their attractive properties like efficiency and simplicity. They are successfully applied and shown to be easily amenable to the problems studied. Parameter optimization is explored for Differential Evolution (DE) and Bat Algorithm (BA) to arrive at recommendations for best performance in solving the problem. A comparative study of the two algorithms is also included. Both DE and BA are efficient in solving the models, requiring less than 150 function calls in all cases, which on the typical personal computer of today, would run in only fractions of a second. In terms of yearly average costs, DE produces solutions that outperform Bat Algorithm on model 1 while the reverse is the case on the two scenarios of model 2; BA proved slightly more efficient than DE.

Finally, GRASP is shown to be adaptable for the blood platelet daily production amount problem. It is observed that there is a linear relationship between the number of iterations and the run time. The specific relationship or model can therefore be estimated and used to determine the appropriate design choice or predict expected run time for a given choice. For the highest number of iterations in the case study (500), the average run time was between 1.6 and 1.8 seconds for $\beta = 5$ and $\beta = 10$ and even lower for $\beta = 15$. The algorithm is therefore suitable for applications with low time budget. The results show that the computational cost per iteration is quite low. More so, it is capable of arriving at good solutions within a few iterations.

CHAPTER ONE

INTRODUCTION AND BACKGROUND

1.0 Introduction

This chapter presents an overview of this thesis. Some background is presented on the research topic, after which the problem statement is described. Then the research objectives are highlighted, followed by clarification of scope of the study as well as overview of the methodology adopted. Finally, a few important terms are defined as used in this thesis, before concluding the chapter with description of organization of the rest of this thesis.

1.1 Background and Motivation

Blood platelets (PLTs) are a vital life-saving perishable product. Despite substantial developments in artificial blood products, the need for natural human blood as well as its derived components remains prevalent [1]. Patients needing chemotherapy, organ transplants, bone marrow transplants and radiation treatments often require PLT transfusions. There is therefore the need for a readily available inventory of PLTs at hospital centers. PLTs can be derived from a unit of whole blood together with other two main components: Red Blood Cells (RBCs) and Plasma, or obtained directly from a donor through the process of apheresis which separates and retains the PLTs while returning the other blood components to the donor's blood system [2]. Generally, each blood component has a known shelf life after which the product is counted as unusable. According to materials from the South African National Blood Service (SANBS) [3], among the various blood components, PLTs have the shortest shelf life which ranges from 5 to 7 days, and they are the most expensive.

Generally, blood product management is a problem that has attracted much societal interest because of a number of complicating factors. Supply is quite irregular due to dwindling availability of donors. Blood donors have to meet strict requirements such as being free from certain diseases, having normal blood pressure and pulse rates, falling into particular age groups and being of a minimum weight. While on one hand, a chunk of the populace is not eligible, on the other, a large percentage of the eligible adults actually do not donate blood. SANBS reports that less than 1% of the South African population are regular donors [4]. Eligible donors also have to allow for a period of 56 days between two whole blood donations [5]**.** The supply of blood also depends on other factors ranging from the capacities for collecting and processing blood at the blood banks to the availability of transport infrastructures [6]. On the demand side of the process, demand for blood products is uncertain even with the information of treatment plans and planned surgeries. Emergency cases account for part of this uncertainty. In addition, the variety constituted by the eight different blood types, introduces complexity in predicting demand. The very short shelf life of PLTs as compared to RBCs and plasma is a major factor that poses problems for managing their inventory. The operational costs involved in producing and managing inventories of blood PLTs are also high. Production volumes have to be set carefully to prevent high outdate as there are great cost and ethical implications. Shortages that put lives at risk should also be minimized. The blood PLT producer therefore usually has difficulty in identifying optimal production policy that balances wastage, shortages and costs. This optimization problem is the concern of this thesis.

Exact methods have been proposed in the literature to handle the blood platelet production and inventory management problem (BPPIP). One of such methods is Dynamic Programming (DP) [7-9]. These methods are limited by the fact that they can only solve small or moderate size problems due to the explosive growth of computational cost as the problem size increases. Some of these methods have also been reported to be very difficult to implement in practice [10].

Because of these limitations of exact methods, most studies have focused on the use of either approximate models or heuristic techniques to produce usable solutions [10]. Belien and Force [1] in their review pointed out the need for further research to develop fast and robust heuristics to solve the PLT inventory problem as they conclude that “there is no proof yet whether a solution to the PLT ordering problem exists involving simple order-up-to rules resulting in both low levels of outdate and wastage”.

This research work therefore explores the use of metaheuristics in solving the BPPIP. Two solution approaches are presented and the performance of three metaheuristic algorithms are evaluated, namely, Differential Evolution (DE), Bat Algorithm (BA) and greedy random adaptive search procedure (GRASP).

1.2 Problem Statement

The inventory management of blood PLTs is of high importance in healthcare practice. PLTs are a critical component of modern therapies and their production and inventory management is challenging, due to the very short shelf life associated with this valuable blood product [11]. Costs are incurred by the blood banks in processing, storing and transporting blood products. Shortage can result in higher costs like loss of lives, hence it should be kept at minimum. Outdates are also undesirable because they lead to tangible and intangible penalty costs. There is the tangible costs to the blood producer of a waste of production costs and the intangible costs to donors who may be less inclined to donate if they feel their precious gift will be scrapped. Large outdate rates are thought to be a threat to the stability of the PLT supply chain because donor participation rates are typically small [4, 12]. PLT production volumes must therefore be set carefully at blood banks to prevent large outdate and shortage rates as well as minimize costs. Exact solution methods to the BPPIP have been found difficult to implement because of the problem of curse of dimensionality.

This research explores heuristic optimization techniques that are capable of producing good solutions to the BPPIP. Two approaches to solving the problem are presented and the performance of metaheuristic algorithms, with respect to efficiency and accuracy, are investigated and reported.

1.3 Research Questions

The research questions examined in this research are outlined as follows:

- How can the BPPIP be realistically modeled to capture practical constraints?
- Which proven metaheuristic technique(s) are relatively easily amenable to the BPPIP, and how can each be actually adapted to solve the problem using the different models?
- How does each of these algorithms perform in terms of efficiency as well as accuracy, the quality of solutions being measured by overall cost, shortage rate and outdate rate?

1.4 Research Objectives

The objectives of this research work are:

- To model mathematically, the operations of the blood PLT producer for optimization of order-up-to policy in terms of cost, while satisfying practical constraints relating to shortage and outdate.
- To adapt and implement two metaheuristic algorithms (DE and BA), specifically chosen for their simplicity and easy amenability, for solving the order-up-to policy models; to

empirically determine optimal parameter selection for the algorithms and to compare both on the basis of the performance criteria mentioned in section 1.2.

- To explore another metaheuristic algorithm, GRASP, chosen for the same reason as in the second objective, for optimizing daily PLT production amounts over a specified planning horizon.

1.5 Research Methodology

Performances of the algorithms are studied empirically. The datasets used in the study are simulated based on parameters and distribution information from [9, 11], on demand, initial inventory, PLT shelf-life and cost.

Data analysis is done using descriptive statistics and relevant visualizations. Statistical hypothesis testing techniques are also employed for generalizing comparison between performances of algorithms. The criteria for comparison are accuracy and efficiency.

All implementations are done in MATLAB 2015b, on an Intel(R) Core(TM) i7-3632QM 2.20GHz CPU, operating on a 64bit system.

1.6 Scope and Limitation

This research work focuses on the BPPIP at the producer level using metaheuristics. This is primarily because the blood center is the source of PLTs production. As long as the blood producer can keep making optimal production volume decision every day, outdates and shortages will be reduced in the entire PLT supply chain. In addition, reduction of costs made possible by optimal production volume decisions will also reduce the price of blood PLTs and make it more affordable to the patients who are in need of it.

Selected algorithms are chosen on the basis of simplicity, efficiency and being easily amenable to the problems studied. These properties are typically of high priority in software tools used in such practical settings. The study is limited to two solution approaches to the BPPIP:

- the optimization of order-up-to policy
- optimization of daily production amounts over a specified planning horizon

1.7 Significance of the Study

This study holds some significance for research and practice relating to the BPPIP, in a number of ways, highlighted as follows:

- First, on the theoretical front, the model of [11] developed for supply chain inventory optimization for short-shelf-life goods, is improved in this work to capture cost for the blood producer while satisfying practical constraints of limits on shortage and outdate.
- Adaptations of metaheuristics are presented, for solving the blood platelet production and inventory problem. Research into this important real-world problem among computational scientists is relatively young. This is particularly true among metaheuristics researchers. While many metaheuristics have generally proved efficient and effective for a wide range of optimization problems, a few are identified that are easily amenable to the solution approaches considered in this work.
- The successful adaptations in this work provide a good foundation for further research in this area which might portend promising arena for incorporation into decision support systems for the BPPIP.

1.8 Definition of Terms

A few terms are defined here, as used throughout this dissertation:

- Inventory: This refers to a listing or store of raw materials, in-process and finished goods considered to be the portion of an organization's assets that are ready or will be ready for sale. Goods in this case are blood PLT units.
- Order-up-to policy: This is a rule that governs order for new blood PLT units in order to bring the inventory level to a certain base stock.
- Metaheuristics: a procedure, algorithm or technique that solves an optimization problem by conducting a non-exhaustive search through the solution space. The final solution may not be the global optimum but an effective technique will generally produce good quality solutions. Metaheuristics are popular because of their capacity to handle practical problems which typically have solution spaces that are too large to be handled by exact techniques or exhaustive enumeration.
- Solution: any hypothetical vector of possible values of decision variables is referred to as a solution. Feasible solutions are those that result in expected shortage and outdate rates less than or equal to specified percentages.

1.9 Overview of Chapters

The rest of this dissertation is structured as follows:

Chapter two presents a review of related literature.

Chapter three presents a study of metaheuristics on the order-up-to policy solution approach. In this chapter, the models and methodology are described in detail. Results from various related empirical studies are also presented and discussed. DE and BA are adapted for the problem and compared on the grounds of accuracy and efficiency.

Chapter four presents the adaptation of GRASP for the optimization of daily PLT production amounts.

Finally, Chapter five presents the summary and conclusion of this research work, including recommendations for future work.

CHAPTER TWO

LITERATURE REVIEW

2.0 Introduction

This chapter provides an overview of the inventory management of perishables with an emphasis on blood products. It then gives a review of works done in the area of blood PLT inventory management. Several themes are identified in literature: scope of operation, major model characteristics and model solution approaches. An account into the use of metaheuristics to solve the BPPIP is also presented.

2.1 Perishables Inventory Management

Inventory refers to stock of materials or goods that is held available for use. Inventory is held to ensure operations continue at an organization in the event of a time lag between the order and arrival of a given product. For example, time elapses between when a blood bank recruits donors and collect, test and prepare blood products. Inventory is also necessary to cater for uncertainties in production, demand and supply. Such uncertainties result from the fact that neither the availability of donors nor the demand for blood products is known ahead of time. Inventory could be a means of achieving economies of scale in the sense that the fixed costs of a blood bank can be spread over a number of blood units in order to reduce the overall cost of operations [10].

Perishable goods are items that become unusable through natural processes or legal statutes after a period of time [13]. The lifetime of perishable items can be fixed, for example in blood products, or stochastic, as is the case with fruits and vegetables. Perishability adds complexity and cost to any inventory problem [10].

Research into perishable product inventory management has been active for a few decades. One of the earliest research efforts on the management of inventory of perishable products, including blood products, is the work of Van Zyl [14] published in the 1960s. Nahmias [13] took it further in 1982, giving a survey of works that studied periodic review policies. He also considered the applications of the models to blood bank management. In 1984, Prastacos [15] reviewed contributions from the field of Operations Research to the theory and practice of blood inventory management. Also, there is a survey of continuous inventory perishable models up to 1991 by Raafat [16]. Goyal and Giri [17] review and classify literature on perishable inventory between the early 1990s and 2000, according to shelf life and the nature of demand, considered in the studies. According to their classifications, shelf lives are either fixed or random. Similarly, demand is either deterministic or stochastic. They also incorporate real-world conditions like delay in payment, price discount, and so on in their classification of literature. In another review, Karaesmen et al. [22] gave an overview of literature on management of perishable products with respect to supply chain, having fixed or random shelf lives. Particular attention is paid to food supply chains. Bakker et al. [18] reviewed inventory models of perishable items that have been published since the aforementioned review of Goyal and Giri in 2001. The authors suggested that more focus be placed on stochastic modelling to better represent inventory control practice.

2.2 Blood Product Inventory Management

The earliest review found to focus specifically on the inventory management of blood is that of Prastacos [15] in 1984. Pierskalla [19] discusses both supply chain and blood inventory management while Belien and Force [1] give the latest review of advancements made in inventory and supply chain management, of blood products. The authors observed two peaks in the distribution of papers published on blood products management. The first is between 1976 and

1985 and the more recent one is between 2001 and 2010. In terms of focus, they note that most of the papers are works on red blood cells or whole blood with a few studies found on the inventory management of PLTs.

2.2.1 Red Blood Cell Inventory Management

Authors often use the term “RBCs” and “blood” interchangeably. This is probably because RBCs are mostly in demand and they are transfused into surgical and intensive care patients to improve the delivery of oxygen to the tissues. They are also used in the treatment of premature infants and those suffering from anemia [1]. Therefore, a ready inventory of this blood product needs to be maintained at hospitals. Approaches to the inventory management of RBCs are discussed in this section.

Pierskalla and Roach [20] used a DP formulation to show that first in first out (FIFO) policies lead to optimal solutions in problems involving perishable inventory. Using a simulation methodology, Jennings [21] focuses on trade-off between shortages and outdates for a hospital region using exchange curves derived under different operating policies. Brodheim et al. [22] suggest an equation for setting target inventory level that depends on average daily demand and pre-specified acceptable shortage rates. Adopting a similar approach, Cohen and Pierskalla [23] propose a simple decision rule for setting optimal target inventory levels for a decentralized regional blood banking system or hospital blood bank, that makes it unnecessary for blood bank administrators to explicitly set shortage rates. Using simulation, they identify the minimum cost inventory policy in which only shortage and outdate costs are considered, and from the analysis of the results, a target inventory level that depends on daily demand, average cross match release and transfusion to cross match ratio period, is identified. Friedman at al. [24] describes blood management policies from a clinician’s view, suggesting an empirical approach to inventory policy in which safety stocks are gradually reduced. The authors also use simulation to set inventory levels under the assumption of an extended 35-day shelf life. Stanger et al. [25] reviewed the inventory practice in seven UK hospitals that had recorded low wastage in a year in order to identify the key drivers for good blood inventory performance. From their findings, skilled and regularly trained transfusion staff, electronic cross matching, simple management procedures and transparency of the inventory are key drivers for realization of low wastage and good inventory management practice. Gunpinar and Centeno [26] present stochastic and deterministic models to minimize costs, shortage and outdates of RBCs and PLTs at a hospital within a planning horizon.

