METAHEURISTIC APPROACHES FOR MAXIMUM BLOOD COLLECTION PROBLEM

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ABSTRACT

Thanks to recent technological and medical advances, blood components can now be extracted from whole blood after a donation. One of such components is the platelet, which has a wide range of uses in medical fields, including cancer treatment and other surgical procedures. Due to the perishable nature of platelets, it is recommended that the separation occurs within six hours after the donation. Moreover, platelets constitute less than one percent of the whole blood volume, yet they are highly demanded. Thus, it becomes apparent that there is a need for an effective platelet supply chain that meets patient needs. Given the importance of platelets in healthcare, their perishability, and their limited supply, an effective platelet supply chain leans on well-managed whole blood collection operations. In this study, we consider a *blood collection problem* (BCP) focusing on the collection of whole blood donations from the *blood donation sites* (BDS). Different from the basic form of BCP, we consider processing time limit of blood and arbitrary donation patterns of donors as well as relaxing the assumption of assigning each *blood collection vehicle* (BCV) to a set of BDSs. Therefore, we define the *non-clustered maximum blood collection problem* (NC-MBCP) as a variant of BCP. In this problem, the goal is to maximize the total platelets collected from numerous BDSs utilizing a set of BCVs that collect blood from those BDSs and transfer it to a central processing facility before it becomes non-usable for platelet production. In this study, we examine routing decisions for platelet collections while relaxing the clustering requirement from the BDSs, resulting in a significant increase in the complexity of the problem. In order to solve the problem, we propose a hybrid genetic algorithm and an invasive weed optimization algorithm that provide considerable improvements over the best solution in the

literature for the clustered variant of the problem and outperform it by 9.40% improvement by the hybrid genetic algorithm and 9.14% improvement by the invasive weed optimization algorithm on average.

ÖZETÇE

Son teknolojik ve tıbbi gelişmeler sayesinde, kan bileşenleri artık bir bağıştan sonra tam kandan elde edilebilmektedir. Bu bileşenlerden biri de, kanser tedavisi ve diğer cerrahi işlemler de dahil olmak üzere tıp alanlarında geniş bir kullanım alanına sahip olan trombosittir. Trombositlerin çabuk bozulan yapısı nedeniyle, bağıştan sonra altı saat içinde ayrılması önerilmektedir. Ayrıca, trombositler tam kan hacminin yüzde birinden daha azını oluşturmasına rağmen oldukça talep görmektedir. Böylece, hasta ihtiyaçlarını karşılayan etkin bir trombosit tedarik zincirine ihtiyaç olduğu ortaya çıkmaktadır. Trombositlerin sağlık hizmetlerindeki önemi, çabuk bozulabilirlikleri, sınırlı tedarikleri ve etkili trombosit tedarik zinciri, iyi yönetilen tam kan alma işlemlerine dayanmaktadır. Bu çalışmada, *kan bağışı merkezlerinden* (BDS) tam kan bağışlarının toplanmasına odaklanılan bir *kan alma problemi* (BCP) ele alınmaktadır. BCP'nin temel halinden farklı olarak, her bir *kan toplama aracını* (BCV) bir dizi BDS'lere atama varsayımını esnetmenin yanı sıra, kanın işlem süresi sınırını ve donörlerin keyfi bağış modellerini ele almaktayız. Bu nedenle, *kümelenmemiş maksimum kan alma problemini* (NC-MBCP) BCP'nin bir çeşidi olarak tanımlanmaktadır. Bu problemdeki amaç, BDS'lerden kan toplayan ve trombosit üretimi için kullanılamaz hale gelmeden önce bir merkezi işleme tesisine aktaran bir dizi BCV'yi kullanarak çok sayıda BDS'den toplanan toplam trombositleri maksimize etmektir. Bu çalışmada, problemin karmaşıklığında önemli bir artışla sonuçlanan BDS'lerden kümeleme gereksinimini esnetirken trombosit toplamaları için rotalama kararları incelenmektedir. Problemi çözmek için, problemin kümelenmiş varyantı için literatürdeki en iyi çözüm üzerinde önemli iyileştirmeler sağlayan bir hibrit genetik algoritma ve bir istilacı yabani ot optimizasyon algoritması önerilmektedir. Önerilen hibrit genetik algoritma

ortalama %9,40 ve istilacı yabani ot optimizasyon algoritması ile ortalama %9,14 iyileştirme ile daha iyi performans göstermektedirler.

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CHAPTER I

INTRODUCTION

Blood and its products are essential to human existence, and despite all technological advancements, no synthetic equivalent has so far been approved by the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) [1, 2]. Furthermore, donors' blood is the only source of supply for the constant and high blood needs. Patients require blood products during surgical procedures, emergencies, and even everyday medical therapies. According to a study conducted by [3], one out of every seven people who enter a hospital require blood or its products. According to [4], more than 1.9 million new cancer cases are projected in the United States in 2022, with 609,360 people dying as a result of it. During their treatment, the majority of those patients will require *whole blood* (from blood donation) or its components (which are derived from whole blood) dependent on their treatment procedure. Furthermore, victims of accidents and natural catastrophes may require blood for treatment. For example, in the four days following the 2003 Bam earthquake, the average daily amount of blood units transfused in the city was 3.7 times the typical level [5]. Also, a person involved in an automobile accident may require up to 100 units of blood [6]. Thus, healthcare systems rely heavily on blood availability. However, the supply of donated blood cannot meet the growing demand for whole blood and its components.

Despite the fact that only 118.5 million blood donations were performed worldwide in 2018, the majority of these donations were provided by unpaid volunteers. However, in 56 countries, paid donors and family donors account for more than half of the blood supply [7]. Based on country-specific medical needs, [8] estimate the gap between worldwide blood supply and demand. According to their research, there is a shortfall

of more than 100 million units of blood in 119 countries where demand exceeds supply. Consequently, blood donation organizations face a supply-demand imbalance that directly threatens human survival.

There is an ongoing need for blood products around the world; therefore, the *blood supply chain* (BSC) plays a vital role in meeting these needs, which leads to patient survival in hospitals. It is responsible for collecting, extracting, and distributing blood and its products to hospitals and medical centers in a timely manner. In normal circumstances, an effective BSC could increase the performance of the healthcare system. Furthermore, because any long-term interruption, such as a pandemic, can substantially upset the blood supply and demand balance, resulting in a blood supply shortage, an effective BSC could increase the resilience of healthcare systems under abrupt and long-term pressures.

Although *blood supply management* (BSM) is an essential component of the healthcare system, there are certain obstacles to implementing an effective BSM. Despite the efforts of the World Health Organization and the Red Cross around the world, barely 10% of eligible donors donate blood [9]. Due to demographic trends, some academics predict a substantial blood scarcity in the following years [10]. Moreover, there are some requirements for becoming a blood donor. If they are in excellent health, only people over the age of 17 and weighing at least 110 lbs are allowed to donate blood [11]. Donors may also be deferred for a variety of reasons, either permanently or temporarily, based on particular parameters set to take into account the donors' health status better. Furthermore, to avoid health complications such as iron deficiency anemia, a healthy donor should refrain from donating blood for a while following a donation. The minimum interval between whole blood donations varies between 8 and 16 weeks depending on country legislation and donor's gender [12]. This minimum delay is referred to as *deferral time*. A strict limit on the number of donations considerably impacts the schedule of donations made by recurring donors.

A donor's limited ability to donate in a period also reduces the number of available donors and donations within that period, emphasizing the value of BSM.

Another factor that makes the BSM difficult is that blood is classified as a *perishable product*. Perishable products are those that have a short shelf-life or decay quickly [13]. Blood is a complex perishable product since it might expire before or after component extraction. When blood is donated, it should be separated into its essential components within 5-8 hours; otherwise, some of its potential products may perish [14]. This critical period of time from donation to the separation of components is known as the *processing time limit* [15]. Besides, the demand for each blood product makes it necessary to separate whole blood into its components. These derived components, however, are also perishable. Each component of the blood has a special shelf-life to transfuse after being separated. Platelet has the shortest shelf-life of five days. The shelf-life of whole blood is 21-35 days, that of red blood cells is 42 days, and that of plasma is about 365 days [16]. Dealing with time constraints in the procedure is critical for improving the effectiveness of the BSM. Considering the time dependency and perishability of all blood products, it is clear that platelets are the most critical ones.

Platelets are essential in cancer treatments, organ transplant procedures, and other surgical procedures, and in the United States, platelets are required every 15 seconds [17]. Furthermore, it accounts for less than one percent of total blood volume, while to produce one unit of platelet, four to six units of whole blood are needed [18]. It means that the platelet amount derived from one unit of donated blood is insufficient to meet an adult patient's one-unit platelet requirement. The *pooling* of platelets (combining the platelets extracted from four to six donors) is vital to producing a therapeutic dose for an adult patient in the *platelet supply chain* [19]. Therefore, it is critical to improve the effectiveness of the platelet supply chain.