2.2.2 Platelet Inventory Management

The limited studies on the inventory management of PLTs can be classified at three levels: the hospital blood bank level, the producer or regional blood bank level, and the entire supply chain level. Most of the works done in PLT inventory management have also been qualitative in nature. They are mostly case studies [11].

2.2.2.1 Hospital Blood Bank Level

Focusing on the hospital level of PLT management, Sirelson and Brodheim [27] test a class of PLT ordering policies using simulation. They present a predictive model that relates the base stock level and mean demand to the rates of outdate and shortage. Zhou et al. [28] investigated the inventory management of PLTs with a three-day shelf life. For a single hospital, they came up with an optimal dual-mode replenishment policy comprising one regular order every two days and an expedited order in between the two days, if necessary. Blake et al. [12] developed a model for hospitals that attempts to find a PLT ordering policy that jointly satisfies pre-specified bounds on outdates and shortages while minimizing ordering costs. Civelek at al. [29] show that a protection level policy can improve the blood PLT inventory management performance under various conditions.

2.2.2.2 Producer/Regional Blood Bank Level

At the regional blood bank level, Haijema et al. [6, 30] explore near-optimal inventory policies that belong in the category of simple order-up-to rules. The quantitative method proposed by these researchers is described by van Dijk et al. [31] for readers without much background in operations research. Blake [10] follows with an editorial write-up, describing the strengths and limitations of the solution method employed in the van Dijk paper. Abdulwahab and Wahab [32] developed a discrete-event, multi-period model for a single blood bank serving a single hospital. They also studied O-percentage within the inventory. de Kort et al. [33] did a practical implementation study to minimize outdate and extend time till outdating. A software tool designed specifically for this purpose is presented and named Thrombocyte Inventory Management Optimizer. Ghandforoush and Sen [34] in their work developed a decision support system to aid the realization of an efficient production plan as well as mobile assignment schedule to hospitals for a regional blood center.

2.2.2.3 Entire Supply Chain Level

Blake et al. [9] solved an instance of the PLT inventory management problem involving two-level supply chain for a single producer and a single hospital. A DP model is formulated and implemented for both supplier and consumer to optimize ordering policies. These policies are then simulated to select those that practically reduce outdate and shortage rates within the entire supply chain. Fontaine et al. [35] worked on improving the PLT supply chain by means of collaboration between the blood centre and hospital. The interaction between processes such as inventory management, collection, and rotation were studied, and recommendations made to improve the performance of supply chain. A post implementation analysis was also done to reflect the improvement in outdates and costs reduction. Mustafee et al. [36] studied the supply chain of the UK national blood service and demonstrated the usefulness of simulation in the timely execution of such supply chains.

Duan and Liao [11] proposed a framework for supply chain management of highly perishable items based on simulation-optimization with focus on PLTs. They also developed a technique for arriving at a new replenishment policy based on a old inventory ratio. This was tested using a single-supplier-multi-consumer supply chain and their policy performed better than two other policies from the literature, consistently yielding good solutions for all cases considered.

Figure 2.1 shows the different scopes of operation for the blood PLT inventory problem while figure 2.2 shows the distribution of works according to the scope of operation.

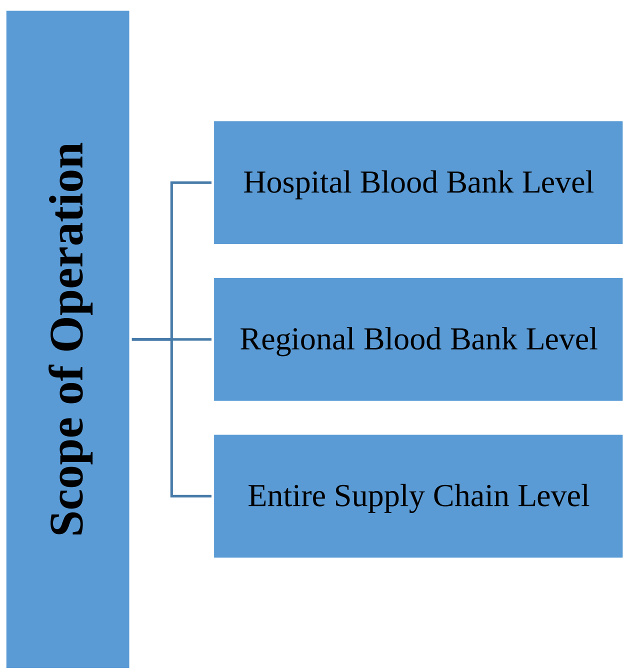

Figure 2.1: Scope of Operation for the Blood PLT Inventory Problem

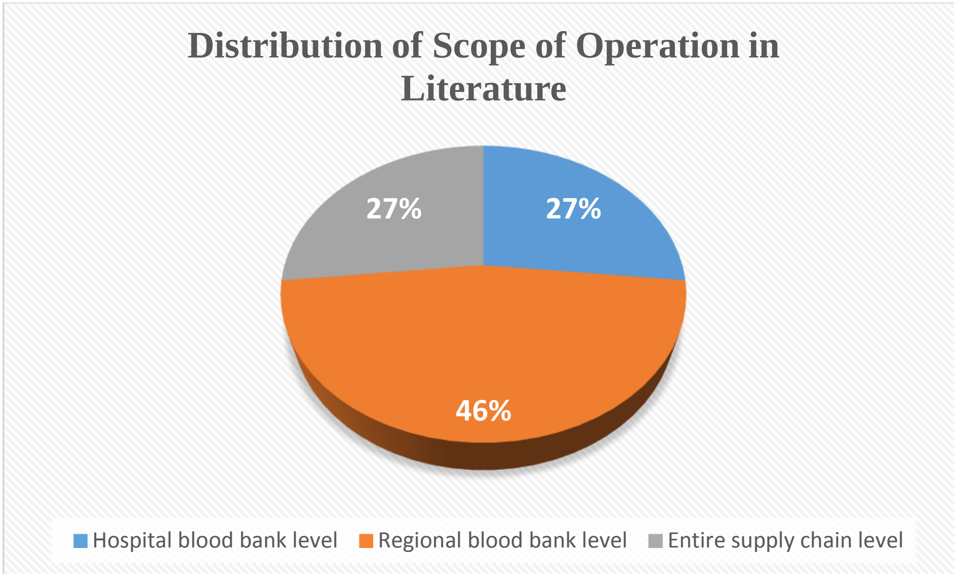

Figure 2.2: Distribution of Scope of Operation in Literature

2.3 Blood Platelet Inventory Problem: Model Characteristics

The BPPIP is a real life problem involving various complex dynamics. As such, models try to incorporate different characteristics to capture the real life processes as much as possible. Also, the assumptions made and factors considered in any model considerably affects the solutions generated [32]. The table 2.1 is a summary of major characteristics and assumptions considered in various models.

Table 2.1: Major characteristics and assumptions considered in various models.

Objective Function	**Major Model Characteristics**	**Major Assumptions**	**Reference**
Minimize platelet shortage and outdate while maximizing the total rewards and keeping minimum inventory level.[32]	• Stochastic demand and supply. • Deterministic lead time. • Six days shelf life. • Reward function used in place of costs.	• Maximum inventory capacity for each blood type. • Production occurs six days a week. • Shortage is served by expediting order from outside source. • Distinction between blood types with ABO substitution system (RH not a must).	Abdulwahab and Wahab [32]
Minimize total costs, shortage and outdating levels within a planning horizon.	• Stochastic demand and demand for two types of patients are differentiated.	Capacity of blood center is limited.	Gunpinar and Centeno [26]

	• Five days shelf life including two days of testing. • Zero lead time for blood supply. • Cross match--transfusion and cross match release period are considered. • Purchase, holding, shortage and wastage costs are considered.		
Select an order size that minimizes the cost of operations over a planning horizon.	• Deterministic supply. • Stochastic demand. • Five days shelf life. • One day lead time. • Constraints on inventory capacity. • Order, holding, shortage and	• Donation occurs five days a week. • Production decision is made before demand for the day is experienced. • Shortage is served by expediting	Blake, et al. [9]

	disposal costs are considered.	order from outside source.	
Minimize average costs over a planning horizon.	• Two types of demand (“young” and "any age") are distinguished. • Alternative supply rules for the two types of demand. • Six days shelf life. • One day production lead time. • Production, outdating, inventory, shortage and mismatch costs are considered.	• Production only takes place during weekdays. • No restrictions on production nor storage capacity. • Shortage is served by expediting order from outside source. • No distinction of blood types.	Haijema, et al. [6] [30]
Minimize the expected total costs over an infinite time horizon.	• Age-differentiated stochastic demand (young, mature, old). • Three days shelf life.	• Shortage is served by expediting order from outside source. • No distinction of blood types.	Civelek, et al. [29]

	• Zero lead time. • Replenishment, holding, outdating, shortage and substitution costs are considered.		
Minimize the system outdate rate under a pre-specified fill rate constraint.	• Stochastic demand following Poisson distribution. • Shelf life of 5 days. • Lead time of one day. • Performance measures are shortage and outdate rates. • Costs are not considered.	• Shortage is served by expediting order from outside source. • No restriction with respect to production and storage capacity. • Production only takes place during weekdays.	Duan and Liao [11]
Find a platelet ordering policy that jointly meets defined bounds on outdates and shortages while	• Stochastic demand assumed to be Poisson distributed.	• Hospital specifies target service level and outdate rate.	Blake, et al. [12]

minimizing the overall number of orders placed.	• Six days shelf lifeObjective is to find a PLT ordering policy that jointly meets defined bounds on outdates and shortages while minimizing the overall number of orders placed.	• ABO and Rh status of donor and recipient are ignored. • Demand for platelets is assumed to occur in doses rather than individual units. • All stock arriving on a given day of the week is of an identical age.	

2.4 Existing Solution Methods for the BPPIP

In this section, a review of some common model solution methods in literature for the BPPIP is presented. The advantages and limitations of each method are noted where applicable.

2.4.1 Dynamic Programming

The perishable product inventory management problem has been defined in a DP format in the early works of Nahmias [7] and Fries [8]. However, DP problems suffer from the "curse of dimensionality" [10]; the formulations cannot be solved for problems of realistic size as it becomes too large for computation. In addition to this, DP solutions have been reported to be very difficult to implement in practice. This is because the solution depends not only on the actual number of units available, but also on age distribution and the specific day of the week [1, 10]. Because of this limitation, Blake et al. [9] adopted a simplification within the DP framework through aggregation of data to reduce the problem search space and make the problem tractable. They reported that their model has the potential to lower costs by 18% while reducing shortages and outdates.

Haijema and colleagues [6] in their own work followed the same approach, using DP and dimension reduction through aggregation of units into doses combined with a computer simulation method. They distinguished between two types of periodic demand namely demand for "young" PLTs and demand for PLTs of "any" age bounded by the maximum shelf life, while varying the supply rules for both demand types. After a downsizing of the problem and solving exactly by standard successive approximations, the researchers showed the complexity of the optimal policy. They also showed the near-optimality of simple single and double-order-up-to replenishment rules. In their opinion, the double level order-up-to rules, with one level corresponding to "young" PLTs and the other to the total inventory, perform better and can be shown to be nearly optimal when distinguishing between demand for "young" and "any" PLTs. They set up a simulation frequency table by for the optimal strategy to identify the order-up-to level that appears most frequently for each day of the week. The strategy was simulated over a large number of weeks and a best-fit order-up-to rule was determined from the various inventory state and production size combinations. By simulation, the best-fit order-up-to rule for the downsized problem was verified to compete closely with the real optimal strategy. They then proceeded to rescale the solution to the original problem size, and repeat simulation to verify that the feasibility of the solution for the original problem. Finally, a local search procedure based on simulation was used to fine-tune these simple order-up-to levels. In their sensitivity analyses, it was shown that increasing shelf life of PLTs from 4 to 5 days substantially reduces shortages and outdating while less benefit was found by extending from 5 to 7 days. It was also proved that distinguishing between the eight blood types and accounting for Rhesus factor was unnecessary. Their justification lies in the fact that less than 50% of the whole blood donations are processed for PLTs production. They however mention that it may become necessary to create a distinction between blood groups, when there are restrictions on PLTs production because of a limited availability of whole blood donations. Using sensible cost functions, the authors estimated outdating to reduce from 20% to about 1%. In their practical application of the results from the approach above for the routine supply of PLTs using a real-world dataset spanning 3 years obtained from a Dutch regional blood bank, van Dijk et al. [31] reported that outdating could be reduced from 15-20% to less than 0.1% of the annual demand, with shortages virtually lowered to zero. Haijema et al. [30] extended their combined DP-Simulation approach to accommodate irregular production breaks such as holidays, and reported that with the maintenance of outdating and shortage rates below 1%, the simple order-up-to rule remains optimal. They discovered the possibility of integrating the periods with production.

While Blake [10] agrees that the method suggested by van Dijk et al. [31] provides insights into the PLT inventory problem by suggesting relatively simple and easy to implement policies, he disagrees with their assumption. Van Dijk et al. [31] adopted the assumption that the stock age distribution can be ignored when making optimal ordering decisions and Blake [10] proved that their assumption is incorrect. Blake [10] also cautions against making broad generalizations of the proposed solution based on the results from a single case study. Furthermore, he noted an error in their results presentation which prevents direct comparison with other heuristics thus precluding confirmation of their solution quality.

One author, de Kort et al. [33] reported a practical implementation study of the combined stochastic DP and simulation approaches. The study adopted a theoretical approach towards minimizing outdating and shortages while extending the time till outdating. They also discussed the design of the earlier-mentioned Thrombocyte Inventory Management Optimizer, a dedicated software tool used to address the problem. A significant improvement and more structured platelet inventory management has resulted from the adoption of their theoretical approach.

2.4.2 Approximate Dynamic Programming

Identifying this limitations of problem downsizing because of the "curse of dimensionality", Abdulwahab and Wahab [37] used an approach that combines a news-vendor model, Linear Programming (LP) and Approximate Dynamic Programming (ADP), to develop a blood platelet inventory model. Factoring into their proposed model the eight different blood types and their ages, the daily demand distribution and periodicity of demand and supply, as well as demand of each blood type and the inventory level. The researchers evaluated the model in terms of shortage, outdate, inventory level, and the gained total reward. The developed model was solved without any downsizing and their results show cost reductions and low inventory level. In addition, shortages and outdates are reduced to 3.9% and 4.6% of the annual demand and production respectively.

2.4.3 Integer Programming

Gunpinar and Centeno [26] in their study developed Integer Programming (IP) models aimed at minimizing total cost, shortage and outdate rates of PLTs and RBCs for a hospital inventory within a given planning horizon. Their models explicitly accounted for the age of units in the inventory as well as two types of demand (as also found in the work by Haijema et al. [6]). In addition, their model captured uncertainty in blood demand and cross match to transfusion ratio. Their results showed average wastage reduction from 19.9% to 2.57%. They also incorporated cross-match to transfusion ratio into the model using the hospital's average value. However, only single cross matching policy was considered in the models, and cross-match to transfusion requirements for specific patient groups were not incorporated.