Although donated whole blood from donors at BDSs must be separated into components in less than 18 hours, platelet extraction should be performed within six hours of donation. In light of this constraint, [20] proposes a *vehicle routing problem with time windows* (VRPTW) to minimize the cost of blood collection while collecting a given amount of extractible platelet. [21] also study a vehicle routing problem with multiple interdependent time windows to reduce the cost of blood collection routing when we collect all blood units within a given period which is suitable for platelet production.

Both of the aforementioned studies propose routing problems for platelet production regarding the perishable nature of platelet. [22] present the *maximum blood collection problem* (MBCP), which is a routing problem designed to maximize the total number of platelets collected by focusing on a consistent and continuous pattern of donation. In addition to the complexity of collecting donated blood due to the perishable nature of platelets, they consider a more realistic version where the pattern of donations is arbitrary and not uniform. The arbitrary pattern of donations introduces significant complexity to the problem, and the authors deal with this complexity by using a "cluster-first route-second" approach. In this study, we define a new variant of MBCP in which there is no prior clustering, and due to that, the complexity is even higher. In other words, based on the plan, multiple BCVs can visit the same BDS because it is a non-clustered variant of MBCP. This variant of BCP, which we call *non-clustered maximum blood collection problem* (NC-MBCP), considers both random and discrete-time donation patterns and processing time limit to extract platelets and assigns no BCV to the BDSs beforehand. More specifically, not only can BCVs visit a BDS more than once, but the BDSs can also be visited by more than one BCV. However, this, in turn, increases the complexity of the problem and complicates the timing aspect, which will be explained later in detail. To explain NC-MBCP setting and its complexities further, we show a simple example for

a single-day blood collection of two BCVs as illustrated in Figure 1. To clarify the tour and route terms we are using in this thesis, we define a route as a sequence of BDSs visited by a BCV beginning at the blood processing center and ending at the blood processing center. In order to define a tour, we look at it as a series of routes completed in order by a BCV in a single day.

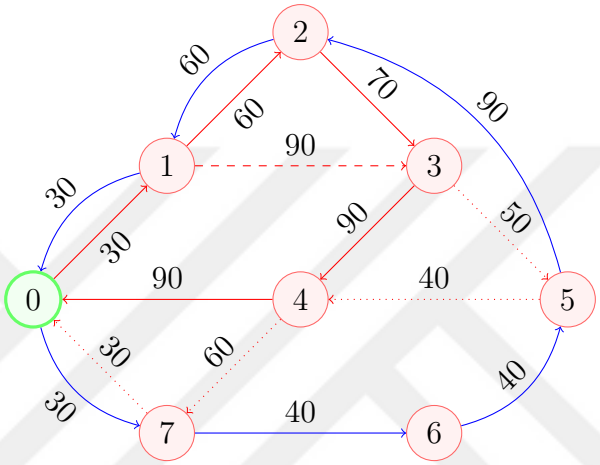

Figure 1: An illustrative example of NC-MBCP.

As illustrated in Figure 1, we assume two BCVs, one blood processing center (denoted by "0"), and seven BDSs (denoted by "1" to "7"). The numbers on the edges represent the time it takes to travel between nodes in minutes. BDSs are open from 10:00 a.m. to 06:00 p.m. If platelet extraction takes one hour at the blood processing center, we have at most five hours to bring the donated blood to the blood processing center after donation; otherwise, any donated blood kept for more than five hours after donation would not be suitable for platelet extraction. It is assumed that donors visit the BDSs according to an arbitrary schedule. Thus, the number of donations and the associated completion time are given based on the scheduled donations in Table 1.

The first column in Table 1 represents the donation completion times. Columns 2-8 show the number of donations received in BDSs 1-7, respectively. As shown in Figure 1, we differentiate the two BCVs by using different colors. First, we investigate

Table 1: The number donations and their completion times for each BDS.

Donation completion time	# donations for each BDS						
	1	2	3	4	5	6	7
10:00	2	3	1	0	0	2	2
10:30	3	2	1	2	0	1	2
11:00	1	0	1	1	0	3	3
11:30	2	2	2	2	2	0	3
12:00	3	0	3	2	0	3	2
12:30	0	3	0	2	3	3	0
13:00	2	1	2	0	0	0	1
13:30	1	3	2	1	3	0	3
14:00	1	1	0	1	0	0	3
14:30	0	0	1	0	1	0	0
15:00	2	0	1	1	0	0	1
15:30	0	2	0	3	0	1	2
16:00	1	2	0	3	3	0	1
16:30	1	3	0	2	1	1	3
17:00	3	2	0	0	2	0	0
17:30	2	3	1	0	2	1	2
18:00	3	2	2	2	2	3	0
Total number of donations	**27**	**29**	**17**	**22**	**19**	**18**	**28**

each BCV's performance separately. In this case, the first BCV departs from the blood processing center at 10:00, visits BDSs 1–4 in order, and returns to the blood processing center at 15:40 (the red arrows). The BCV collected 31 units of blood during this route, 17 units of which could be used for platelet extraction. If we change the route to skip node 2 (the dashed line), the BCV will return to the blood processing center at 15:00 with 23 units of collected blood, all of which would be used for platelet extraction. Therefore, skipping a node may increase the number of extracted platelet units at the end of the day. Furthermore, it is only worth collecting blood units if the processing time limit is not violated. If we add new BDSs to the previous route (the dotted lines), the order would be 1, 3, 5, 4, and 7. In this case, the total number of blood units collected is 47 units, and all of them are suitable for platelet extraction. The removal of BDS 2 and replacing it with BDSs 5 and 7 increase the amount of blood collected by 16 units and platelet production by 30

units. As a result, both adding and removing donations BDSs can significantly alter the effectiveness of blood collection.

Separately examining the second BCV shows that it begins a route from the blood processing center toward the BDSs at 7, 6, 5, 2, and 1, then returns to the blood processing center (the blue lines). The BCV begins the route at 10:00 and ends at 14:50 by returning to the blood donation center. During this route, the BCV collects 38 units of blood, all of which can be used for platelet production. Therefore, we could improve a BCV's effectiveness in a route even if we changed BDSs to visit and the order of visit those BDSs.

It is even more challenging to compare the performance of two BCVs collecting blood rather than just one. Because some routes by different BCVs may intersect, the collection of one BCV may have an effect on the performance of the other one. In our example, the first BCV begins collecting blood units at 10:00 in a red line route with orders 1, 3, 5, 4, and 7, then returns to the blood processing center at 15:00. The second BCV begins the blue-lined tour at 10:00 and returns to the blood processing center at 14:50. Three nodes in this example are visited by both BCVs: 1, 5, and 7. Node 1 is to be visited by the first BCV first, while nodes 5 and 7 are to be visited by the second BCV first. In this case, the first BCV collects 41 units of blood, while the second BCV collects 33 units suitable for platelet extraction. Using only one BCV for the same tour results in 47 units for one tour and 38 units for another, whereas using two BCVs at the same time results in 74 units of blood suitable for platelet extraction.

Another aspect of the problem's complexity is determining the best time to begin a tour. The starting time can have a significant impact on the collected blood units and extractible platelet units. If the first BCV in the above example begins the initial tour with order 1, 2, 3, and 4 at 11:00 instead of 10:00, it will return to the blood processing center at 16:40, with 42 units of collected blood but with 18 units

suitable for platelet extraction. The above example illustrates the dependence of the number of extractible platelets collected in a day on departure time from the blood processing center, the number and order of nodes to visit in a single tour, the order of tours, and the interlude between tours in NC-MBCP. In fact, NC-MBCP is a complex routing problem with a "time dimension." As part of NC-MBCP, BCVs perform tours during the day, while a single BCV may cross routes with other BCVs along its route. The time between visits to the crossed part of routes by different BCVs can affect the amount of collected blood by the BCV. However, any start time of any route can produce a different solution. Thus, in this problem, time aspects of routing are affecting the solutions from several points. In NC-MBCP, the objective function maximizes collected blood units suitable for platelet extraction. Besides, in classic routing problems, a BCV visits a node only once. MBCP allows any BCV to visit a node multiple times due to the cumulative nature of blood donations. In addition, NC-MBCP has a six-hour limit for any blood unit after donation to be collected, making it more complicated than other routing problems.

In this thesis, we create a framework for making routing decisions without clustering BDSs first. Since clustering is removed from this framework, the degree of freedom for the BCVs grows, resulting in higher-quality solutions by collecting more donations. Nonetheless, removing clustering expands the feasible region, thus raising the difficulty level. To this end, as solution methods, we propose *invasive weed optimization* (IWO) algorithm and a *hybrid genetic algorithm* (HGA).

The algorithm greedily constructs tours for the vehicles one after the other in a backward manner. Following that, the previous node to be visited is determined based on the highest possible collectible processed blood. To determine the total number of donations that can be collected from a site, say i, the donations between $t-K$ and $t-t_{i0}$ are considered assuming that the vehicle arrives at the BDS at time t. The BDS with the highest possible amount is then selected as the node for the

current time.

These solution methods are proposed based on BDSs diversity and processing time limit to optimize collection operations to extract platelets. To evaluate the performance of the proposed heuristic algorithms, we compare them against a solution method proposed by [22] as the best solution for MBCP in the literature. The proposed algorithms yield better solutions in almost all cases when compared to the aforementioned algorithm. The main contributions of our study are as follows:

- We remove the clustering assumption from MBCP to obtain better solutions.
- We propose effective heuristic algorithms to maximize the amount of collected blood that can be used for platelet production without the need for BDSs to be clustered and outperform the clustered solutions by 9.40% by HGA and 9.14% by IWO on average.

The remainder of this thesis is organized as follows. Section 2 is a systematic review of the relevant literature to determine the state-of-the-art methods in MBCP. Section 3 presents the problem definition as well as the mathematical model of the problem. Section 4 discusses the solution approaches proposed to solve the problem. Section 5 focuses on testing and comparing the performance of the proposed heuristics against both each other and a benchmark algorithm from the literature. Finally, concluding remarks are provided in Section 6.

CHAPTER II

LITERATURE REVIEW

The related literature explores BCP from different perspectives. For instance, [23] study staff scheduling for BDSs based on predefined scenarios. In this study, the authors consider both a deterministic demand model and a stochastic demand model of blood donors based on the number of donors arriving at BDSs. Their findings reveal that the proposed models require fewer staff when facing adequate staff scenarios and fewer donors when facing inadequate staff scenarios. Also, [24] analyze strategies for managing the blood inventory system using discrete-event simulation in order to determine how to order blood, resulting in a reduction in blood shortages and wastage in hospitals. In this study, we focus on two main categories of BCP literature: BSC and vehicle routing for BCP. Hence, the literature is reviewed under two separate parts in this section.

2.1. Blood Supply Chain

[25] first mentions BSM in a dissertation on perishable commodities inventory control. [26] investigates optimal and sub-optimal order policies for perishable products such as blood, taking both deterministic and stochastic demand into account. [27] investigates the theory and application of blood inventory management for the first time by introducing the BSC. BSC has also received much attention in recent years. We refer the reader to studies by [28], [29], and [30] for recent reviews of the literature on BSC.

[31] present a mixed-integer linear programming model to minimize the total cost of the platelet supply chain network while including costs of establishment and repositioning of BDSs, blood units transportation, platelet production, and inventory costs.

[32] synthesize the BSC literature and categorize it into different decision-making environments, issues related to the design of the blood supply chain, operational processes, and planning decisions.

[33] investigate a platelet allocation problem inspired by an experience at an Indian hospital. First, they consider the issue from the perspective of a social planner. Then, using simulation and sensitivity analysis, they propose a heuristic method based on revenue management principles to maximize total social benefit in a highly supply-constrained environment and evaluate the heuristic. Performance comparison shows that their policy outperforms sequential first-come-first-serve and two fixed proportion-based rationing policies. [34] consider a supply chain network optimization model for managing BDSs, testing and processing centers, and the distribution sector in a complex BSC. They propose a network model for determining the optimal allocation of perishable blood products in order to reduce blood waste and excess costs. [35] address a bi-objective, two-stage robust optimization model for designing a disaster-resilient BSC. This model aims to minimize the time and cost of delivering blood to consumers while taking into account the risk of a disaster and the resulting disruptions in the BSC infrastructures. They apply the model to a blood bank in Jordan and solve the problem with a Lagrangian heuristic method.

[36] propose a bi-objective mixed-integer linear mathematical programming model to design a BSC that takes ABO blood group compatibility into account in order to maximize unsatisfied demand while minimizing total cost. [37] present an integrated age-differentiated platelet supply chain problem with three deterministic and two stochastic models to manage blood collection and platelet production to keep shortages at a minimum. They then propose a bi-objective model based on first-in-first-out and last-in-last-out policies to minimize total cost while maximizing platelet freshness. [38] consider a bi-objective model that establishes a trade-off relationship between network costs and platelet freshness while accounting for the uncertainty of

network facility performance. Their robust model results in a significant reduction in the level of relative regret while disrupting the network.

Some of the relevant works associated with our study include reducing blood product shortages and waste in BSCs. [39] propose that cost minimization is not an appropriate goal for platelet inventory and ordering policy. They concentrate on a model for ordering platelets that consider scarcity and waste at an acceptable rate in order to simplify the problem and its solution. The authors test the model's applicability using practical scenarios based on demand profiles from nine different hospitals in Ontario, Canada. They demonstrate that their model is better suited to stable platelet demands rather than variable platelet demands. [40] make recommendations on blood inventory management to minimize red blood cell losses due to time expiry in hospital transfusion laboratories while keeping enough stock to meet blood demands. [41] create a mixed-integer stochastic programming model to determine the platelet ordering policy, which includes the amount and the time of ordering. This model's objective function is to minimize platelet wastage while maintaining a specified service level. [42] use a multi-objective stochastic integer programming model to determine BSC policies. This model's goal is to reduce wastage and platelet shortages. Furthermore, they propose a modified genetic algorithm to solve the model for large-size problems. [43] address a two-stage stochastic programming model to reduce blood wastage and shortage costs in the face of uncertain hospital demand from a central blood bank.

Some studies look into the scheduling of blood donor appointments as well. [44] deal with the modeling and simulation of blood collection systems in France, with a focus on the scheduling of plasma and platelet donors. [45] present a mixed-integer linear programming model for a blood collection problem to maximize platelet production considering the processing time limit. They propose an integrated blood collection and appointment scheduling framework for the problem. In order to solve

the problem, they propose an integer programming heuristic algorithm. [46] present the blood donation appointment scheduling problem and propose a mixed-integer linear programming model to balance the production of blood units of different types so that they have an adequate amount on hand during the day while minimizing the penalty of weighted dispersion.

2.2. Vehicle Routing for Blood Collection Problem

Another major body of literature on BCPs focuses on the routing aspect of BCVs, defining their problems as a VRPTW. The VRPTW is perhaps the most well-known extension of VRP, in which each client should receive service during an associated time window. To solve the VRPTW, a variety of heuristics and meta-heuristics methods are proposed [47, 48, 49, 50].

[20] presents the first study that focuses on vehicle routing operations in BSC. The author of this study constructs a VRPTW model for collecting blood from BDSs. They solve the problem according to a lower bound on the number of extractible platelets from the collected blood. Using column generation, they solve the problem. In a real-life case study in the United States, his proposed method reduces collection costs by up to 60%. [51] consider a multi-objective fuzzy mathematical programming model for bloodmobile collection systems. The goal of this model is to maximize the amount of blood collected while minimizing operational costs. In order to study the BCV's routing problem, they present a VRPTW and formulate it as a clear multi-objective linear programming model. They then use a tailored simulated annealing algorithm to solve it. [52] present an integer programming model for a BCP to determine the number of BCVs to operate while minimizing the distance traveled by the BCVs concurrently. To find the best solution, they use the CPLEX solver and the branch-and-price algorithm. [53] address a new model for a selective VRP to determine the best tours of the bloodmobiles and shuttles, as well as their

lengths of stay at each stop. The proposed model aids in the collection of blood from bloodmobiles while accounting for logistic costs. In addition, they propose another model to maximize the total number of blood collected in a given time frame. [54] formulate the donation collection problem as a variant of the network routing problem using mixed-integer linear programming. They propose several heuristic policies to solve the problem and demonstrate that these heuristic policies perform well. [22] analyze routing decisions in MBCP and propose an integrated clustering and routing framework to collect and process the maximum number of donations for platelet production. They cluster the BDSs so that only a single BCV serves the BDSs in each cluster. They propose several heuristic algorithms for the routing step, two of which are greedy and others based on an a priori algorithm to create and select tours.

Another problem focusing on routing to maximize the collection is *Team Orienteering Problem* (TOP) which is a general form of orienteering problem. [55] first introduces the Orienteering problem as maximization of rewards collected from nodes by finding a route for a vehicle. [56] present a multiple tour maximum collection problem called TOP. They seek to maximize their total collected profit by meeting a time limit for each vehicle. The main differentiating factor between TOP and MBCP is the time limit. Under the MBCP, the donated blood in each BDS (node) has a limited amount of time to be processed in the blood center. TOP, however, limits the amount of time each vehicle can travel on edges and visit nodes. Accordingly, due to the processing time limit of the donated blood, the rewards in the MBCP change over time. The rewards collected from a BDS depend on the time the BDS visited and when it arrived at the blood processing center. Changes in reward behavior have a significant impact on the order in which the nodes in the route are visited. As well, in the MBCP some BDSs may be visited more than once to collect more rewards due to the processing time limit for donated blood.

CHAPTER III

PROBLEM DEFINITION

This section provides a formal definition of NC-MBCP, and it lists assumptions for the problem. We assume that the daily donations at BDSs are known and the BDSs have a fixed location. Table 2 shows the sets, parameters, and decision variables.