2.4.4 Simulation Studies

Other researchers have addressed the platelet inventory problem through simulation studies. Sirelson and Brodheim [27] came up with a predictive model that relates the base stock level to the outdate and shortage rate. Katz et al. [38] also developed computer a simulation model to generate daily platelet orders. Both groups of researchers found ample reductions to outdate rate from 10-20% to 2-5%. However, since they used simulation models, their solutions cannot be proven to be optimal and the extent to which the solutions are robust and generalizable is not clear [10, 31].

2.4.5 Metaheuristics

Metaheuristic algorithms generally refer to optimization methods that implement certain strategies for searching a solution space and finding the global best solution. These algorithms have been reported to find very good solutions although there is no theoretical guarantee that they will always find the global optima. In addition, they are known to have advantage in dealing with optimization problems that are difficult to be modeled explicitly [39]. Due to corresponding increase in complication of optimal/sub-optimal solution search and formulation of constraints or the presence of conflicting objectives with increase in problem size, exact algorithms have been found to be much slower, causing additional computational costs [40]. Meanwhile, the solution space of practical problems easily gets too large to preclude exhaustive enumeration. For this reason, metaheuristics, which are non-exhaustive search techniques have gained popularity in many practical fields. Particle Swarm Optimization (PSO), Ant Colony Optimization (ACO), Genetic Algorithm (GA), Tabu Search (TS) and Simulated Annealing (SA) are examples of metaheuristic algorithms.

Metaheuristics have been applied to different aspects of blood management in literature. Dufourq et al. [41], Adewumi et al. [42] and Olusanya et al. [43] applied metaheuristics to optimize the assignment of blood in a blood banking system. Dufourq et al. [41] presented a comparative study of GA, Hill Climbing and Simulated Annealing while Olusanya et al. [43] reported the performance of PSO for the blood assignment problem. For the BPPIP, Duan and Liao [11] applied a hybrid metaheuristic comprising of two cooperative metaheuristic algorithms (DE and Harmony Search) and one local search (Hooke and Jeeves) method. The authors demonstrated the effectiveness of this hybrid metaheuristic in generating near-optimal solutions in their simulation-optimization framework. Based on this precedence and recommendations in literature, this work also considers the application of DE, BA and GRASP to the different models of the BPPIP as is presented in subsequent chapters. However, an overview of the three underlying techniques is provided in the subsections below.

2.4.5.1 Differential Evolution

DE is a global optimization algorithm based on evolutionary techniques introduced by Storn and Price [44] in 1996, and in congruence with other evolutionary-type algorithms, is stochastic and population-based. It is one of the most popular optimization algorithms currently [45].The general evolutionary algorithm procedure is as shown in figure 2.3:

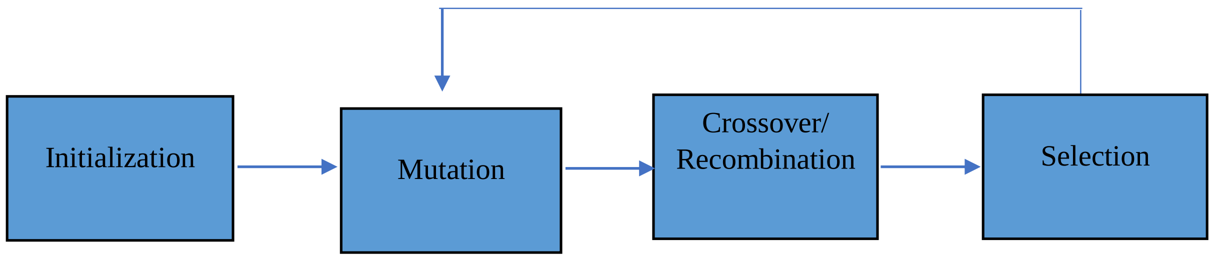

Figure 2.3: General Evolutionary Algorithm Procedure

In each generation G, population is made of N-D parameter vectors in its parallel direct search procedure. The parameter vectors are of the form:

$$x_{i,G} = [x_{1,i,G}, x_{2,i,G}, \dots, x_{D,i,G}] \;\; i = 1,2, \dots, N \qquad (2.1)$$

Where N is the population size and D is the number of parameters. Upper and lower bounds are defined for each parameter and the initial vector population is chosen randomly from within these bounds. Each of the N parameter vectors undergoes mutation, crossover and selection. In the mutation process of the DE algorithm, a mutant vector is generated by taking the weighted difference between two population members (randomly selected) and adding a third member to the result. Crossover is then done with the aim of generating a trial vector by combining the mutant vector with the target vector. Thereafter, a selection operator is applied with the aim of comparing the fitness function value of the target and trial vectors to determine which of them moves to the next generation [46].

Each of these steps are described more specifically as follows:

- **Mutation**

For each parameter or target vector $x_{i,G}$, three other vectors $x_{r1,G}$, x_{r2G}, $x_{r3,G}$, are randomly selected such that the indices $i, r1, r2$ and $r3$ are distinct. A mutant vector is generated of the form:

$$v_{i,G+1} = x_{r1,G} + F(x_{r2,G} - x_{r3,G}) \tag{2.2}$$

Where F ∈ [0,2] is a real and constant factor which controls the amplification of the differential variation.

- **Crossover**

Crossover is introduced to achieve the goal of cumulatively improving solutions such that successful solutions obtained from previous generations are incorporated in the current solution. To this end, a trial vector $u_{i,G+1}$ is developed from the elements of the target vector $x_{i,G}$ and the elements of the mutant vector $v_{i,G}$:

$$u_{i,G+1} = [u_{1,G+1}, u_{2,G+1}, \dots, u_{D,G+1}] \tag{2.3}$$

where

$$u_{j,i,G+1} = \begin{cases} v_{j,i,G+1} \ if \ rand_{j,i} \leq CR \ or \ j = I_{rand} \\ x_{j,i,G} \ if \ rand_{j,i} > CR \ and \ j \neq I_{rand} \end{cases} \tag{2.4}$$

In (2.4), $rand_{j,i} \sim U[0,1]$ and I_{rand} is a random integer from $[1,2, \dots D]$ which ensures that $u_{j,i,G+1}$ gets at least one parameter from $v_{i,G+1}$. CR is the crossover constant ∈ $[0,1]$

- **Selection**

The trial vector $u_{i,G+1}$, generated at the crossover stage is compared with the target vector $x_{i,G}$ using the objective value function. The one with the lower value function is admitted to the next generation $G + 1$:

$$x_{i,G+1} = \begin{cases} u_{i,G+1} \ if \ f(u_{i,G+1}) \leq f(x_{i,G}) \\ x_{i,G} \ otherwise \end{cases} \tag{2.5}$$

The entire procedure is repeated until some stopping criterion is met.

The general DE pseudocode is presented below [47]:

DE Algorithm

Initialize population: Set $X(0) = \{x_1(0), \dots, x_m(0)\}$

Set $g = 0$

Compute $\{f(x_1(g)), \dots, f(x_m(g))\}$

While (*stopping criterion not met)*

    for *i from 1 to m, do*

        Set $y_i = mutate(x(g))$

        Set $z_i = crossover(x_i(g), y_i)$

        Compute $f(z_i)$

        if $f(z_i) < f(x_i(g))$ *then*

            Set $x_i(g+1) = z_i$

        $\boldsymbol{else}$

            Set $x_i(g+1) = x_i(g)$

        end if

    end for

    Set $g = g + 1$

end while

Algorithm 2.1: Pseudo-code of the DE

DE has been shown to be highly effective in handling Combinatorial Optimization Problems (COPs) related to the problem under study. For example, Maryam and Farid [48] presented a DE algorithm for the single-item resource-constrained Aggregate Production planning Problem (APP). They showed that DE has a strong ability to reduce the infeasibility of the addressed problem, and is capable of handling linear and multiple-constrainted non-linear objective functions. In addition, Piperagkas et al. [49] combined PSO and DE to address a highly-constrained mixed integer optimization problem known as the multi-item inventory optimization model with supplier selection. The showed that the DE and PSO hybrid algorithm was highly competitive with other GA-based methods reported in literature. Radhika et al.[50] applied DE in solving the Master Production Scheduling Problem with positive results. Their analysis of results revealed that the DE algorithm performed better than GA in providing the optimal solution within reasonable computational time. Hence. DE has been successfully applied to large-scale, constrained, multi-objective and uncertain optimization problems [45]. DE was also chosen as one of the metaheuristic algorithms to use in solving the BPPIP because of its simplicity, robustness and good convergence properties [44].

2.4.5.2 Bat Algorithm

BA was recently introduced by Yang [51] in 2010 from the study of bats' echolocation behavior in finding their prey. Even in the dark, the bats are able to differentiate between various insect types by emitting pulses of varying loudness and listening for the echoes that bounce back [40]. By following the delay of the returning echo, the bats are able to measure the distance from their prey and also to identify the location of other objects. The echolocation pulses have three characteristics: pulse emission rate, pulse frequency and intensity. The pulse frequency for most bat species is usually between 25kHz and 150kHz. This pulse emission rate can be sped up to about 200 pulses per second upon approaching prey. The pulse loudness varies from the loudest (110dB) to the quietest (50dB) as they come close to the prey.

The BA uses the rules presented in [51]:

- The use of echolocation to sense distance and differentiate between prey and surrounding barriers.
- Random flight is conducted with velocity v_i, at position x_i, emitting pulses with a fixed frequency f_{min}, of varying wavelength λ and loudness A_0 in search for prey. Wavelength and rate of pulse emission can be adjusted by the bats depending on the nearness of their prey.
- The loudness or intensity of the pulse is assumed to vary from a large positive value A_0 to a minimum constant value A_{min}

The BA pseudo-code is presented next [51]:

Bat Algorithm

Objective function f(x), $x = (x_1, \dots x_d)^T$
Initialize population $x_i (i = 1, 2, \dots, n)$ *and* v_i
Define pulse frequency f_i *at* x_i
Initialize pulse rates r_i *and loudness* A_i
While (*t < Max number of iterations)*
    Generate new solutions by adjusting frequency,
    Update velocities and locations/solutions according to equations (2.6) to (2.8)
    if *(rand >*r_i*)*
        Select a solution among the best solutions
        Generate a local solution around the selected best solution
    end if
    Generate a new solution by flying randomly
    if $(rand < A_i \,\&\, f(x_i) < f(x_*))$
        Accept the new solutions
        Increase r_i *and reduce* A_i

```
    end if
Rank bats and find current best x_*
end while
Post process results and visualization
```

Algorithm 2.2: BA pseudo-code

The bat population is first initialized with position x_i, velocity v_i and random frequency f_i drawn uniformly from $[f_{min} - f_{max}]$. The bats' motion is given as an iterative updating their velocities v_i^t and positions x_i^t at time step t using equations (2.6) to (2.8) as follows:

$$f_i = f_{min} + (f_{max} - f_{min})\beta \tag{2.6}$$

$$v_i^t = v_i^{t-1} + (x_i^{t-1} - x_*)f_i \tag{2.7}$$

$$x_i^t = x_i^{t-1} + v_i^t \tag{2.8}$$

where $\beta \in [0,1]$ is a randomly generated vector drawn from a uniform distribution and x_* denotes the current global best solution which is obtained by comparing all the solutions found within the population.

A new solution is generated locally for each bat using random walk:

$$x_{new} = x_{old} + \varepsilon A^t \tag{2.9}$$

where $\varepsilon \in [-1,1]$ is a random number, while $A^t = < A_i^t >$ is the average loudness of all the bats at the current time step.

Furthermore, as the iterations proceed, the loudness A_i and the rate of pulse emission r_i are updated by equations (2.10) and (2.11) respectively:

$$A_i^{t+1} = \alpha At_i^t \tag{2.10}$$

$$r_i^{t+1} = r_i^0[1 - \exp(-\gamma t)] \tag{2.11}$$

Where α and γ are constants. A solution is accepted if a randomly generated number is less than loudness A_i and $f(x_i) < f(x_*)$. The search process continues until some specified termination criterion is reached.

BA has also been successfully implemented in literature to address similar problems to BPPIP. In [52], a hybrid BA with optimally tuned parameters was implemented to solve a bi-objective inventory model of a three-echelon supply chain. The proposed Hybrid BA was compared with a GA algorithm and found to perform better on tested problem instances. Another improved BA algorithm was also employed in [53] to solve a proposed portfolio selection model, with results showing that the algorithm performed well in achieving the optimal results for the proposed model. BAs have been also used to address other COPs as can be seen in [51, 54-56].

2.4.5.3 Greedy Randomized Adaptive Search Procedure

GRASP is a metaheuristic which was first described in 1989 by Thomas A. Feo and Mauricio G. C. Resende [57]. It is an iterative technique that comprises of a construction phase and a local search phase. A feasible solution is built in the construction phase, and its neighborhood is explored for a local minimum during the local search stage. The best solution found is usually maintained and updated over successive iterations.

The construction phase is an iterative process which involves building the feasible solution one element at a time. The next element to be incorporated into the partial solution is determined according to a greedy function which estimates the benefit of selecting each element in the candidate list. The list of best candidates, called the restricted candidate list (RCL), consists of the elements with the greatest gains. The size of the RCL can be restricted either by value using the parameter $\alpha \in [0,1]$ (i.e. all candidate elements that are not more than α percent away from the greedy choice are included in the RCL. $\alpha = 0$: purely greedy; $\alpha = 1$: purely random), or by cardinality (i.e. the RCL consists of only the β best candidate elements), or a merge of both criteria. The probabilistic aspect of GRASP is demonstrated by randomly selecting one element from the RCL (not necessarily the best), this gives a bias towards god solutions and at the same time allows for the discovery of different solutions at each GRASP iteration. Therefore, some constructed solutions will be worse and some others better than the average solution quality. Once an element has been selected to be incorporated into the partial solution, the candidate list is updated to reflect the changes resulting from the selection of the previous elements; this is the adaptive part of the algorithm.

The local search phase involves an iterative refinement of each constructed solution until no better solution can be found within the neighborhood.

The GRASP technique is attractive because of its ease of implementation as only two main parameters need to be set: the stopping criterion (usually the maximum number of iterations) and the parameter to restrict the size of the RCL. Also, as mentioned earlier, at each iteration, a different solution is obtained, and in general, the higher the number of iterations, the higher the probability of finding a good solution and the higher the computation time required also.

The basic GRASP procedure is described below [58]:

```
Procedure GRASP (stopping_criterion, α)

Read Input_Instance ();
While GRASP stopping_criterion not satisfied
Solution ← ConstructGreedyRandomizedSolution (α)
     LocalSearch (Solution)
    UpdateSolution (Solution, BestSolutionFound)
end while
return BestSolutionFound
end GRASP
```

Algorithm 2.3: Basic GRASP Pseudo-Code

The algorithm has been applied to a variety of problems including the set covering, production planning and scheduling, and location problems with great success [57]. Igwe et al. [59] used GRASP to solve the multiple knapsack model of the blood assignment problem, finding it to be better in efficiently handling data than DP. In addition, Jin [60] applied a GRASP algorithm to solve the facility location problem for logistics networks, and tested the effectiveness of the GRASP method using various data sets. The GRASP algorithm was found to perform successfully in achieving solution to the highlighted problem.