Table 2: Nomenclature for NC-MBCP

Sets	
V	set of BDSs ($\{1, 2, \ldots, n\}$) – indexed by i
V_0	set of blood processing center and BDSs ($\{0, 1, 2, \ldots, n\}$) – indexed by i
E	set of edges connecting the nodes in V_0 – indexed by (i, j)
F	set of vehicles ($\{1, 2, \ldots, M\}$) – indexed by k
$\mathcal{T}$	set of routes performed by a vehicle in a single day ($\{1, 2, \ldots, L\}$) –indexed by m
T_i	set of discrete time units for BDS i ($\{a_i, \ldots, b_i\}$) –indexed by t
Parameters	
t_{ij}	travel time on edge (i, j)
a_i	opening time associated with BDS i ($a_i \in Z^+$)
b_i	closing time associated with BDS i ($b_i \in Z^+$)
T_s	start time of planning horizon zone ($T_s := \min_{i \in V}\{a_i\}$)
T_e	end time of planning horizon zone ($T_e := \max_{i \in V}\{b_i\}$)
d_t^i	number of blood donations at time t at BDS i
K	processing time limit
H	a large enough number
θ	temperature $(0, ..., \theta_0)$
Decision variables	
x_{mk}^{it}	1, if donations completed at time t at BDS i are picked up in tour m of vehicle k; 0, otherwise
y_{ijmk}	1, if location j is visited after location i in tour m of vehicle k; 0, otherwise
z_{mk}	1, if vehicle k performs tour m; 0, otherwise
e_{mk}	arrival time of vehicle k at the blood processing center after completing tour m
v_{imk}	arrival time of vehicle k at BDS i in tour m

Given a graph $G = (V_0, E)$ where V_0 is the union of the set of blood processing center (0), V is the set of BDSs, and E is the set of edges that connect the nodes in V_0. BCV starts a tour from the blood processing center and collects the donated blood from a subset of V and travels on a combination of edges in E with a given order in t_{ij} units of time for each edge (i, j), and finally, returns to the blood processing center. We assume that the travel times satisfy the triangle inequality. There are opening (a_i) and closing (b_i) times associated with each BDS i for $i \in V$, t where a_i, $b_i \in Z^+$. BDS i donations are assumed to occur at discrete times between a_i and b_i. The start time (T_1) and end time (T_2) of the planning horizon are defined as follows: $T_1 := \min_{i \in V} a_i$, $T2 := \max_{i \in V} b_i$. We use d_t^i $(\in Z^+)$ to denote the number of blood donations at time $t(\in a_i, ..., b_i)$ at BDS i. The BCVs are responsible for collecting donated blood and delivering it to the blood processing center within K units of time. Otherwise, the collected blood units, which are delivered to the blood processing center later than the processing time limit units of time after donation, cannot be used for platelet production. Thus, the objective of NC-MBCP is to collect and process as much blood as possible within K time units of donation time, with no restrictions on BCVs visiting the BDSs. In other words, the primary distinction between NC-MBCP and MBCP is a greater degree of freedom for a BCV in visiting BDSs in NC-MBCP. Hence, the difference between the mathematical model we proposed and the one proposed by [22] is the constraint dealing with the clustering of BDSs. In fact, we do not limit a BCV to perform its tour on a single cluster of BDSs daily. Note that in this mathematical model, we need an upper bound on the number of tours for any BCV to perform during the planning horizon. We use the upper bound proposed by [22], based on the minimum distance to the depot for any given BDS as follows: $L = \frac{T_s - T_e + 2K}{\min\limits_{i \in V}\{2t_{0i}\}}$.

In the next, we present the mathematical model, using the sets, parameters, and decision variables presented in table 2.

$$\max \quad \sum_{m\in\mathcal{T}}\sum_{k\in F}\sum_{i\in V}\sum_{t\in T_i} d_i^t x_{mk}^{it} \tag{1}$$

$$\text{s.t.} \quad \sum_{j\in V_0\setminus\{i\}} y_{ijmk} = \sum_{j\in V_0\setminus\{i\}} y_{jimk} \qquad \forall i,m,k \tag{2}$$

$$\sum_{j\in V_0\setminus\{i\}} y_{ijmk} \le 1 \qquad \forall i,m,k \tag{3}$$

$$\sum_{j\in V} y_{0jmk} + \sum_{j\in V} y_{j0mk} = 2z_{mk} \qquad \forall m,k \tag{4}$$

$$z_{mk} \le z_{m-1,k} \qquad \forall m,k \tag{5}$$

$$\sum_{i\in V_0}\sum_{j\in V_0} y_{ijmk} \le H z_{mk} \qquad \forall m,k \tag{6}$$

$$v_{imk} + t_{ij} \le v_{jmk} + H(1-y_{ijmk}) \qquad \forall i,j,m,k \tag{7}$$

$$e_{m-1,k} + t_{0i} \le v_{imk} + H(1-y_{0imk}) \qquad \forall i,m,k \tag{8}$$

$$v_{i1k} \ge a_i \qquad \forall i,k \tag{9}$$

$$a_i + H\sum_{j\in V_0} y_{ji1k} \ge v_{i1k} \qquad \forall i,m,k \tag{10}$$

$$v_{i,m-1,k} + H\sum_{j\in V_0} y_{jimk} \ge v_{imk} \qquad \forall i,m,k \tag{11}$$

$$v_{imk} \ge v_{i,m-1,k} \qquad \forall i,m,k \tag{12}$$

$$v_{imk} + t_{i0} \le e_{mk} + H(1-y_{i0mk}) \qquad \forall i,m,k \tag{13}$$

$$x_{mk}^{it} \le \sum_{j\in V_0} y_{jimk} \qquad \forall i,m,k,t \tag{14}$$

$$\sum_{m\in\mathcal{T}}\sum_{k\in F} x_{mk}^{it} \le 1 \qquad \forall i,t \tag{15}$$

$$e_{mk} - K \le t + H(1-x_{mk}^{it}) \qquad \forall i,m,k,t \tag{16}$$

$$v_{imk} \ge t - H(1-x_{mk}^{it}) \qquad \forall i,m,k,t \tag{17}$$

$$x_{mk}^{it} \in \{0,1\} \qquad \forall i,m,k,t \tag{18}$$

$$y_{ijmk} \in \{0,1\} \qquad \forall i,j,m,k \tag{19}$$

$$z_{mk} \in \{0,1\} \qquad \forall m,k \tag{20}$$

$$v_{imk} \ge 0 \qquad \forall i,m,k \tag{21}$$

$$e_{mk} \ge 0 \qquad \forall m,k \tag{22}$$

The objective function (1) seeks to maximize the total number of donations collected and processed. Constraints (2) and (3) guarantee that any BDS is only visited once in a single tour by a given BCV. Constraints (4) state that all BCVs must end their tour at the blood processing center. Constraints (5) ensure that a BCV cannot begin a new tour if it has not completed the previous one. Constraints (6) refer to a logical constraint emphasizing that a BCV cannot visit any of the BDSs in a tour if the tour is not performed by the BCV. The visiting time of each BDS in each tour performed by each BCV is determined by constraints (7) to (13). Constraints (14) and (15) ensure that a site's donation can only be collected once and that it can be collected by a BCV visiting the BDS. Constraints (16) and (17) impose the visiting time of a BDS in a tour as well as the completion time of this tour if a donation is picked up from this BDS on this tour at a specific time. Finally, constraints (18) to (22) impose binary, integer, and non-negativity constraints on decision variables.

CHAPTER IV

SOLUTION APPROACHES

The substantial part of NC-MBCP is that different BCVs can collect blood at the same time from a given BDS. This event can cause overlaps between visited BDSs by different BCVs. Since the BCVs are allowed to perform concurrently, the problem becomes more challenging. The collections performed by any BCV during a BDS visit would affect the amount of available donated blood units at the BDS during subsequent visits by other BCVs due to the overlap in visits.

To meet this challenge, we present a framework to count the collected blood amount for each BCV separately from the other BCVs in order, considering overlaps of BCVs on visiting BDSs. This concept reduces the multi-vehicle problem to several single-vehicle sub-problems with overlaps. This framework finds the near-optimal solution for any sub-problem in order, but each sub-problem affects the amount of available donated blood units at the visited BDSs. Therefore, according to the order of sub-problems, the framework updates the amount of available donated blood units of BDSs for the next sub-problem based on the collection performed in the current sub-problem. Finally, the framework aggregates the collected blood units appropriate for platelet extraction for each vehicle and solves the multi-vehicle problem, which is NC-MBCP. We propose two meta-heuristic approaches to address NC-MBCP: an *invasive weed optimization* (IWO) algorithm and a *hybrid genetic algorithm* (HGA).