2.5 Identified Gaps in Literature

The review presented in this chapter shows that the exploration of metaheuristics for optimizing blood PLT production and inventory, is relatively young. Although the limitation of exact methods in practice is widely acknowledged, researchers only began to explore metaheuristics which have generally been shown in a few works to be effective, while offering much better efficiency than many other existing techniques. However, the field of metaheuristics itself is fast-growing, hence the need to keep up with state of the art. There is still much need for research effort to explore those that are easily amenable to the PLT production and inventory problem. Comparative studies are also needed in order to evaluate the performances of known metaheuristics and how they compare to one another, in order to make good choices for applications. Neither of these is abundant in literature.

Another area that needs much more attention is in the area of modelling. Solution techniques may be good but conclusions drawn from studies are only as good as the model adopted. This review identifies progressive evolution of practical details catered for in mathematical models developed to represent the real-life PLT production and inventory process. While progress has been made in moving from overly simplistic models to those that capture more detail, there is much room for improvement. Specifically, we identify the model of [11] successfully developed for entire supply chain inventory optimization for short-shelf-life goods with a focus on PLTs. The model does not capture costs for the blood producer.

Some of these identified gaps are addressed in the subsequent chapters of this thesis.

2.6 Summary

In this chapter, an overview of works in the inventory management of perishables with an emphasis on blood products have been given. Studies done in the area of blood PLT inventory management have also been reviewed. Some of the commonly used solution methods have been presented. From the review, it is observed that the use of metaheuristics in solving this real-world problem has not really been explored. This research, therefore, focuses on investigating the performance of metaheuristic algorithms in solving this problem. This is significant in providing a good foundation for further research in this area which might portend promising arena for incorporation into decision support systems for the blood platelet production and inventory problem.

CHAPTER THREE

OPTIMIZATION OF ORDER-UP-TO POLICY FOR THE BPPIP

3.0 Introduction

In this chapter, the first solution approach to the BPPIP is presented. The operations of the blood PLT producer are described and modeled in two ways, giving rise to models 1 and 2. Two scenarios of model 2 are studied: one gives priority to adherence to bounds on shortage rates over outdate, in the event that a choice has to be made between two infeasible solutions during the search process, while the other prioritizes outdate rate over shortage rate.

3.1 The Blood Platelet Producer Models for Optimizing Order-up-to Policy

In this section, the two models (models 1 and 2) for optimizing order-up-to policy for the blood PLT producer are presented. The main difference between the two models is that model 1, is unconstrained, capturing shortage and outdate within the total cost which constitute the objective function to be minimized, while model 2 handles shortage and outdate as constraints.

3.1.1 Model 1: The Unconstrained Blood Platelet Producer Model

Here, the blood PLT producer’s problem is that of deciding simple order-up-to rules that yield production volumes of PLTs which minimize costs over the entire planning horizon. At the beginning of each day, inventory inspection is conducted, and a production decision taken. The inventory inspection involves observing the total number of PLT units available as well as their age distribution. Whole blood units are collected from donors and prepared for separation into several components. An order cost is associated with the collection of whole blood units. It is also assumed that the production volume decision is taken before the demand for the day is observed. The production of that day will be available the next morning. During the day, it is assumed that demand for PLTs from hospitals is satisfied from the inventory according to the FIFO rule. The demand for the day is assumed to be random. If available stock is not sufficient to meet demand, then a shortage cost is incurred to ship in PLTs instantaneously from an outside source. At the end of the day, all PLTs remaining in stock age by one day. Therefore, any PLT in stock with one day to outdate becomes outdated PLT and is removed from the inventory. Accordingly, disposal cost is incurred for the outdated units. Ordered PLT units enter the inventory the next morning as the youngest stock with a minimum of five days to expire. It is assumed that there is no production on weekends, and restrictions on production and storage capacities are negligible [29, 35].

3.1.2 Model 2: The Constrained Blood Platelet Producer Model

The blood PLT producer's problem here is that of deciding simple order-up-to rules that yield production volumes of PLTs which minimize costs over the planning horizon while meeting pre-specified maximum allowable shortage and outdate constraints.

Following the classical unconstrained blood producer operation, the inventory state is inspected at the beginning of each day and a production decision is taken. Demand for the day is also satisfied according to the FIFO policy. However, if there is a shortage, the unmet demand is assumed to have been lost.

According to Blake et al. [29], the important costs of shortage and outdate are non-tangible and difficult to determine. Haijema et al. [6] also confirms that the costs for shortages and outdates are less concrete as compared to inventory costs. The cost of a shortage may be the well-being of a life and the loss of donor good-will associated with an outdate unit cannot really be estimated. Haijema et al. [6] and Cohen and Pieskalla [23] adopted a relative cost approach while noting the difficulty in setting appropriate values for shortages and outdates. With an example, Blake et al. [29] show that the relative cost approach has a significant impact on the actual solutions obtained. They suggest that blood producers are rather comfortable setting operational targets for key performance metrics, such as shortage and outdate rates, than dealing in costs.

Accordingly, the objective function defined for the constrained variant of the blood PLT producer model takes into account order and holding costs only, while meeting pre-specified maximum allowable shortage and outdate constraints.

The following notations are used in the mathematical formulation of models 1 and 2:

- t represents the period/day in the planning horizon. $t = (1, 2, 3, \ldots, T)$
- M represents the maximal residual shelf life. (*M =5 for platelets*)
- r represents the residual shelf life of platelet in stock. $r = (1,2, \ldots, M)$
- a_r represents the amount of PLT units that will expire in r days

  The vector $a(t) = (a_1, a_2, a_3, a_4, a_5)$, presented as a tuple, describes the inventory state at hand at the beginning of a period *t*. a_1 represents the oldest units while a_5 are the youngest units in inventory
- n_j^t represents the total amount of PLT units in inventory at the beginning of a particular period *t* of age j ($j = 1,2, \ldots, 5$) or less. $n_j^t = \sum_{r=1}^{j} a_r$
- d_t is the demand for period *t*, assumed to be Poisson distributed
- q_t represents the production quantity for period t
- S_t represents the shortage quantity for period *t* defined as $s_t = (d_t - n_5^t)^+$

  $t = (1, 2, 3, \ldots, T)$ where $x^+ = max\{x, 0\}$
- SR represents the shortage rate over the entire planning horizon defined as

$$SR = \frac{\sum_{t=1}^{T} s_t}{\sum_{t=1}^{T} d_t}$$

- O_t represents the outdate quantity for period t defined as $o_t = max\{a_1(t),0\}$

  $t = (1, 2, 3, \dots, T)$

- OR represents the outdate rate over the entire planning horizon defined as

$$OR = \frac{\sum_{t=1}^{T} o_t}{\sum_{t=1}^{T} q_t}$$

- OC_t = Cost of placing an order for period t, defined as

$$\begin{cases} 0 & \text{if } q_t = 0 \\ f_o + v_0 qt & \text{if } q_t > 0 \end{cases}$$

Where f_o is the fixed cost of placing an order

v_0 is the variable cost per PLT unit ordered

q_t is the order for period t

- OC represents the order costs over the entire planning horizon defined as

$$OC = \sum_{t=1}^{T} OC_t$$

- HC_t = Cost of holding inventory for period *t* defined as

$$\begin{cases} 0 & \text{if } n_t = 0 \\ f_h + v_h n_t & \text{if } n_t > 0 \end{cases}$$

Where f_h is the fixed cost of holding any units in inventory

v_h is the variable cost per period per PLT unit

n_t is the number of PLT units in inventory at period t

- HC represents the inventory holding costs over the entire planning horizon defined as

$$HC = \sum_{t=1}^{T} HC_t$$

- SC_t = Shortage cost of obtaining PLT units from external sources for period *t*

$$\begin{cases} 0 & if\, s_t = 0 \\ f_s + v_s s_t & \text{if } s_t > 0 \end{cases}$$

where f_s is the fixed cost of obtaining units from outside sources

v_s is the variable cost per PLT unit obtained from external source

s_t is the number of PLT units obtained from external sources for period t

- SC represents the shortage costs over the entire planning horizon defined as

$$SC = \sum_{t=1}^{T} SC_t$$

- DC_t = Cost of disposing outdated PLT units for period *t* defined as

$$\begin{cases} 0 & if\, o_t = 0 \\ f_d + v_d o_t & \text{if } o_t > 0 \end{cases}$$

where f_d is the fixed cost of disposing outdated PLT units

v_d is the variable cost per PLT unit disposed

o_t is the number of outdated PLT units for period t

- DC represents the outdate costs over the entire planning horizon defined as

$$DC = \sum_{t=1}^{T} DC_t$$

The objective functions for the Model 1 and 2 respectively are defined in equations (3.1) and (3.2):

Model 1

$$min\{E_p(C)\} \text{ where } C = OC + HC + SC + DC \tag{3.1}$$

Model 2

$$min\{E_p(C)\} \text{ where } C = OC + HC \tag{3.2}$$

subject to $$max\{E_P(SR)\} \leq 1 - \varphi \tag{3.3}$$

and $$max\{E_P(OR)\} \leq \beta \tag{3.4}$$

where

E_P represents the function of expected value function, with respect to stochastic demand distribution P

φ is the target availability or fill rate service measure

β is the maximally acceptable outdate rate

The day-to-day transitions between inventory states is jointly determined by the quantity produced for the day, demand for the day, the rule by which the demand is served and the replenishment policy. Haijema et al. [6] suggest that order-up-to policies be adopted to approximate optimal policies, due to the fairly complicated structure of actual optimal policies which makes them impractical to implement. From the results of their study, Duan and Liao [11] reported the superiority of policies that account for distribution of age of stocks are to policies that do not account for age. The old inventory ratio policy proposed by these researchers is therefore employed in this study. In this policy, quantity to be produced is firstly arrived at based on the traditional order-up-to level, which only accounts for the current amount of items in inventory. The fraction of old items among the total items in inventory is then calculated. If the calculated proportion exceeds a particular threshold δ, there is an addition to the production quantity to cater for outdates that could possibly arise as a result of the old items. The size of this addition is equal to the total number of old items in stock. The policy is described by the equations (3.5) and (3.6):

$$If\ TIS_t < SS_t\ then\ q_t = SS_t - TIS_t \tag{3.5}$$

Secondly,

$$If\ {n_2^t}/{n_5^t} \geq \delta\ then\ q_t = q_t + n_2^t \tag{3.6}$$

Where TIS_t is the total inventory size on day *t*

SS_t represents the order-up-to level being targeted for day *t*

n_2^t represents the number of old items in inventory on day *t*

n_5^t represents total number of items in inventory on day *t*

3.2 Solution Framework

The solution framework adopted in this study is the optimization-simulation framework proposed by Duan and Liao [11]. While simulation has proven to be useful in performance evaluation of complex systems, it is often insufficient to use simulation only. "An advanced optimizer that searches for the best combination of decision variables based on the output of a simulation model of the system may be needed in the form of simulation optimization" [11, 61]. In the framework adopted for this work, a metaheuristic algorithm generates solutions which are evaluated by the simulation model. The method of sample average approximation proposed by Kleywegt et al. [62] is adapted in the solution framework to estimate the expected operational costs. Random samples of the demand experienced by the blood PLT producer are generated, followed by approximation of their expected value functions by means of the corresponding sample average function.

Let $D^1, D^2, \dots, D^K$ represent a set of K realizations of identically distributed independent random samples of demand data experienced by the blood PLT producer. The expected operational costs,

$E_p(C)$, is approximated as ${}^{1}/_{K}\sum_{k=1}^{K}(C|D^k)$ where $C|D^k)$ is the operational cost computed based on the kth realization. Similarly, the expected shortage rate, $E_P(SR)$, and outdate rate, $E_P(OR)$, are approximated as ${}^{1}/_{K}\sum_{k=1}^{K}(SR|D^k)$ and ${}^{1}/_{K}\sum_{k=1}^{K}(OR|D^k)$ respectively where $(SR|D^k)$ is the computed shortage rate and $(OR|D^k)$, the outdate rate computed based also on the kth demand realization. This is because

$$E[{}^{1}/_{K}\sum_{k=1}^{K}(C|D^k)] \to E_p(C),$$

$$E[{}^{1}/_{K}\sum_{k=1}^{K}(SR|D^k)] \to E_P(SR)$$

$$\text{and } E[{}^{1}/_{K}\sum_{k=1}^{K}(OR|D^k)] \to E_P(OR)$$

$$\text{as } K \to \infty.$$

For Model 2, the parameter-les constraint handling method proposed by Deb 2000 [63] is adapted to handle the shortage and outdate constraints in the objective function. A solution that results in expected shortage and outdate rates less than or equal to $1-\varphi$ and β respectively is considered feasible; otherwise they are counted infeasible. In the adapted constraint handling method, a pair of solutions is compared at a time with the enforcement of the following conditions:

- The feasible solution with a better objective function value option is preferred.
- For infeasible solutions, two scenarios are considered:
    - Scenario 1 (Model 2a): The outdate constraint is relaxed, and between two solutions violating the shortage constraint, preference is given to the one that violates the constraint less.

- Scenario 2 (Model 2b): The shortage constraint is relaxed, and between two solutions violating the outdate constraint, the one with a smaller constraint violation is preferred.

This constraint handling method is adopted in this study because of its efficiency resulting from the fact that solutions are not compared on fitness value and amount of constraint violation at the same time.

The optimization and simulation modules are separate entities but they interact with each other. The simulation model evaluates the fitness of a solution and the output of the simulator is passed as input to the metaheuristic algorithm working in the optimization module to derive new solutions. The algorithm aims at improving the quality of the best solution iteratively by repeating the optimization-simulation loop and this process continues until successive iterations are found to return the same solution. The distinctness of the optimization and simulation modules allows the comparison of the performance of three metaheuristic algorithms as stated in the research objectives.

3.2.1 Dataset

The demand data is simulated following a Poisson distribution with independently varying daily means. Table 3.1 gives a description of the dataset used, most of which are obtained from literature [9, 11]. A summary of the values of cost parameters also obtained from literature [9] is given in Table 3.2. A 5-day PLT shelf life is assumed and a planning horizon of one year (52 weeks) is used with the Poisson distributed demand daily means given as in the table:

Table 3.1: Model Parameters

Parameter	***Value***
Daily demand means over the days of the week – d	[29, 32, 33, 31,33, 22, 20]
Initial Inventory at the beginning of planning horizon	[0 0 20 0 0]
PLT shelf Life (in days)	5
Length of Planning Horizon	1 year or 364 days
Maximally Allowable outdate rate	5%
Maximally Allowable shortage rate	1%

Table 3.2: Cost Parameters

Parameter	***Fixed ($)***	***Variable ($)***
Order Costs	21.85	0.00
Holding Costs	0.00	0.05
Disposal Costs	10.00	0.45
Shortage Costs	100.00	0.00

3.3 Adaptation of Differential Evolution for the BPPIP

A DE solution to the BPPIP consists of a vector of order-up-to levels for each day of production i.e. Monday to Friday. Therefore, the number of decision variables is 5. An upper and lower bound is defined for each decision variable using the method suggested by Blake et al. [12]. The lower bound is set as the minimum order-up-to level, I_{min}, representing the smallest number of units that must be available in inventory after replenishment. It is the smallest integer such that the probability that demand is not greater than this value is φ where φ is the target availability measure:

$$I_{min} = P^{-1}(\lambda, \varphi) \tag{3.7}$$

where $P^{-1}(\lambda, \varphi)$ is the inverse Poisson cumulative probability function having mean λ.