4.1. Hybrid Genetic Algorithm

The genetic algorithm is a powerful method for solving natural selection-based optimization problems. In this study, we propose HGA for NC-MBCP pseudocode of

which is presented in Algorithm 1. We call it a hybrid algorithm because it is a combination of algorithms. HGA collects as many blood units per BCV as possible using a genetic algorithm while considering the processing time limit for platelet production. Due to the fact that there are several BCVs, we aggregate collected blood units using a greedy algorithm. As a final step, we use a *simulated annealing algorithm* (SA) to improve the solution.

Algorithm 1 *Hybrid Genetic Algorithm*

$\mathcal{N} := min$(Number of sufficient routes,Number of feasible routes)
$\mathcal{R}$:= Set of routes with one BDS
while $Size(\mathcal{R}) \leq \mathcal{N}$ **do**
  $\mathcal{R} := \mathcal{R}$+Set of routes with one more BDS than $\mathcal{R}$
end while
$Size(\rho) := 10 \times \ln(Size(\mathcal{R}))$
G :=Number of generations
for $k \in F$ **do**
  ρ := Random tours from $\mathcal{R}$
  t_ρ := Random departure times for ρ
  for $g \in G$ **do**
    $Rand$:=Random rational number$\in (0, 1)$
    if $Rand \leq MutationRate$ **then**
      $Q := \alpha \times Size(\rho)$
      Replace Q weakest tours of ρ with Q random tours from $\mathcal{R}$
    else
      Select $Parent1$ & $Parent_2$ by Roulette Wheel Selection
      Divide randomly $Parent_1$ to $Parent_1(a)$ & $Parent_1(b)$
      divide randomly $Parent_2$ to $Parent_2(a)$ & $Parent_2(b)$
      $Offspring_1 := Parent_1(a) + Parent_2(b)$
      $Offspring_2 := Parent_1(b) + Parent_2(a)$
      for $i \in \{1, 2\}$ **do**
        $t_{Offspring_i}$:= random departure times for $Offspring_i$
        if $Offspring_i$ with $t_{Offspring_i}$ is feasible **then**
          $\mathcal{L} := \rho_{minFitenss}$
          if $Fitness_{Offspring_i, t_{Offspring_i}} \geq Fitness_{\mathcal{L}, t_\mathcal{L}}$ **then**
            Replace $\mathcal{L}$ of ρ with $Offspring_i$
          end if
        end if
      end for
    end if
  end for
  $\rho^* := \rho_{maxFitness}$
  $t_{\rho^*} := t_{maxFitness}$
  $\theta := \theta_0$
  while $\theta \geq 0$ **do**
    $Rand$:= Random number($\in \{-1, +1\}$)
    $t_{temp} := t_{\rho^*} + 5\% * t_{\rho^*} * Rand$
    if $Fitness_{\rho^*, t_{temp}} \geq Fitness_{\rho^*, t_{\rho^*}}$ **then**
      $t_{\rho^*} := t_{temp}$
    else if $e^{-\frac{Fitness_{\rho^*, t_{temp}} - Fitness_{\rho^*, t_{\rho^*}}}{\theta}} > 0.9$ **then**
      $t_{\rho^*} := t_{temp}$
      $\theta := \theta - 1$
    end if
  end while
  $MaximumCollected_{vehicle} := Fitness_{\rho^*, t_{\rho^*}}$
  Update blood collection schedule regarding ρ^* & t_{ρ^*}
end for
$MaximumCollected := \sum_{vehicle \in Vehicles} MaximumCollected_{vehicle}$

In HGA, the first BCV follows the best routes available to collect the maximum blood units while keeping the processing time limit in mind for the platelet extraction process. When the first BCV completes its tour, the following BCV begins its tour on the same day, but it is assumed that there is no BCV performing before it, and it is the first BCV, while the collected blood units by the first BCV are subtracted from the BDS's inventory. For example, if the first BCV's tours run from 10:30 to 14:30, the second BCV can run from 10:00 to 12:00. The only difference between the first and second BCVs is that the collected blood units by the first BCV are not available for the second one. We allow the BCVs to complete tours simultaneously in a day. To simplify the simultaneous collection, we consider counting collected blood units by BCVs independently and sequentially in the solution method. Moreover, BCVs are free to travel to any BDS without being restricted. In other words, the BCVs are collecting blood units simultaneously, just as they would in the real world, but we count the blood collected by each BCV individually and sequentially. Thus, taking into account the remaining uncollected blood units, the second BCV completes its tour by a greedy collection of blood units while considering the processing time limit, and completes its task for the day. The same procedure is also applied to the rest of the BCVs.

4.1.1 Solution Encoding

To establish HGA, we first define the solution encoding so that it fits NC-MBCP. Figure 2 shows a simple example of this encoding structure for a single BCV problem. The illustration depicts a chromosome with several genes. Each gene represents a different route performed by the BCV. Thus, the entire chromosome is a series of routes that we call a tour.

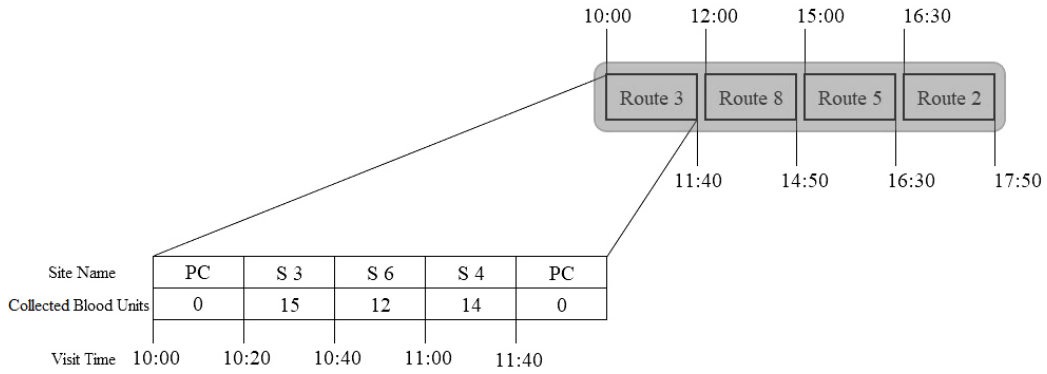

Figure 2: A sample chromosome encoding of a solution

The entire chromosome shown in Figure 2 is formed by combining four routes. The BCV begins the tour by Route 3, which is the chromosome's first gene, at 10:00 a.m. It takes 100 minutes to visit BDSs on Route 3. The blood processing center is denoted by PC in Route 3 and S3, S6, and S4 denote the BDSs. At 10:00 a.m., the BCV begins its journey from the blood processing center to BDS S3. It continues its journey to BDS S6 after collecting 15 units of blood at 10:20. At 10:40, it arrives at BDS S6 and collects 12 units of blood. The BCV then moves toward BDS S4. Finally, at 11:40 a.m., the BCV returns to the blood processing center, having collected 41 units of blood from the BDSs visited during the tour. After 20 minutes of rest, the BCV proceeds to Route 8, following the same procedure as in Route 3. Then it proceeds to the following route until all routes have been executed. At 17:50, the BCV's final route of the tour is completed by traversing Route 2, and all of the collected blood units for platelet production are calculated for the chromosome. Therefore, each chromosome represents a solution for a BCV, and multiple chromosomes can be a solution for NC-MBCP with multiple BCVs.

Since the main goal of solving NC-MBCP is the maximization of platelet production, considering a six hours time limit between donation and platelet production in which one hour of the six hours should be assigned for the platelet extraction process in the blood processing center seems essential in the example shown in figure 2. Thus,

all donated blood units before 11:30 a.m. at BDSs visited on Route 5 cannot be used for platelet production. Likewise, for Route 2, Route 8, and Route 3 any blood units donated before 12:50 a.m., 9:50 a.m., and 6:40 a.m., respectively, are inappropriate for platelet extraction. Moreover, some blood units lose the chance to be used in platelet production because the donations after the visiting time of each BDS will not be collected.

4.1.2 Initial Population

In this section, we explain the process we use to build an initial population using possible good routes. Because allowing BCVs to try all feasible combinations of feasible routes would take a significant amount of time, we use an algorithm to generate a set of possible routes that is a subset of the feasible routes set. Longer routes, in fact, require a large proportion of the available daily time of BCVs. Longer routes have a lower chance of creating an optimal tour by connecting to each other, whereas shorter routes can create tours with a large number of route combinations within a tour. Therefore, as stated in Algorithm 1, we first create a set of possible routes, starting with the shortest routes and working our way up until we have a sufficient number of routes. As a parameter, we use a Taguchi method to find a sufficient number of routes [57]. Limiting the number of viable routes helps in reducing the size of the routing problem. Thus, it saves a significant amount of time for our neighborhood solution search in any algorithm. This is a trade-off between the expected time to reach a semi-optimal solution and the quality of the solution. The routes from the set of possible routes we created in this phase are used to create initial solutions for HGA. It also has a filter that uses a greedy policy to limit the size of feasible routes in order to avoid creating routes that have a low chance of being part of optimal or near-optimal solutions.