Similarly, the upper bound, I_{max}, is set as the maximum possible stock that can be held in inventory after replenishment such that the probability of outdating will not exceed the maximum allowable outdate rate, β. Since daily demand is assumed to be distributed independently and identically, the demand can be estimated for a platelet unit arriving on day i with residual shelf life of r_i days by the cumulative demand over the r_i days, $CD(i, r_i)$:

$$CD(i, r_i) = \sum_{t=i}^{i+r_i-1} d_t. \tag{3.8}$$

where d_t is the demand for day t

Therefore,

$$I_{max} = max_y \left\{ \frac{\sum_{x=0}^{y} (y-x) p(x, CD(i, r_i))}{y} \leq \beta \right\} \tag{3.9}$$

where $p(x, \mu)$ is the probability mass function of a Poisson random variable with mean μ, evaluated at x and β is the maximally accepted outdate rate.

An initial population is generated within these bounds and each of the population members undergoes mutation and crossover. The blood PLT producer model is simulated to evaluate the fitness of each population member and the trial vector generated from the crossover operation. The better of the solutions is selected to move on to the next generation. Iterative improvement of the best solution is continued until the stopping criterion is satisfied; that is, until it is found that there is no improvement between successive iterations.

DE was originally designed for problems involving continuous variables rather than discrete optimization problems. However, it does not require that the problem being optimized be differentiable as other classical optimization methods do. As a result, it can be used on non-continuous optimization problems [64]. For the BPPIP, values of the order-up-to levels in newly generated solutions in lines 12 and 15 of Algorithm 2.1, are restricted to integers by rounding.

3.3.1 Validation of Computed Upper and Lower Bounds

The upper bound and lower bound for the element of the solution vector were computed following the method suggested by Blake et al. [12]. To validate the computed upper and lower bounds, an attempt is made to reproduce the results of [12].

According to the authors, for an hospital with demand vector $d = (4,4,4,4,4,4,4)$ with service level $\alpha = 97.5\%$ and target outdate rate $\beta = 5\%$, the minimum and maximum inventory that must be on hand after replenishment is 8 units and 22 units respectively. Over the six days until product outdate, the expected demand is 24 units and the outdate rates for different inventory sizes according to equation (3.12) are given in table 3.3:

Table 3.3: Outdates vs. Maximum Inventory assuming a six-day shelf life [12]

Inv_{max}	Expected Outdates	Outdate Rate
19	0.346	1.8%
20	0.527	2.6%
21	0.769	3.7%
22	1.083	4.9%
23	1.475	6.4%

Using the bounds computed in this study yields exactly the same results. Hence, the computed bounds which constitute an important component of the solutions techniques are adopted.

3.3.2 Factorial Experiment for Parameter Selection in Differential Evolution

The goal of the empirical studies reported is to arrive at optimal settings for the combination of parameters upon which the performance of the algorithm depend. This subsection describes the particular design followed in the experiments for reliable results.

3.3.2.1 Experimental Design

Considering the fact that performance is affected not only by main effects of the individual parameters but also by the interaction among parameters, regular one-factor-at-a-time (OFAT) design, in which each experimental run varies the values of one parameter while keeping others constant, may be misleading. Therefore, a factorial design [65] is adopted, precisely the full-factorial design. This experimental design type has been widely applied for years in many fields including various areas of engineering [66], social science [67], agriculture [68], computer science [69, 70] and general research [71]. In such a design, parameters are coded as factors with discrete levels. Then each possible combination of levels of all parameters are run and the values of the performance criteria recorded. In this way both main and interaction effects are accounted for. To account for randomness inherent in the algorithm, each combination is run thrice, so the costs, shortage and outdate are averaged over the 3 runs. It is these averages that are compared.

The low, mid and high levels for the DE control variables, (F,CR and N) were chosen according to the rules of thumb suggested by Storn and Price [44]. The authors suggest 0.5 and 0.1 as good low levels for F and CR respectively. They also recommend 5 to 10 times the number of decision variable as a reasonable choice for N.

Table 3.4: Variable levels for full factorial design of experiment for the DE algorithm

	Low	Mid	High
F	0.5	1	2
CR	0.1	0.5	1
N	25	35	50

Where F refers to a real constant factor $\in [0,2]$, CR is the crossover constant $\in [0,1]$ and N is the population size. The Table 3.3 shows the average costs taken over 3 runs for each of the 27 (3^3) possible combinations. Should it arise that the average cost realized from multiple combinations are the same, such ties are resolved using average runtime measured by the number of function calls.

Table 3.5: Factorial Experiment for Parameter Selection in Differential Evolution

Combination	**np**	**F**	**cr**	**Average cost**	**Average function calls**
1	L	L	L	7000	50
2	L	L	M	4940	75
3	L	L	H	5290	50
4	L	M	L	4680	50
5	L	M	M	5170	100

6	L	M	H	5070	100
7	L	H	L	4750	100
8	L	H	M	5120	75
9	L	H	H	5040	125
10	M	L	L	5180	70
11	M	L	M	5120	140
12	M	L	H	5120	140
13	M	M	L	5090	70
14	M	M	M	4560	140
15	M	M	H	5220	70
16	M	H	L	4710	210
17	M	H	M	5790	70
18	M	H	H	4780	105
19	H	L	L	4790	200
20	H	L	M	5030	100
21	H	L	H	4790	200
22	H	M	L	5220	250
23	H	M	M	5040	200
24	H	M	H	5330	100
25	H	H	L	5040	100
26	H	H	M	5020	100
27	H	H	H	4560	100
			best	**4560**	

3.4 Adaptation of Bat Algorithm for the BPPIP

Similar to the DE solution to the BPPIP, a BA solution also consists of a vector of order-up-to levels for each production day. Upper and lower bounds are also set for each decision variable using the method suggested by Blake et.al [12] as used for the DE algorithm. Every step involving in the adaptation of BA for the problem is exactly same as for DE, the only difference being the search strategy. An initial population is generated within these bounds and each of the population members is updated to constitute a new generation, according to the process outlined in Algorithm 2.2. The blood PLT producer model is simulated to evaluate the fitness of each population member, while record is kept of the personal best of each bat as well as the global best. The process continues, and the global best is then returned as the optimal solution when the termination criterion is met.

Although originally designed for continuous optimization problems, just like DE, BA is easily amenable to discrete optimization problems such as the one being studied in this work, by restricting values on each dimension to integers, while maintaining every other component of the original algorithm. This is achieved simply by rounding to integers, every element of hypothetical solution vectors generated in line 6 of Algorithm 2.2.

3.4.1 Factorial Experiment for Parameter Selection in Bat Algorithm

As done for DE in section 3.3.2, the goal of the empirical studies reported, is to arrive at optimal settings for the combination of parameters upon which the performance of the BA depend. Again, a factorial design is adopted, to account for main effects as well as interaction among parameters. The coded levels for each parameter is described in table 3.6.

Table 3.6: Factor Levels for Bat Algorithm Parameters

Parameter	Low	Mid	High
Np (population size)	25	35	50
a (loudness)	0.1	0.5	1
pr (pulse rate)	0.1	0.5	1
Qmax (maximum frequency)	1	5	10

Table 3.7: Factorial Experiment for Parameter Selection in Bat Algorithm

Combination	**np**	**A**	**pr**	**Qmax**	**Average Cost**	**Average function calls**
1	L	L	L	L	9443.1	100
2	L	L	L	M	6819.45	100
3	L	L	L	H	13638.7	150

4	L	L	M	L	8228.2	100
5	L	L	M	M	6003.8	150
6	L	L	M	H	14585.3	100
7	L	L	H	L	8896.05	100
8	L	L	H	M	15114.25	100
9	L	L	H	H	8114.1	100
10	L	M	L	L	16964.25	100
11	L	M	L	M	9216.75	100
12	L	M	L	H	6532.05	150
13	L	M	M	L	7081.1	150
14	L	M	M	M	8468.6	200
15	L	M	M	H	13006.55	100
16	L	M	H	L	8300.4	150
17	L	M	H	M	5941.1	150
18	L	M	H	H	12652.85	150
19	L	H	L	L	8103.15	100
20	L	H	L	M	5153.8	300
21	L	H	L	H	5423.5	200
22	L	H	M	L	5587.5	150
23	L	H	M	M	5743	150
24	L	H	M	H	6444.9	150
25	L	H	H	L	5444.4	100
26	L	H	H	M	4800.8	100
27	L	H	H	H	5423.5	150
28	M	L	L	L	11303.6	50
29	M	L	L	M	13698.5	100
30	M	L	L	H	8355.25	100
31	M	L	M	L	12184.3	50
32	M	L	M	M	11285.05	50
33	M	L	M	H	8599.4	100
34	M	L	H	L	7985.2	200
35	M	L	H	M	8699.45	50
36	M	L	H	H	6140.25	100
37	M	M	L	L	6552.45	100
38	M	M	L	M	5205.5	100
39	M	M	L	H	13319.1	50
40	M	M	M	L	5816.75	50
41	M	M	M	M	5423.5	100
42	M	M	M	H	9686.6	100
43	M	M	H	L	10190.15	200
44	M	M	H	M	6333.05	100

45	M	M	H	H	9520.9	50
46	M	H	L	L	5372.2	150
47	M	H	L	M	5171.6	100
48	M	H	L	H	5475.35	150
49	M	H	M	L	5861.05	100
50	M	H	M	M	6296.95	150
51	M	H	M	H	6354.3	200
52	M	H	H	L	8451.95	100
53	M	H	H	M	5161.2	100
54	M	H	H	H	10198.35	100
55	H	L	L	L	6492.4	100
56	H	L	L	M	12301.65	100
57	H	L	L	H	13259	100
58	H	L	M	L	13138.95	100
59	H	L	M	M	11744.8	100
60	H	L	M	H	11757	100
61	H	L	H	L	7612.65	100
62	H	L	H	M	5910.75	100
63	H	L	H	H	7593.35	100
64	H	M	L	L	15165.35	100
65	H	M	L	M	19707.15	100
66	H	M	L	H	6612.7	200
67	H	M	M	L	6493.5	200
68	H	M	M	M	11743.15	100
69	H	M	M	H	10531.2	100
70	H	M	H	L	13826.5	100
71	H	M	H	M	5385.2	200
72	H	M	H	H	5165.6	100
73	H	H	L	L	6731.9	100
74	H	H	L	M	6540.7	100
75	H	H	L	H	5107.9	150
76	H	H	M	L	10938.35	150
77	H	H	M	M	5386.2	200
78	H	H	M	H	5296.8	150
79	H	H	H	L	8241.2	100
80	H	H	H	M	5423.5	100
81	H	H	H	H	5386.2	150
				best	**4800.8**	

3.5 Comparative Study of Differential Evolution and Bat Algorithm for the BPPIP

In this section, the performances of DE and BA are evaluated on the blood platelet production and inventory problem, and compared. First this study is carried out using model 1 described in section 3.1.1. Then they are compared on model 2 described in section 3.1.2, under two different scenarios highlighted in section 3.2.

Table 3.8: Results for Model 1

	DE				Bat			
Realization	**Cost**	**Shortage rate**	**Outdate rate**	**Function calls**	**Cost**	**Shortage rate**	**Outdate rate**	**Function calls**
1	4438.50	0.0022	0.0059	100	5452.20	0.0014	0.0076	100
2	4476.75	0.0022	0.0059	150	5238.80	0.0014	0.0206	100
3	5037.00	0.0004	0.0000	100	5628.80	0.0014	0.0076	100
4	4982.80	0.0000	0.0033	100	10694.00	0.0543	0.0444	100
5	5288.80	0.0000	0.0083	150	6366.60	0.0018	0.0000	100
6	4427.30	0.0011	0.0084	100	9431.20	0.0301	0.0007	50
7	4940.05	0.0000	0.0000	150	6651.10	0.0014	0.0079	100
8	4786.05	0.0023	0.0099	200	5452.20	0.0014	0.0076	100
9	5184.30	0.0018	0.0000	100	6852.05	0.0039	0.0069	150
10	4989.40	0.0000	0.0000	100	5401.45	0.0014	0.0090	100
11	4993.30	0.0001	0.0000	100	13876.25	0.1680	0.0777	100
12	5050.40	0.0000	0.0033	150	5436.60	0.0014	0.0076	100
13	5284.15	0.0000	0.0083	100	6507.50	0.0189	0.0154	100
14	4434.30	0.0010	0.0088	150	5139.00	0.0014	0.0000	150
15	4365.25	0.0010	0.0083	100	6073.00	0.0014	0.0000	250
16	5091.35	0.0000	0.0001	100	5155.55	0.0014	0.0019	200
17	4473.05	0.0026	0.0091	100	5422.90	0.0014	0.0076	150
18	4930.15	0.0000	0.0001	200	10657.90	0.0351	0.0000	100
19	5226.40	0.0000	0.0083	100	6363.80	0.0014	0.0019	100
20	4408.30	0.0010	0.0084	100	5422.90	0.0014	0.0076	100
21	5039.35	0.0004	0.0000	100	5703.15	0.0014	0.0000	150
22	5209.05	0.0000	0.0043	100	6580.75	0.0016	0.0019	200
23	5183.95	0.0057	0.0293	250	14551.80	0.0892	0.0000	100
24	4980.20	0.0000	0.0033	100	5452.20	0.0014	0.0076	150
25	5288.80	0.0000	0.0083	150	5452.20	0.0014	0.0076	100
26	5194.40	0.0012	0.0000	100	6716.45	0.0048	0.0110	150
27	4800.45	0.0013	0.0202	150	6332.85	0.0108	0.0443	100
28	4460.55	0.0010	0.0093	100	5138.50	0.0057	0.0083	150

29	4449.00	0.0027	0.0054	150	5630.60	0.0070	0.0270	100
30	5068.15	0.0010	0.0000	100	5452.20	0.0014	0.0076	100
Averages	**4882.72**	**0.0010**	**0.0059**	**125**	**6807.82**	**0.0152**	**0.0116**	**122**

Table 3.9: Results for Model 2, Scenario 1

	DE				**Bat**			
Realization	**Cost**	**Shortage rate**	**Outdate rate**	**Function calls**	**Cost**	**Shortage rate**	**Outdate rate**	**Function calls**
1	5283.35	0.0016	0.0017	100	6330.25	0.0027	0.0000	50
2	6742.05	0.0016	0.0109	250	5250.05	0.0031	0.0011	150
3	8680.75	0.0384	0.0000	150	5193.65	0.0014	0.0019	200
4	5966.80	0.0060	0.0001	100	5534.95	0.0112	0.0113	100
5	9966.30	0.0349	0.0002	150	6393.75	0.0014	0.0006	100
6	6480.65	0.0016	0.0017	100	5503.70	0.0029	0.0004	100
7	9817.40	0.0285	0.0311	100	6735.95	0.0014	0.0080	100
8	5762.45	0.0016	0.0109	200	5427.55	0.0014	0.0080	100
9	9792.35	0.0493	0.0002	150	4657.45	0.0031	0.0120	100
10	7272.25	0.0163	0.0018	100	6319.90	0.0025	0.0080	50
11	8741.15	0.0376	0.0000	200	5850.95	0.0075	0.0456	150
12	6548.30	0.0119	0.0035	100	4535.15	0.0025	0.0091	100
13	5483.90	0.0016	0.0107	200	5191.95	0.0030	0.0000	150
14	8165.75	0.0389	0.0169	150	5850.95	0.0075	0.0456	100
15	9832.85	0.0590	0.0430	100	6058.80	0.0046	0.0131	250
16	6835.75	0.0037	0.0000	150	5524.15	0.0014	0.0080	150
17	6558.05	0.0016	0.0017	150	5524.15	0.0014	0.0080	100
18	9803.45	0.0370	0.0002	150	5533.75	0.0056	0.0081	300
19	9941.80	0.1235	0.0633	100	5331.25	0.0019	0.0046	150
20	6757.05	0.0016	0.0109	150	6432.35	0.0053	0.0000	100
21	7840.30	0.0115	0.0036	100	5524.15	0.0014	0.0080	100
22	5798.50	0.0077	0.0414	100	6411.00	0.0031	0.0000	250
23	9450.30	0.0137	0.0000	300	5524.15	0.0014	0.0080	100
24	8818.35	0.0155	0.0000	100	5524.15	0.0014	0.0080	100
25	10895.80	0.1463	0.0376	200	5572.75	0.0047	0.0000	200
26	8057.35	0.0334	0.0127	100	5406.60	0.0014	0.0029	50
27	11037.35	0.0590	0.0430	100	5389.65	0.0014	0.0365	150
28	9666.10	0.0606	0.0132	100	5775.05	0.0052	0.0155	150
29	9765.35	0.0611	0.0415	150	5091.20	0.0018	0.0157	150
30	5858.70	0.0023	0.0017	150	5524.15	0.0014	0.0080	100
Averages	**8054.02**	**0.0303**	**0.0134**	**142**	**5630.78**	**0.0032**	**0.0099**	**132**

Table 3.10: Results for Model 2, Scenario 2

Realization	DE				Bat			
	Cost	Shortage rate	Outdate rate	Function calls	Cost	Shortage rate	Outdate rate	Function calls
1	10601.00	0.0427	0.0259	100	9754.45	0.0529	0.0427	100
2	5315.65	0.0000	0.0071	100	6623.20	0.0004	0.0047	100
3	7607.00	0.0000	0.0071	150	5264.05	0.0004	0.0008	100
4	6691.80	0.0000	0.0071	100	5433.85	0.0004	0.0047	100
5	5314.55	0.0000	0.0071	100	6161.10	0.0004	0.0047	100
6	10477.25	0.0357	0.0000	100	5433.85	0.0004	0.0047	150
7	10833.90	0.0544	0.0420	150	5403.25	0.0004	0.0047	100
8	8822.85	0.0363	0.0050	100	5159.05	0.0004	0.0000	150
9	5078.15	0.0009	0.0000	100	5097.90	0.0005	0.0000	100
10	5350.20	0.0000	0.0071	150	5433.85	0.0004	0.0047	150
11	6239.35	0.0008	0.0000	100	5209.05	0.0004	0.0001	150
12	9395.85	0.0115	0.0000	150	5314.50	0.0004	0.0014	100
13	6530.05	0.0000	0.0071	100	5403.25	0.0004	0.0047	100
14	8768.40	0.0093	0.0000	100	7130.75	0.0104	0.0029	100
15	12528.45	0.1309	0.0000	100	9468.10	0.0672	0.0012	150
16	10521.50	0.0971	0.0000	100	10816.80	0.0542	0.0410	50
17	5715.55	0.0023	0.0077	150	8085.80	0.0153	0.0000	150
18	5291.15	0.0000	0.0071	150	5909.05	0.0004	0.0026	100
19	4977.35	0.0000	0.0000	200	6843.95	0.0004	0.0047	150
20	6317.55	0.0000	0.0000	100	6303.80	0.0095	0.0448	100
21	8728.80	0.0351	0.0000	150	5327.85	0.0004	0.0047	100
22	5451.60	0.0011	0.0135	250	5433.85	0.0004	0.0047	150
23	7438.90	0.0335	0.0000	150	6401.45	0.0149	0.0233	100
24	5345.00	0.0000	0.0071	100	4482.90	0.0009	0.0048	100
25	6042.20	0.0085	0.0000	100	4914.65	0.0004	0.0000	100
26	5160.15	0.0010	0.0000	100	7373.75	0.0123	0.0032	150
27	5350.20	0.0000	0.0071	100	5398.70	0.0004	0.0047	100
28	7197.10	0.0000	0.0000	200	6227.40	0.0007	0.0000	100
29	5195.80	0.0000	0.0000	150	6303.80	0.0095	0.0448	100
30	4945.40	0.0000	0.0000	150	5500.50	0.0010	0.0390	100
Averages	**7107.76**	**0.0167**	**0.0053**	**128**	**6253.82**	**0.0085**	**0.0101**	**113**

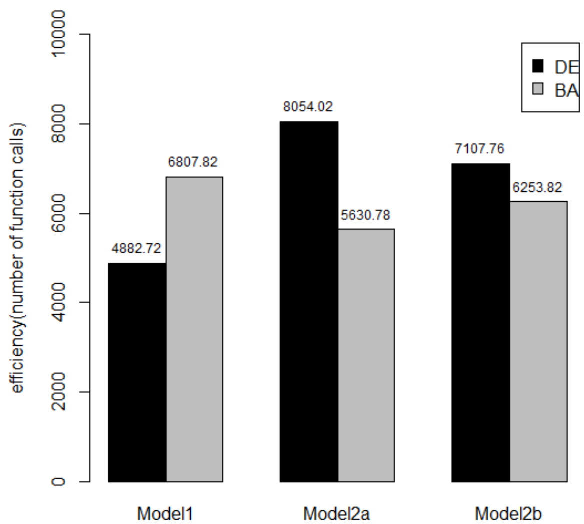

Figure 3.1: Average Yearly Costs associated with solutions from DE and BA

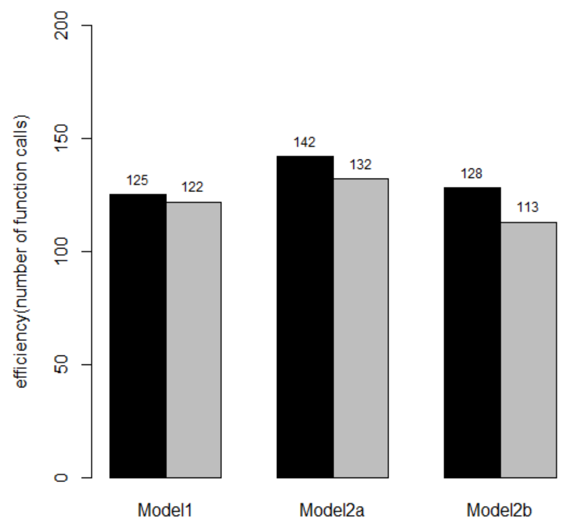

Figure 3.2: Efficiency (average number of function calls)

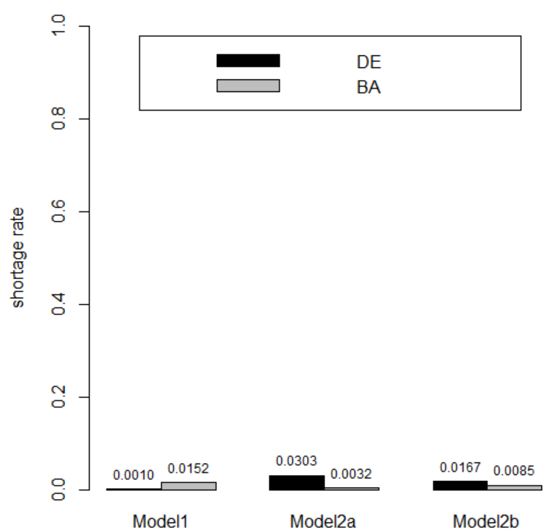

Figure 3.3: Average shortage rates

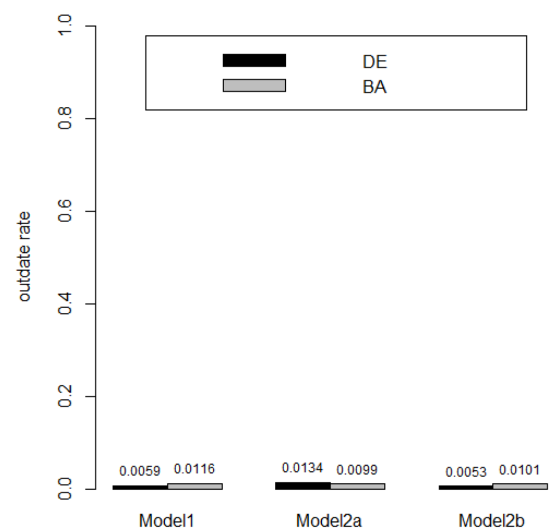

Figure 3.4: Average outdate rates

A number of interesting observations are made from the experimental data presented. Firstly, a glance at Tables 3.8 – 3.10 and Figures 3.1 – 3.3 shows that both DE and BA algorithms quite often find solutions with shortage rates and outdate rates that are within the specified threshold of 0.01 and 0.05 for shortage and outdate rates respectively. Although violations are recorded, in most cases the excess percentage is marginal. The reason for such violations may be the fact that the algorithms terminate too early at an infeasible solution, since they are terminated based on the fact that solution in successive iterations does not change. It is also observed that the average shortage rate and outdate rate corresponding to solutions produced by both algorithms for Model 1 produced are generally low. They even fall below the thresholds explicitly imposed on Model2a and Model2b, which are not imposed on Model 1. One observation is that the cost function of Model1 has four components while that of Model 2 has just two, of which shortage cost which is one of the absent components is the most dominant in magnitude. This may also have contributed to the observed behavior of the algorithms on Model 2 compared to Model 1, by reducing the power of their search strategies to discriminate between hypothetical solutions as well as to explore the solution space.

Concerning efficiency, both DE and BA perform remarkably well, generally performing less than an average of 150 function calls for any of the instances. This would take only fractions of a second to run on the typical personal computer.

3.5.1 Comparing Yearly Costs

Figure 3.1 shows comparison between average yearly costs associated with solutions returned by DE and BA. On model 1 DE outperforms BA, while the reverse is the case on models 2a and 2b.

3.5.1.1 Statistical Test of Significance of Difference in Costs from Model 1

To test whether the observed difference between the costs of DE and BA is statistically significant or not, the two-sample t-test is used. This tests the likelihood that the two samples of the 30 results are from populations that are indeed different or the observed difference is due to chance. Notice that there are two sources of variation: variation in realizations and variation due to inherent randomness in the algorithms.

Null hypothesis: $\mu_{DE} = \mu_{BA}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{DE} < \mu_{BA}$ i.e. the population represented by the sample of 30 costs of DE is significantly better (lower) than that of BA.

p-value: The test is performed using the T.TEST function provided in Microsoft Excel 2013. The reported p-value is 4.6444E-05: almost zero. Since the p-value < 0.05, then at 0.05 significance level (95% confidence level), the null hypothesis can be confidently rejected. It can be safely concluded and generalized that on this problem set, DE is significantly more accurate than BA.

3.5.1.2 Statistical Test of Significance of Difference in costs from Model 2

To test whether the observed difference between the accuracy of DE and BA is statistically significant or not, the two-sample t-test is used. This tests the likelihood that the two samples of the 30 results are from populations that are indeed different or the observed difference is due to chance. Notice that there are two sources of variation: variation in realizations and variation due to inherent randomness in the algorithms.

Null hypothesis: $\mu_{DE} = \mu_{BA}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{BA} < \mu_{DE}$ i.e. the population represented by the sample of 30 costs of BA is significantly better (lower) than that of DE.

p-value: The test is performed using the T.TEST function provided in Microsoft Excel 2013. The reported p-value is 0.042293

Since the p-value < 0.05, then at 0.05 significance level (95% confidence level), the null hypothesis can be confidently rejected. It can be safely concluded and generalized that on this problem set, BA is significantly more accurate than DE.

3.5.1.3 Statistical Test of Significance of Difference in costs from Model 2b

To test whether the observed difference between the accuracy of DE and BA is statistically significant or not, the two-sample t-test is used. This tests the likelihood that the two samples of the 30 results are from populations that are indeed different or the observed difference is due to chance. Notice that there are two sources of variation: variation in realizations and variation due to inherent randomness in the algorithms.

Null hypothesis: $\mu_{DE} = \mu_{BA}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{BA} < \mu_{DE}$ i.e. the population represented by the sample of 30 costs of BA is significantly better (lower) than that of DE.

p-value: The test is performed using the T.TEST function provided in Microsoft Excel 2013. The reported p-value is 7.66976E-10: almost zero.

Since the p-value < 0.05, then at 0.05 significance level (95% confidence level), the null hypothesis can be confidently rejected. It can be safely concluded and generalized that on this problem set, BA is significantly more accurate than DE.

3.5.1 Comparing Shortage Rates

Figure 3.3 shows comparison of average shortage rates associated with solutions produced by DE and BA. DE produces lower average shortage rate than BA on model 1 while the reverse is the case on models 2a and 2b

3.5.1.1 Statistical Test of Significance of Difference in Shortage Rates in solving Model 1

Null hypothesis: $\mu_{DE} = \mu_{BA}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{DE} < \mu_{BA}$ i.e. the population represented by the sample of 30 shortage rates of DE is significantly better (lower) than that of BA.

p-value: 0.04

Since p < 0.0.5, the null hypothesis can be confidently rejected while the alternate hypothesis is accepted, resulting in the inference that DE produces better (lower) shortage rates than BA on model 1.

3.5.1.2 Statistical Test of Significance of Difference in Shortage Rates in solving Model 2a

Null hypothesis: $\mu_{DE} = \mu_{BA}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{DE} < \mu_{BA}$ i.e. the population represented by the sample of 30 shortage rates of DE is significantly better (lower) than that of BA.

p-value: 0.00

Since p << 0.0.5, the null hypothesis can be confidently rejected while the alternate hypothesis is accepted, resulting in the inference that BA produces better (lower) shortage rates than DE on model 2a.