We generate the initial population –initial chromosomes– using a random tour generation method. The chromosomes in the initial population are created by randomly selecting routes from the set of possible routes and combining them to create a new chromosome (tour), considering the time constraints. Since a solution for NC-MBCP should contain tours of BCVs and their associated departure times that consider the working hours of BDSs as well as the PTL for each vehicle. The associated departure times of tours should consider the working hours of BDSs as well as the processing time limit. The associated departure times of routes in a tour are obtained by using a Dirichlet distribution [58] on a randomly distributed departure time. First, we calculate a BCV's total time to complete a tour when there is no idle time between two successive routes. Next, we calculate the BCV's total idle time during a working day by subtracting the time BCV is busy from the daily working time of that BCV. Finally, we distribute the BCV's idle time between routes of the tour using a Dirichlet distribution. Since a chromosome fitness value is the number of collected blood units that can be used for platelet production, different associated departure times for routing of a BCV on a route can change the fitness value of that chromosome. Hence, we try several random departure times for each route in a tour and select the one with the highest fitness to increase the quality of our solution.

4.1.3 Crossover Operator

The crossover operator is one of the genetic algorithm's neighborhood search structure features. This operator is a tool for increasing the quality of initial population solutions. In general, solutions in a genetic algorithm are encoded by equal-size chromosomes. This feature simplifies the use of one-point and k-point crossover operators. However, due to the solution encoding used in our solution approach, we need a different crossover operator to handle the size-inequality of chromosomes. The unequal

crossover operator is used to mate parents of different sizes in order to produce offspring. To begin with, the algorithm uses the Roulette Wheel Selection method to select two parents from the initial population with varying probabilities of selection based on the fitness value of each chromosome within the initial population. The unequal crossover operator generates a unique random integer ranging from one to the size of each parent. These are the points at which the unequal crossover operator cuts parents to produce offspring. Thus, it is similar to the one-point crossover operator, except that the points in both parents are not the same.

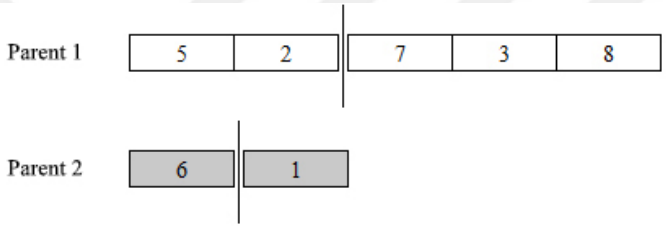

Figure 3: Performance of unequal crossover operator on parents

As shown in the example in Figure 3, parents are divided into two parts by randomly drawn lines across the chromosomes. As shown in Figure 4, the right parts of parents exchange with each other, resulting in the generation of new pair of offspring. During the crossover procedure, because the chromosomes are divided into parts randomly, they may reproduce new chromosomes that need time to perform more than possible or chromosomes. Therefore, in the crossover procedure, the feasibility of the solution can be lost. As a result, the algorithm evaluates the viability of new solutions. If both offsprings are viable, they will be added to the initial population; otherwise, they will be eliminated.

Any new solution obtained by using the crossover operator is a BCV tour, whereas this solution requires departure times of routes beginning at the blood processing center. Any solution obtained in this phase takes associated departure times using the same timing method used for the initial population.

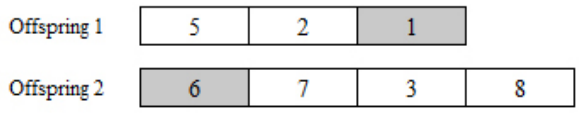

Figure 4: Pair of off-springs created using crossover operator

4.1.4 Mutation Operator

The genetic algorithm employs a mutation operator to avoid becoming stuck in a local optimum. This operator is not used in every iteration, but it occurs with a certain probability known as the mutation rate; it generates an entirely random solution in some iterations. This operator ensures that the current population is diverse. The mutation rate used in this study is 0.1, which means that with a 10% chance, a mutation occurs in each iteration. When no mutation occurs in an iteration, the crossover operator will reproduce new chromosomes. We forbid mutation and crossover operators within the same iteration. There is also another parameter for the mutation operator, which we call it the mutation volume. The mutation volume determines the number of chromosomes in the population that will be replaced by newly generated chromosomes when the mutation operator works. The nominated chromosomes to be replaced are selected based on their quality among the available chromosomes in the population. The chromosomes with the purest fitness value are replaced by the new generation. In the proposed algorithm, the mutation volume is a proportion of the population. We show the proportion by α, which is set to ten percent in this problem, which is determined by experimenting with different values in the algorithm. The mutation operator generates new chromosomes by selecting random routes from a set of possible routes, using the same method that we use to generate the initial population.

4.1.5 Selection

After adding new solutions to the initial population using crossover or mutation operators, the number of chromosomes in the population increases. The algorithm then computes all fitness values for the new augmented population in order to improve the quality of the chromosomes in the initial population by replacing the weakest chromosomes with better alternatives. The main idea behind the genetic algorithm is to eliminate the weakest chromosomes while keeping the remaining chromosomes, hoping to strengthen them. In order to have a fixed-sized population, the chromosomes are sorted and truncated in each iteration.

4.1.6 Simulated Annealing for Departure Times

HGA solution consists of a set of routes and a set of departure times for each related route. To find the best solution, HGA should look for the best tour with the best-associated departure times. To address this issue, we try two methods of fitting departure times to routes. First, we propose a random search heuristic method for determining appropriate departure times for any given route while searching for neighborhood solutions. Following that, as explained in Algorithm 1, once we have found the tour and its associated departure times with the largest fitness value, we use SA to find any better departure times for the tour. In other words, SA seeks better departure times for the solution. To do so, the SA produces neighbor associated departure times by adjustıng associated departure times for the best tour. If the SA could find any associated departure times for the best tour leading to a larger amount of platelet production, the HGA accepts it as the associated departure times for the tour, otherwise, the algorithm tries new associated departure times.

Additionally, SA part of HGA accepts some transitions to a worse neighbor solution with a probability determined by Boltzmann in the equation ($P = e^{-\frac{Fitness_{\rho^*,t_{temp}} - Fitness_{\rho^*,t_{\rho^*}}}{\theta}}$) to avoid getting stuck in local optima [59]. The difference between the best solution

fitness value so far and the newly generated solution fitness value is denoted by $Fitness_{\rho^*,t_{temp}} - Fitness_{\rho^*,t_{\rho^*}}$, and θ is the temperature that is decreasing during the algorithm iterations till the termination criteria are activated.

4.2. Invasive Weed Optimization Algorithm

IWO is a numerical stochastic optimization algorithm that is inspired by weed colonization in nature, and it was first introduced by [60]. It is weeds that infest and occupy vacant land between crops in a cropping field. An invading weed tries to use the field's resources depending on the fitness of the weed in the area and reproduces seeds fast. The more adapted weeds to the vicinity can distribute more than new seeds grown randomly in the field. Hence, those weeds that have better adoption and are located in a highly enriched part of the field have a higher chance of reproducing more seeds. Therefore, the newly reproduced seeds will be randomly distributed over the field and will grow to reproduce new seeds. Dependent on the resources available in the field, the growth will continue. Hence, the weeds that have higher fitness in the field have more chances to reproduce. This reproduction strategy is the main idea behind IWO. In IWO, each weed represents a solution, and solutions with better fitness will survive and reproduce heavily, while solutions with weak fitness will not be able to reproduce significant seeds; accordingly, weak solutions will be extinct. The steps of IWO are presented in Algorithm 2.

As it is presented in Algorithm 2, IWO algorithm has four main steps. First of all, an initial population of weeds will be distributed over the field. Then, according to the fitness of each weed, the reproduction of new seeds will occur. After reproduction, seeds will disperse over the field. Finally, weeds with better fitness will survive, and weeds with weak fitness will be excluded from the field. In this problem, the fitness value of a weed is the number of collected blood units that can be used for platelet production.