3.5.1.3 Statistical Test of Significance of Difference in Shortage Rates in solving Model 2b

Null hypothesis: $\mu_{DE} = \mu_{BA}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{DE} < \mu_{BA}$ i.e. the population represented by the sample of 30 shortage rates of DE is significantly better (lower) than that of BA.

p-value: 0.1078

Since p > 0.0.5, the null hypothesis cannot be confidently rejected. The implication is that the difference in shortage rates produced by the two algorithms on model 2b is not significant enough.

3.5.1 Comparing Outdate Rates

Figure 3.4 shows comparison of outdate rates associated with solutions produced by DE and BA. DE produces lower average outdate rate than BA on model 1 and 2b while the reverse is the case on models 2a.

3.5.1.1 Statistical Test of Significance of Difference in Outdate Rates in solving Model 1

Null hypothesis: $\mu_{DE} = \mu_{BA}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{DE} < \mu_{BA}$ i.e. the population represented by the sample of 30 outdate rates of DE is significantly better (lower) than that of BA.

p-value: 0.0451

Since p < 0.0.5, the null hypothesis can be confidently rejected while the alternate hypothesis is accepted, resulting in the inference that DE produces better (lower) outdate rates than BA on model 1, although the difference is only slightly significant.

3.5.1.2 Statistical Test of Significance of Difference in Outdate Rates in solving Model 2a

Null hypothesis: $\mu_{DE} = \mu_{BA}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{DE} < \mu_{BA}$ i.e. the population represented by the sample of 30 outdate rates of DE is significantly better (lower) than that of BA.

p-value: 0.1841

Since p >0.0.5, it is inferred that no significant difference is detected between outdate rates produced by both algorithms on model 2a.

3.5.1.3 Statistical Test of Significance of Difference in Outdate Rates in solving Model 2b

Null hypothesis: $\mu_{DE} = \mu_{BA}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{DE} < \mu_{BA}$ i.e. the population represented by the sample of 30 outdate rates of DE is significantly better (lower) than that of BA.

p-value: 0.06

Since p >0.0.5, it is inferred that no significant difference is detected between outdate rates produced by both algorithms on model 2b.

3.5.2 Comparing Efficiencies

Figure 3.2 shows comparison between the measure of efficiency, that is, the function of function calls performed by DE and BA. In all three cases, BA performs less function calls than DE, although the competition is quite close.

3.5.2.1 Statistical Test of Significance of Difference in efficiency in solving Model 1

Similar to the comparison done on accuracy, to test whether the observed difference between the efficiency of DE and BA is statistically significant or not, the two-sample t-test is used. This tests the likelihood that the two samples of the 30 results are from populations that are indeed different or the observed difference is due to chance.

Null hypothesis: $\mu_{DE} = \mu_{BA}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{DE} < \mu_{BA}$ i.e. the population represented by the sample of 30 numbers of function calls of DE is significantly better (lower) than that of BA.

p-value: 0.373606

Since p > 0.05, the null hypothesis cannot be confidently rejected. The implication is that there difference in efficiency between both algorithms is not significantly different. They compete closely.

3.5.2.2 Statistical Test of Significance of Difference in efficiency in solving Model 2a

Null hypothesis: $\mu_{DE} = \mu_{Bat}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{Bat} < \mu_{DE}$ i.e. the population represented by the sample of 30 numbers of function calls of Bat is significantly better (lower) than that of DE.

p-value: 0.041708

Since $p < 0.05$, the null hypothesis can be confidently rejected. The implication is that the difference in efficiency between both algorithms is significant, although slight. They still compete closely, but Bat is more efficient.

3.5.2.3 Statistical Test of Significance of Difference in efficiency in solving Model 2b

Null hypothesis: $\mu_{DE} = \mu_{Bat}$ i.e. there is no difference in the population means

Alternate hypothesis: $\mu_{Bat} < \mu_{DE}$ i.e. the population represented by the sample of 30 numbers of function calls of Bat is significantly better (lower) than that of DE.

p-value: 0.243535

Since $p > 0.05$, the null hypothesis cannot be confidently rejected. The implication is that the difference in efficiency between both algorithms is not significant. They compete closely.

3.6 Summary

In this chapter, DE and BA are adapted for the blood PLT inventory problem. First the problem is described along with relevant models. A description is given for how the basic formulation presented by [11] developed for supply chain inventory optimization for short-shelf-life goods, is modified to capture cost for the blood producer while satisfying practical constraints of limits on shortage and outdate. Full factorial experiments are reported, concerned with the arriving at optimal parameter selection for both algorithms. The performances of both algorithms are also compared. The study shows that both algorithms are effective, efficient and easily amenable to the PLT inventory problem. The two algorithms are shown to be quite easily amenable to the problem without the adoption of complicated discretization operators. This fulfils one important design goal of this research: simplicity, which is valued for industrial software implementation.

With respect to any of the models studied, the quality of the solutions produced by both algorithms is generally good, judged by the associated shortage and outdate rates. The quality appears better when the unconstrained model in which shortage and outdate are captured in the cost function rather than as constraints, although it is noted that this may have more to do with inherent properties of the algorithms rather than the models. Both DE and BA are remarkably efficient in solving the models, requiring less than 150 function calls in all cases, which on the typical personal computer of today, would run in only fractions of a second. In terms of yearly average costs, DE produces solutions that outperform BA on model 1 while the reverse is the case on the two scenarios of model 2. BA proved slightly more efficient than DE.

CHAPTER FOUR

OPTIMIZATION OF DAILY PRODUCTION VOLUME FOR THE BPPIP

4.0 Introduction

In this chapter, a variation of the blood PLT producer operations and model is described. The goal here is to decide on the daily amount of blood PLTs to produce that minimizes the operational costs over an entire planning horizon. GRASP is adapted to solve this problem and results obtained show that the algorithm is computationally efficient, fast and structurally simple for this problem.

4.1 Blood PLT producer Operation and Mathematical Model

The model version used in this chapter is adapted from the work of Blake et al. [9]. The problem here is that of deciding on daily basis, the production volume of PLTs that minimizes shortage and outdate as well as the total costs of operations, not only for the day, but over the planning horizon [9].

At the beginning of each day, production decision is taken based on inventory inspection. The inventory inspection involves observing the total number of PLT units available as well as their age distribution. Whole blood units are collected from donors and prepared for separation into several components. An order cost is associated with the collection of whole blood units. It is also assumed that the production volume decision is taken before the demand for the day is observed. The stock produced on a particular day will be available for supply the next morning. During the day, it is assumed that demand for PLTs from hospitals is satisfied from the inventory according to the FIFO rule. The demand for the day is assumed to be random. If available stock is not sufficient to meet demand, then a shortage cost is incurred to ship in PLTs instantaneously from an outside source. At the end of the day, all PLTs remaining in stock age by one day. Therefore, any PLT in stock with one day to outdate becomes outdated PLT and is removed from the inventory. Accordingly, disposal cost is incurred for the outdated units. Ordered PLT units enter the inventory the next morning as the youngest stock with a minimum of five days to expire. It is assumed here that the inventory has a maximum capacity and that there is a maximum number of units that may be ordered.

The blood PLT producer's problem can therefore be stated as:

$$\min_{y} \sum_{t=1}^{T} \mathrm{C_t}$$

Where

- $\mathrm{C_t} = \mathrm{OC} + \mathrm{HC} + \mathrm{SC} + \mathrm{DC}$
- t = (1, 2, 3,…, T) represents the planning horizon
- Decision variable y is the amount of PLTs to produce in a day
- OC = Cost of placing an order defined as

$$\begin{cases} 0 & \text{if } y = 0 \\ f_o + v_0 y & \text{if } y > 0 \end{cases}$$

Where f_o is the fixed cost of placing an order

v_0 is the variable cost per PLT unit

y is the order

- HC = Cost of holding inventory defined as

$$\begin{cases} 0 & \text{if } x = 0 \\ f_h + v_h x & \text{if } x > 0 \end{cases}$$

Where f_h is the fixed cost of holding any units in inventory

v_h is the variable cost per period per PLT unit

x is the number of PLT units in inventory

- SC = Shortage cost involved in obtaining PLT units from external sources

$$\begin{cases} 0 & \text{if } w = 0 \\ f_s + v_s w & \text{if } w > 0 \end{cases}$$

where f_s is the fixed cost of holding any units in inventory

v_s is the variable cost per PLT unit obtained from external source

w is the number of PLT units obtained from external sources

- DC = Cost of disposing outdated PLT units defined as

$$\begin{cases} 0 & \text{if } z = 0 \\ f_d + v_d z & \text{if } z > 0 \end{cases}$$

Where f_d is the fixed cost of disposing outdated PLT units

v_d is the variable cost per PLT unit disposed

z is the number of PLT units in inventory

- a_i = amount of PLT units that will expire in *i* days

  The vector $a = (a_1, a_2, a_3, a_4, a_5)$ describes the age of all units at hand at the beginning of a day. a_1 represents the oldest units while a_5 are the youngest units in inventory.

- $n_j = \sum_{i=1}^{j} a_i$ representing the total amount of PLT units in inventory at the beginning of a particular day

- d_t = demand on day *t*

- *A* = maximum inventory that may be held at any time including collected units that is still in the preparation process.

- *B* = maximum amount of units that may be ordered

4.1.1 Model Constraints

The Decision variable y which represents the amount of PLTs to produce on a day is constrained to fall between 0 and the minimum of (B), the maximum amount of PLT units that may be ordered and the remaining inventory capacity$(A - n_5)$.

$$y = (0,1,2,..,\min(B,(A - n_5)))$$

The remaining inventory capacity is constrained to be a non-negative number

$$(A - n_5)) \ \geq 0$$

4.2 GRASP for the BPPIP

4.2.1 GRASP Construction Phase

As mentioned earlier, the GRASP solution construction phase consists in randomly selecting an element from the RCL formed by a greedy function. A solution to the blood producer problem consists of production amounts per day of the entire planning horizon. In this work, we generate the vector of possible production amounts and the corresponding vector of costs for day 1 of the planning horizon using the cost functions and inventory and demand data. The RCL is built by cardinality, it consists of only the β best candidate elements (i.e. the β production amounts with the lowest costs). From the RCL, a production amount is randomly selected and added to the partial solution. The possible production amounts and corresponding costs for the next day are then generated from the randomly chosen RCL element and a new GRASP construction phase iteration will be performed i.e. the greedy function is evaluated again and the RCL built again. A complete GRASP solution is achieved when the planning horizon is over.

4.2.2 GRASP Local Search Phase

For each feasible solution at every iteration of GRASP construction phase, the local search phase finds a better solution. It keeps the solution with the lowest total costs of operations as the best solution until a solution with lower costs is found. It returns the best solution when the total number of iterations are over.

The adapted GRASP is illustrated by flowchart in figure 4.1.

4.3 Experimental Results

In this section, the use of the GRASP algorithm to solve the BPPIP was tested on a simple test case. The test data used is presented and the numerical results obtained from the above model are discussed.

4.3.1 Test Data

Tables 4.1 gives a description of the test data used in the model, most of which are obtained from [9]. A summary of the values of the cost parameters also obtained from the study in [9] is given in table 4.2. A 5-day PLT shelf life is assumed and a planning horizon of 6 days is used with the uniformly distributed demand data over the days given as below.

Table 4.1: Model Parameters

Parameter	***Value***
Sizes of RCL – β	[5,10,15]
Demand over six days – d	[17 19 2 19 13 2]
Initial Inventory	[0 0 20 0 0]
Maximum Inventory Size	40

Maximum Order Size per day	20
PLT shelf Life (in days)	5

Table 4.2: Cost Parameters

Parameter	***Fixed***	***Variable***
Order Costs	21.85	0.00
Holding Costs	100.00	0.00
Shortage Costs	0.00	0.05
Disposal Costs	10.00	0.45

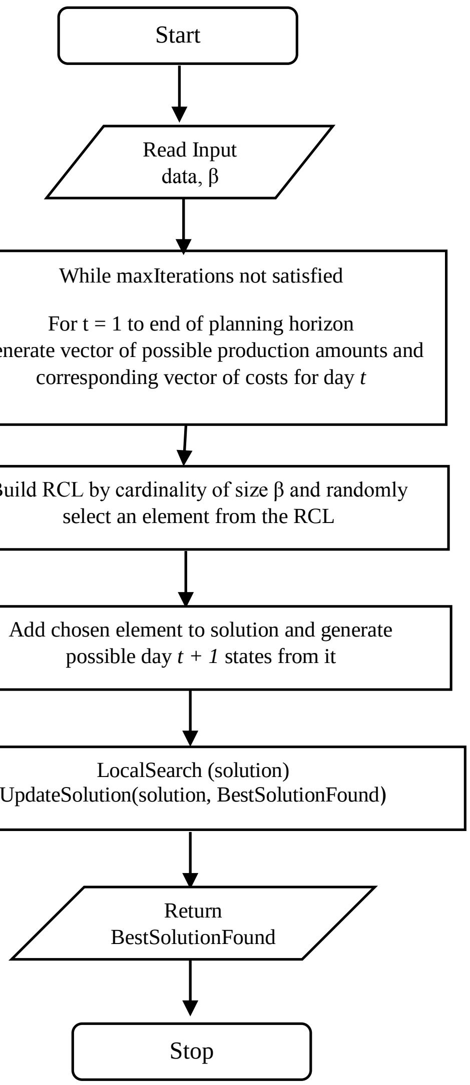

Figure 4.1: Flowchart of GRASP for the BPPIP

4.4 Experimental Results

Simulation was performed on a 2.20GHz PC with 8GB of memory running Windows 7 Professional. The program was written in Matlab 2015 using the data above. Different values of β are used to vary the size of the RCL (5 best candidate elements, 10 best candidate elements and 15 best candidate elements respectively from a total of 21 candidate elements). The number of iterations range from a small value of 50 to a larger value of 500 in steps of 50. The algorithm was run 100 times for each value of β and the results are as shown in the tables and figures below:

Table 4.3: β = 5

Number of iterations	Average best solution over 100 runs (Cost)	Median best solution over 100 runs (Cost)	Average run time over 100 runs in seconds
50	422.056	441.8	0.154288282
100	428.2015	441.85	0.323067651
150	431.1025	441.9	0.374376391
200	419.159	441.7	0.552396771
250	425.075	441.65	0.795072145
300	413.5485	420.05	0.960545434
350	411.2795	420.05	1.004205636
400	405.5115	419.925	1.229097767
450	410.3775	420.025	1.34541556
500	397.484	419.925	1.6243005