Algorithm 2 *Invasive Weed Optimization Algorithm*

$\mathcal{N} :=$ *min*(Number of sufficient routes,Number of feasible routes)
$\mathcal{R} :=$ Set of routes with one BDS
while $Size(\mathcal{R}) \leq \mathcal{N}$ **do**
  $\mathcal{R} := \mathcal{R}$+Set of routes with one more BDS than $\mathcal{R}$
end while
$Seed_{min} := 0$, $Seed_{max} := 5$, $\delta_{initial} := 1$, $\delta_{final} := 0.01$, $iter_{max} := 20$, $P_{max} := 200$
for $vehicle \in F$ **do**
  $\rho :=$ Random tours from $\mathcal{R}$
  $t_\rho :=$ Random departure times for ρ
  $F_{\rho,t} :=$ Fitness value of ρ&t
  for iter $\in iter_{max}$ **do**
    $F_{min}, F_{max} :=$ Min($F_{\rho,t}$), Max($F_{\rho,t}$)
    $\delta_{iter} := \delta_{final} + (\delta_{initial} - \delta_{final}) \times (\frac{iter_{max} - iter}{iter_{max}})^2$
    for $w \in$ Weeds **do**
      $Seed_w := \lceil Seed_{min} + \frac{(Seed_{max} - Seed_{min}) \times (F_{w,t} - F_{min})}{F_{max} - F_{min}} \rceil$
      for $s \in Seed_w$ **do**
        $NewSeed := w$
        $Rand :=$Random rational number$\in (0, 1)$
        if $Rand \geq 10\%$ **then**
          select randomly $Route_1$&$Route_2$ from w
          exchange the position of $Route_1$ with $Route_2$ in $NewSeed$
        else
          select randomly $Route_1$ from w & $Route_2$ from $\mathcal{R}$
          replace the $Route_1$ with $Route_2$ in $NewSeed$
        end if
        $t_{NewSeed} :=$ Random departure times for $NewSeed$
        for $i \in \delta_{iter}$ **do**
          $t_{temp} :=$ Random departure times for $NewSeed$
          if $F_{NewSeed,t_{temp}} \geq F_{NewSeed,t_{NewSeed}}$ **then** $t_{NewSeed} := t_{temp}$
          end if
          add $\rho_{NewSeed,t_{NewSeed}}$ to ρ
        end for
      end for
    end for
    while $size(\rho) \geq P_{max}$ **do**
      Remove the weakest weeds according to the fitness from ρ
    end while
  end for
  $\rho^* := \rho_{maxFitness}$
  $t_{\rho^*} := t_{maxFitness}$
  $MaximumCollected_{vehicle} := F_{\rho^*,t_{\rho^*}}$
  Update blood collection schedule regarding ρ^* & t_{ρ^*}
end for
$MaximumCollected := \sum_{vehicle \in Vehicles} MaximumCollected_{vehicle}$

4.2.1 Initial Population

In this section, we explain how IWO algorithm generates its initial population. To avoid losing good solutions, we try to reduce the number of potential routes, just like we did when creating the initial population of HGA.

As an initial step, the proposed IWO creates a set of potential routes based on a limit in order to keep the number of routes large enough to control the size of the problem. This limit balances the time needed to solve and the quality of that solution. In order to determine the limit, the algorithm creates potential routes starting with

smaller sizes of routes until the set of potential routes size reaches a given number which is the limit. Accordingly, in the first step, a set of potential routes between the locations of the BDSs is created, starting from the blood processing center and ending there. The first group of created routes is the routes visiting only one BDS, and the second group is the routes visiting two BDSs, and so on until the limit for the number of created potential routes allows. To reduce the size of the routing problem, we use the same Taguchi method we used in creating the initial population for HGA. It helps to find a near-optimal solution in a proper time.

The next step in this algorithm is determining a set of initial solutions for the problem. That is to say, a given number of solutions (seeds) initialize the algorithm. In order to generate an initial population for IWO, after picking routes from the set of potential routes randomly, considering the processing time limit, the algorithm combines the picked routes and generates a tour for each BCV. Consequently, the created solution as an initial solution is a tour. This tour requires associated departure times that consider the working hours of BDSs as well as the processing time limit for each BCV. In order to generate the initial population, a given number of solutions are created. These solutions are picked randomly among the set of potential routes and distributed randomly over the solution space. The distribution of routes is based on the departure times of the solutions.

An important part of creating a solution for NC-MBCP is associating departure times from the blood processing center for each tour. A Dirichlet distribution is used to determine departure times for tours, similar to what was discussed in creating the initial population for HGA. Therefore, the algorithm creates several random departure times for any tour to select the one with the highest fitness among the initial population. In IWO, each solution is a seed of weed.

4.2.2 Reproduction

The initial population is formed by seeds that grow in the cropping field according to their fitness to the location and their own fertility level. Fertility level is the number of seeds each weed can reproduce. Weeds are allowed to reproduce new seeds depending on their fitness and fertility. However, the amount of seeds a single weed can reproduce is limited by a lower bound represented by $Fertility_{min}$ and an upper bound represented by $Fertility_{max}$. Also, $Fitness_{min}$ and $Fitness_{max}$ represent the minimum and maximum fitness of all available seeds in the initial population. The proposed algorithm determines the number of seeds that each weed can reproduce, represented by $\sigma_(weed_i)$ according to a formula as follows:

$$\sigma(weed_i) = \lceil Fertility_{min} + \frac{(Fertility_{max} - Fertility_{min}) \times (Fitness_{weed_i} - Fitness_{min})}{Fitness_{max} - Fitness_{min}} \rceil$$

In this formula, the number of seeds that $weed_i$ can reproduce is linearly increasing from the minimum number of seeds to the maximum corresponding to the minimum fitness in the population.

Algorithm 2 produces $\sigma(weed_i)$ new solutions for $weed_i$ using a local search method called 2-opt and an operator called mutation. In a 2-opt method, the algorithm chooses two random routes among the routes in $weed_i$ and exchanges their position to produce a new solution. In addition, the algorithm uses a mutation operator to keep diversity in the population. The algorithm uses a mutation operator to create a new solution by replacing a randomly selected route of $weed_i$ with a randomly selected route from the routes in the set of possible routes. This feature helps the algorithm avoid getting stuck in local optima by creating a new solution with less dependency on the previous solution. In other words, the proposed IWO will not avoid reproduction in the area of cropping field that is free of weeds. For the algorithm proposed to solve NC-MBCP, a weed reproduces a new seed using the mutation operator with a probability of 10%, and with a probability of 90% the weed uses a 2-opt method to reproduce the next generation of seed.

The same associated departure times generating technique in the initial population section, is used to produce associated departure times for each new solution generated in reproduction. Hence, for $weed_i$, there will be $\sigma(weed_i)$ new seeds that will disperse over the cropping field.

4.2.3 Spatial Dispersal

Algorithm 2 distributes the seeds produced in the previous step randomly in the cropping field. This distribution is based on a random normal distribution with a zero mean and a decreasing variance over time. In other words, solutions in initial iterations are in a dispersal distribution, while as iterations go further, the variance of this distribution gets lower and lower. Accordingly, in each iteration, solutions get closer to each other until all seeds are grouped with each other. IWO algorithm eliminates weeds with lower fitness in spatial dispersal, and weak weeds vanish from the cropping field over a period. Calculation of fitness is the same method as used in the creating initial population section. Standard deviation is the square root of variance. In other words, in IWO decreasing variance in each step occurs by decreasing standard deviation. In the first iteration, the standard deviation is set to a given value and during each iteration, the updated standard deviation is determined by using the following equation:

$$\delta_{iter} = \delta_{final} + (\delta_{initial} - \delta_{final}) * (\frac{iter_{max} - iter}{iter_{max}})^n$$

Where δ_{iter} is the standard deviation for iteration iter, $\delta_{initial}$ is the initial value of standard deviation, and δ_{final} is the final value of standard deviation, which is the critical item to stop the algorithm.

Each solution for NC-MBCP has two parts. The first part is the tour composed of routes, and the second part of the solution is associated with the departure times of each route. Tours are used as seeds by the proposed IWO algorithm to generate solutions. The proposed IWO's tour departure times are also derived from spatial

dispersal. The associated departure times are created randomly using a Dirichlet distribution. As mentioned in the initial population section, several associated departure times are tested for any tour to find the best solution. It is good to use lots of random associated departure times for a tour in the first iterations of IWO algorithm. However, after a while, when new seeds are matured, the associated departure times will be fitter than the initial ones. Therefore, it is logical to decrease the number of associated departure times randomly created in each iteration for each new tour (seed). After a while, the associated departure times for a tour will be good, and it does not need to improve too much. Hence, IWO algorithm considering the iteration-based behavior of associated departure times, uses δ_{iter} amount to disperse the seeds reproduced by weeds to the solution space. Using δ_{iter} allows IWO algorithm to disperse in lots of random spaces in the field in initial iterations to keep diversity and avoid getting stuck in a local optimum solution. Besides, later iterations concentrate on solutions that show a higher capability to reproduce near-optimal solutions.

4.2.4 Competitive Deprivation

In the final step, according to a greedy selection, the weeds with higher fitness will remain, and the weaker weeds will be extinct because of low fitness to the environment they are growing. In order to reach a rich weed colony, it is needed to remove the weakest weeds according to a bound, which is called the maximum number of weeds in the colony. The reason to have such a bound is limited sources in the field to feed all the weeds. Besides, dealing with weaker weeds will consume lots of time and sources while there is a lower chance of reaching a good seed from a weak weed. Therefore, the weed with the worst fitness will be removed from the colony so that a determined number of weeds will have remained in the field in every iteration. threeparttable

CHAPTER V

COMPUTATIONAL STUDY

A comprehensive computational study is used to investigate the efficacy of the proposed algorithms. 21 different test instances with randomly generated parameters are solved using the proposed algorithms. The computational experiments are carried out on a 64-bit Windows 11 with two 1.8 GHz i7-8550 CPUs and 8 GB of RAM. The algorithms are implemented using Python 3.8.

5.1. Dataset Configuration

To evaluate the performance of the proposed algorithms, we create a dataset inspired by [22]. The dataset consists of 21 instances with five different numbers of BCVs: {6, 7, 8, 9, 10} and seven different numbers of BDSs: {28, 32, 36, 38, 43, 46, 51} and three different PTLs: {300, 500, 700}. The BDSs and the blood processing centers are randomly placed on a map of 1000 x 1000, with dense areas of BDSs to represent both metropolitan areas and remote areas. Approximately half of the BDSs are located in one of four metropolitan areas, and the rest are uniformly distributed across the map. Different values for K (300, 500, and 700) are considered. The six-hour time limit is considered as the minimum time needed to extract platelets. We take the processing time limit of five hours (300 minutes) to take the time spent in the extraction procedure into account. We consider larger K values since six hours is only the suggested time limit, and longer processing time limits as also possible [61, 21]. Furthermore, we use the same setup parameters and conditions for all proposed algorithms. The best performing heuristic method's results for MBCP proposed by [22] are used as measures of merit in the evaluation of the algorithms.

5.2. Results and Discussion

In order to evaluate the effectiveness of the proposed solutions, we analyze and describe their numerical results in the generated instances. Table 5.2 shows the average relative percentage of improvements of the proposed algorithms for 21 different randomly generated instances with respect to the best performing algorithm proposed by [22] called OEH. The average relative improvement is calculated by dividing the difference between our solution and the best solution in the literature by the best solution's values in percent. The average relative percentage of improvement shows the relative increase in the collected blood units by the new solutions with respect to the older solutions on average.

In addition, we modify two constructive heuristics of [22] in a sequential way that consider the BCVs successively. We call these two constructive heuristics *sequential greedy heuristic* (SGH) algorithm and *sequential recursive greedy heuristic* (SRGH) algorithm.

The SGH algorithm constructs tours for the vehicles one after the other in a backward manner. Following that, the previous node to be visited is determined based on the highest possible collectible processed blood. To determine the total number of donations that can be collected from a site, say i, the donations between $t-K$ and $t-t_{i0}$ are considered assuming that the vehicle arrives at the BDS at time t. The BDS with the highest possible amount is then selected as the node for the current time.

In order to improve SGH's efficacy, we use a more generalized version in which SGH is used recursively, called SRGH. When a decision is about to be made in this algorithm at any point in the heuristic, all of the possibilities are studied, not just the immediate gain but also the future outcomes. This is particularly the reason that the algorithm is used frequently.

The instances are solved for three different K values. For each processing time

limit value, there are different numbers of BDSs and BCVs (denoted by BDSs and BCVs in Table 5.2). In Table 5.2, the first column represents the processing time limit values, the second column represents the number of BDSs, the third column shows the number of BCVs, and columns four to seven represent the improvements with respect to OEH as well as runtimes for HGA, IWO, SRGH, and SGH, respectively.

According to the results, all of the presented algorithms outperform (on average) OEH by a large margin. For the instances with 300 minutes of the processing time limit, IWO outperforms (on average) HGA, SRGH, and SGH by 1.79%, 2.68%, and 7.66%, respectively. However, HGA outperforms other algorithms for the instances with 500 minutes of processing time limit and 700 minutes of processing time limit. The best performing algorithm is HGA, with a 9.40% improvement on average, even though in one of the instances, it cannot outperform OEH. The second best-performing algorithm with a slight difference (0.26%) with HGA is IWO, while in three instances, it is capable of outperforming OEH. It must be noted that the performance of IWO and HGA are so close to each other that they both provide better improvements in comparison with other algorithms. SRGH and SGH are in third and fourth place with 7.25% and 5.09% improvements over OEH, respectively. In spite of OEH outperforming SRGH in two instances, the performance of IWO is better than SRGH on average.

Table 5.2 also represents the runtime performance of the proposed algorithms. IWO is the fastest out of the proposed algorithms, with 441 seconds of runtime on average. Even though the runtime of SGH is so close to IWO (442), the quality of the results provided by SGH is not that high. As expected, whenever the value of the processing time limit increases, the runtime gets higher as well. In that sense, the highest runtime (1186) belongs to HGA for the instance with 51 BDSs and 10 BCVs for 700 minutes of processing time limit.

Table 3: Percentage of improvements of proposed algorithms with respect to OEH algorithm

K	#BDSs	#BCVs	HGA		IWO		SRGH		SGH	
			Imp(%)[1]	Time(s)	Imp(%)	Time(s)	Imp(%)	Time(s)	Imp(%)	Time(s)
300	**28**	**6**	11.65%	89	11.65%	92	13.59%	117	9.71%	113
	32	**6**	16.17%	202	14.97%	242	11.98%	187	4.19%	174
	36	**7**	13.50%	205	15.00%	205	12.00%	224	0.00%	200
	38	**8**	2.13%	643	4.26%	484	1.86%	383	-6.91%	350
	43	**9**	15.71%	456	19.29%	488	17.86%	330	2.14%	286
	46	**10**	18.18%	316	21.36%	282	16.82%	257	30.91%	288
	51	**10**	21.35%	475	24.72%	451	18.35%	316	17.60%	314
	Average		**14.10%**	**341**	**15.89%**	**321**	**13.21%**	**259**	**8.23%**	**246**
500	**28**	**6**	7.24%	199	6.33%	210	1.81%	225	7.69%	238
	32	**6**	4.86%	402	5.71%	391	-0.29%	349	0.86%	353
	36	**7**	11.30%	363	12.15%	344	5.08%	372	13.28%	401
	38	**8**	-1.62%	834	-1.26%	561	-2.88%	539	-2.34%	542
	43	**9**	10.78%	986	8.92%	651	3.35%	556	-2.60%	524
	46	**10**	13.48%	922	13.68%	748	9.86%	546	17.10%	582
	51	**10**	7.43%	1011	0.00%	597	7.26%	635	-12.67%	517
	Average		**7.64%**	**674**	**6.50%**	**500**	**3.46%**	**460**	**3.05%**	**451**
700	**28**	**6**	16.67%	358	18.97%	318	9.20%	380	16.67%	406
	32	**6**	4.91%	718	3.85%	388	2.99%	482	10.47%	517
	36	**7**	13.36%	690	8.77%	362	3.76%	497	5.01%	503
	38	**8**	2.33%	763	3.78%	511	0.87%	693	-1.75%	675
	43	**9**	0.27%	904	-0.13%	581	4.27%	782	-11.87%	661
	46	**10**	6.79%	1176	2.91%	602	14.27%	825	5.96%	765
	51	**10**	0.95%	1186	-2.98%	745	5.96%	889	3.34%	867
	Average		**6.47%**	**828**	**5.02%**	**501**	**5.90%**	**650**	**3.98%**	**628**
Average			**9.40%**	**614**	**9.14%**	**441**	**7.52%**	**456**	**5.09%**	**442**

[1] Imp = $Average\frac{alg_i - alg_{OEH}}{alg_txtOEH}$, where alg_i and alg_{OEH} are the average produced platelets using algorithm i and OEH respectively for a given instance in several runs.

CHAPTER VI

CONCLUSION

Blood and its products, particularly platelets, are critical to human survival. We investigate a blood collection problem BCP that focuses on platelet production effectiveness in this thesis. This problem is designed to maximize the total number of platelets collected by focusing on a consistent and continuous pattern of donation. The main contribution of this study is the presentation of a new variant of BCP via the increasing degree of freedom of BCVs. This variant is called *non-clustered maximum blood collection problem* (NC-MBCP). In NC-MBCP, a number of BCVs attempt to collect blood units from *blood donation sites* (BDSs) with a scheduling leading to produce the maximum possible platelet while considering the *processing time limit*, which is the critical period of time from donation to the separation of components of blood. In this study, the processing time limit for platelet production is at most six hours. This study proposes meta-heuristic algorithms for the first time to solve NC-MBCP in order to design an excellent platelet supply chain. We use a *hybrid genetic algorithm* (HGA), an *invasive weed optimization* (IWO) algorithm, and two greedy-natured heuristic methods to maximize the number of collected blood suitable for platelet production. HGA and IWO meta-heuristic have the advantage of being able to deal with an overwhelming number of solutions by employing a greedy algorithm to eliminate genes with a lower chance of producing a good chromosome as a solution. Furthermore, HGA uses a simulated annealing heuristic to improve solutions by looking for better departure times for a given solution. The obtained numerical results demonstrate that HGA and IWO algorithms are significantly more effective than the currently available algorithms.

Future directions may be based on a more realistic view of MBCP, taking drivers' behavior into account. Drivers who are familiar with a route might perform better than those who are new to it. Moreover, considering the uncertainties of disruptions in routes such as floods and accidents can lead to more resilient solutions to this problem. Furthermore, sharing collected blood units between vehicles can create a new problem with possible better solutions than current ones.

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