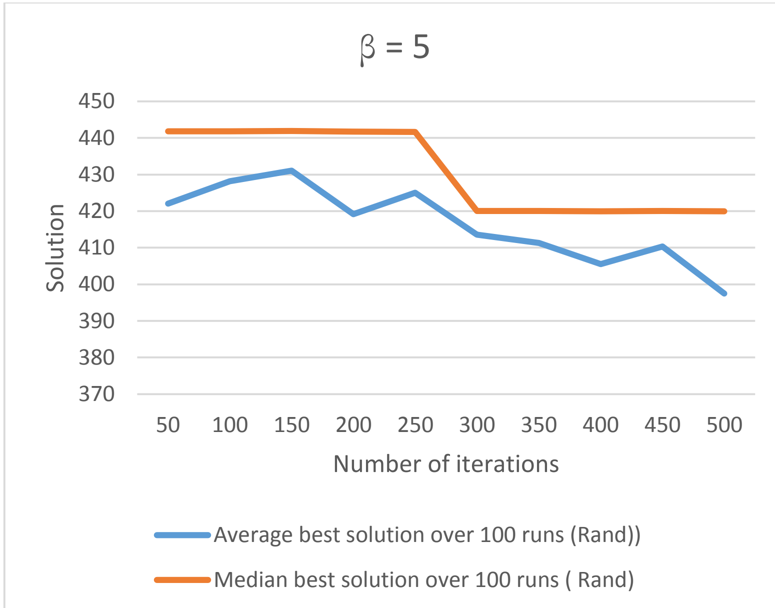

Figure 4.2: Plot of the Average and Median best solutions for $\beta = 5$

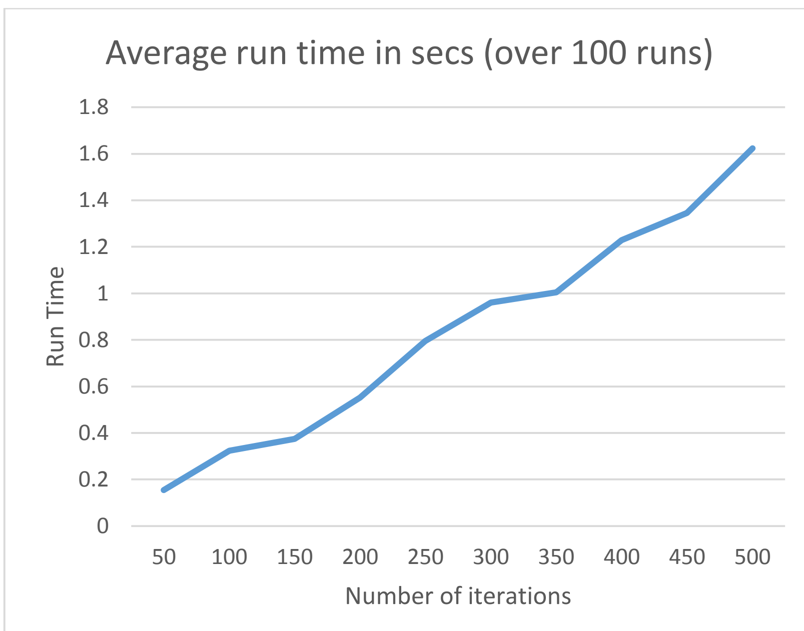

Figure 4.3: Plot of the Average Run Time over 100 Runs for $\beta = 5$

Table 4.4: $\beta = 10$

Number of iterations	**Average best solution over 100 runs (Cost)**	**Median best solution over 100 runs (Cost)**	**Average run time over 100 runs in seconds**
50	426.5255	441.875	0.138349277
100	436.1375	442	0.167026537
150	424.494	441.85	0.29681515
200	422.4855	441.75	0.622425806
250	424.1545	441.7	0.807106747
300	416.845	420.175	1.039582304
350	420.0955	420.275	1.194510796
400	412.76	420.15	1.252349873
450	412.478	420	1.490102701
500	416.928	420	1.742608678

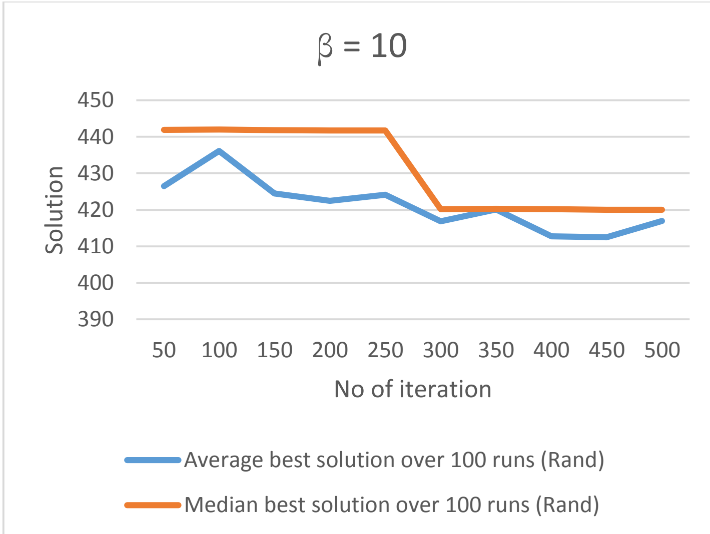

Figure 4.4: Plot of the Average and Median best solutions for β = 10

Figure 4.5: Plot of the Average Run Time over 100 Runs for β = 10

Table 4.5: β = 15

Number of iterations	Average best solution over 100 runs (Cost)	Median best solution over 100 runs (Cost)	Average run time over 100 runs in seconds
50	437.7515	442.1	0.157875976
100	415.7695	441.7	0.320039184
150	406.806	420	0.344628131
200	418.113	441.725	0.525949504
250	426.142	441.65	0.781259956
300	422.219	420.225	0.954247239
350	414.7555	420.1	1.218786461
400	411.895	420.1	0.977898697
450	400.3615	420	0.723163991
500	419.093	420.15	0.806495114

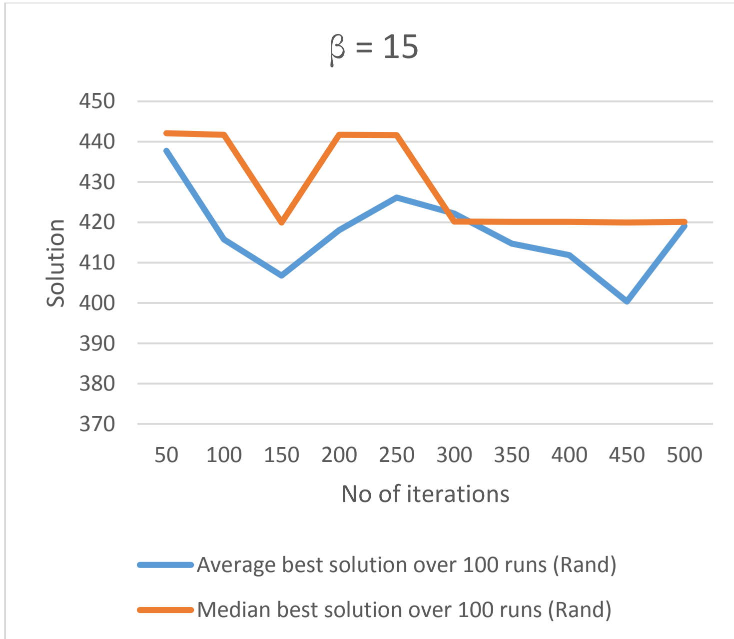

Figure 4.6: Plot of the Average and Median best solutions for β = 15

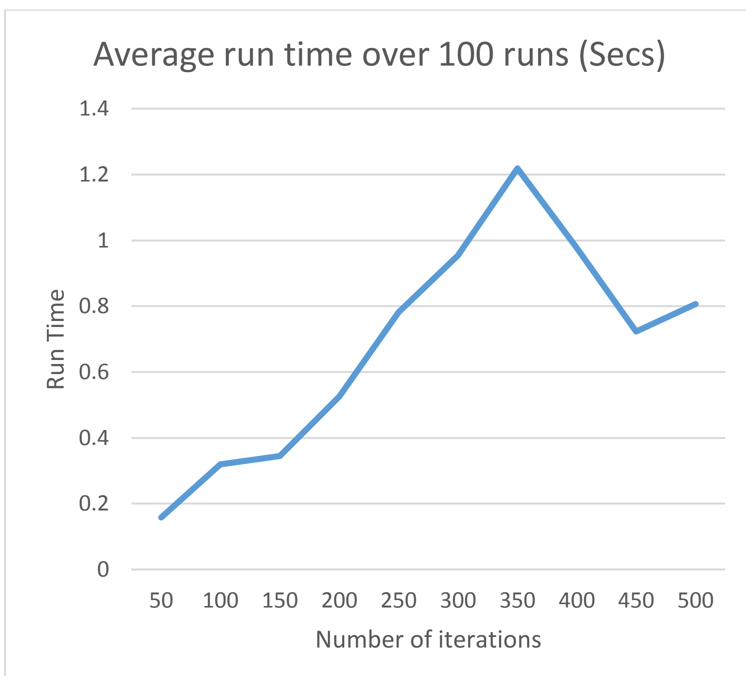

Figure 4.7: Plot of the Average Run Time over 100 Runs for β = 15

It can be observed from the tables and figures for all values of β that the algorithm has a higher probability of arriving at lower costs as the number of iterations increase. $\beta = 15$ seems to produce a more random behavior as the RCL is more random rather than greedy.

The following are also to be noted from the results:

4.4.1 Solution times for all RCL sizes

It is observed that there is a linear relationship between the number of iterations and the run time. The specific relationship or model can therefore be estimated and used to determine the appropriate design choice or predict expected run time for a given choice. For the highest number of iterations in the case study (500), the average run time was between 1.6 and 1.8 seconds for $\beta = 5$ and $\beta = 10$ and even lower for $\beta = 15$. The algorithm is therefore suitable for applications with low time budget.

4.4.2 Efficiency

The algorithm is computationally efficient. Therefore it is capable of handling large problems. It provides facility for efficiently handling the problem of curse of dimensionality, a problem common to large combinatorial optimization problems like blood platelet production and inventory problem. The results show that the computational cost per iteration is quite low. More so, it is capable of arriving at good solutions within a few iterations.

4.5 Conclusion

This chapter presents an adaptation of the GRASP metaheuristic for solving a version of the BPPIP. The combined strength of randomized and adaptive search in the underlying techniques proved efficient as the results show that the computational cost and time per iteration is remarkably low.

CHAPTER FIVE

SUMMARY, CONCLUSION AND RECOMMENDATIONS

5.0 Introduction

This is the concluding chapter of this thesis. The research work is summarized along with evaluation of achievement of research objectives. The direction for future work are highlighted.

5.1 Summary

The problem studied is a practical one with serious impact on society. The need for natural human blood and its derived components remains prevalent despite substantial developments in the area of artificial blood products. Being a critical component of modern therapies, blood platelet inventory management is of high importance in healthcare practice. However, because PLTs have a very short shelf life, their production and inventory management becomes a difficult task. On one hand, production and operational costs are high, while on the other, shortage can result into higher costs of loss of lives. Large outdate rates are also thought to be a threat to the stability of the PLT supply chain because donor participation rates are typically low. The blood PLT producer problem is therefore that of minimizing operational costs while ensuring low shortage and outdate rates.

The prospects of metaheuristics to improve the state-of-the-art in this area are identified. Existing exact methods have been shown to only be able to handle small or moderate sized problems because the required computational expense grows explosively as the problem size increases. Some of these methods have also been reported to be quite difficult to implement in practice. These problems are addressed in this work by the use of metaheuristics. Two different solution approaches for the BPPIP are considered: optimization of order-up-to policy and optimization of daily production amounts. GRASP is explored for the latter, while DE and BA are explored for two different models of the former.

The algorithms are chosen for their attractive properties like efficiency and simplicity. They are successfully applied and shown to be easily amenable to the problems studied. Parameter optimization is also explored for each algorithm to arrive at recommendations for best performance in solving the problem. Comparative study of algorithms is also included.

5.2 Conclusion

For the optimization of the order-up-to policy, DE and BA are successfully adapted for the BPPIP. First the problem is described along with relevant models. A description is given for how the basic formulation presented by [11] developed for supply chain inventory optimization for short-shelf-life goods, is modified to capture cost for the blood producer while satisfying practical constraints of limits on shortage and outdate. The blood PLT producer operation is modeled to capture basic order and inventory holding costs only while shortage and outdate rate were set as constraints. This is because of the findings in literature that shortage and outdate costs are non-tangible, less-concrete and difficult to determine [12] [6].

Factorial experiments are reported, concerned with the arriving at optimal parameter selection for both algorithms. The performances of both algorithms are also compared. The study shows that both algorithms are effective, efficient and easily amenable to the PLT inventory problem. The two algorithms are shown to be quite easily amenable to the problem without the adoption of complicated discretization operators. This fulfils one important design goal of this research: simplicity, which is valued for industrial software implementation.

With respect to any of the models studied, the quality of the solutions produced by both algorithms is generally good, judged by the associated shortage and outdate rates. The quality appears better with the Model 1 in which shortage and outdate are captured in the cost function rather than as constraints, although it is noted that this may have more to do with inherent properties of the algorithms rather than the models. Both DE and BA are remarkably efficient in solving the models, requiring less than 150 function calls in all cases, which on the typical personal computer of today, would run in only fractions of a second. In terms of yearly average costs, DE produces solutions that outperform BA on model 1 while the reverse is the case on the two scenarios of model 2. BA proved slightly more efficient than DE.

For the optimization of daily production amount for the BPPIP, GRASP is shown to be amenable to solve the problem. It is observed that there is a linear relationship between the number of iterations and the run time. The specific relationship or model can therefore be estimated and used to determine the appropriate design choice or predict expected run time for a given choice. For the highest number of iterations in the case study (500), the average run time was between 1.6 and 1.8 seconds for $\beta = 5$ and $\beta = 10$ and even lower for $\beta = 15$. The algorithm is computationally efficient, which makes it suitable for large problems as well as applications with low time budget. It provides facility for efficiently handling the problem of curse of dimensionality, a problem common to large combinatorial optimization problems like BPPIP. The results show that the computational cost per iteration is quite low. More so, it is capable of arriving at good solutions within a few iterations.

Belien and Force [1] in their review pointed out the need for further research to develop fast and robust heuristics to solve the PLT inventory problem as they conclude that “there is no proof yet whether a solution to the PLT ordering problem exists involving simple order-up-to rules resulting in both low levels of outdate and wastage”. The outcomes of this research portend progress for the desired innate in the words of these researchers. Using the solution techniques explored and the models discussed, and data that follow realistic distributions, simple order-up-to rules resulting in both low levels of outdate and wastage, are achieved to a good extent.

5.3 Recommendations for Future Works

The use of metaheuristics in blood PLT inventory management is relatively underexplored. Given the practical nature of this problem, a natural candidate future project would be to apply the models and solution approaches adopted in this study, to real-life data. There is quite a handful of algorithms yet to be studied among this family. It is recommended that future research efforts continue along the direction of this study to explore more of them. Given the efficiency and ease of implementation that metaheuristics usher into this field, it will of great benefit to practitioners to have decision support software developed out of this techniques.

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