BLOOD SUPPLY NETWORK DESIGN

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BLOOD SUPPLY NETWORK DESIGN

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ABSTRACT

BLOOD SUPPLY NETWORK DESIGN

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In our study, we consider a joint location-inventory-routing problem with multiple location layers for a distinctive and regionalized blood supply network design. We formulate the problem as a mixed-integer nonlinear programming model and present an optimal solution method for the problem. However, solving medium and large-sized problem instances for the optimal solution turns out to be impractical. Therefore, we also develop several heuristic methods based on decomposition and simulated annealing techniques. We conduct extensive computational studies on numerous test problems and evaluate the performance of the solution methods proposed. Our results show that simulated annealing heuristic clearly outperforms other solution methods.

Keywords: Joint location-inventory-routing problem with multiple location layers, mixed-integer non-linear programming, blood banking and transfusion services, simulated annealing and decomposition heuristics, blood supply network

ÖZ

KAN TEDARİK AĞI TASARIMI

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Bu çalışmada benzersiz ve merkezileştirilmiş bir kan tedarik ağı için birden fazla katmanda yerleşim yapılacak bütünleşik tesis yer seçimi, envanter ve araç rotalama problemi üzerine çalışılmaktadır. Bu problem karma tamsayılı doğrusal olmayan programlama modeli olarak formüle edilmekte ve problem için kesin bir çözüm yöntemi önerilmektedir. Ancak orta ve büyük boyutlu problemlerin kesin sonuç için çözülmesi pratik olmamaktadır. Bu nedenle benzetilmiş tavlama ve ayrıştırma tekniklerini temel alan dokuz adet sezgisel çözüm yöntemi de önerilmiştir. Örnek problemler üzerinde geniş kapsamlı denemeler yapılarak, önerilen çözüm yöntemlerinin performansları değerlendirilmiştir. Elde ettiğimiz sonuçlar benzetilmiş tavlama sezgiselinin önerilen diğer çözüm yöntemlerinden daha iyi sonuçlar ürettiğini göstermektedir.

Anahtar Kelimeler: Çok katmanda tesis yerleşimi içeren bütünleşik tesis yer seçimi problemi, doğrusal olmayan karışık tamsayılı programlama, kan bankacılığı ve transfüzyon hizmetleri, benzetilmiş tavlama ve ayrıştırma sezgiselleri, kan tedarik ağı

To My Family

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CHAPTER 1

INTRODUCTION

In this chapter, we first present general information about blood, blood banking and the current situation of blood supply network in Turkey. Then we define the motivation and the scope of our study.

1.1. Blood and Blood Banking

Blood is the red fluid that flows through our bodies. The main mission of blood is transporting oxygen and nutrients to our tissues and lungs, and carrying away waste products to the kidneys and liver. It is composed of many different kinds of components. In blood banking applications, except the apheresis process used in special treatment operations, blood is collected as whole blood from donors. After the collection phase, different blood components are extracted from whole blood by using basic processing techniques. Main components of blood are red blood cells, platelets, and plasma. Blood has eight different types according to the ABO and Rh grouping system.

As blood transfusion plays a major role in medical treatment, blood banking has a vital importance in healthcare services. Absence of blood components when needed may cause a negative effect on prognosis of a patient who is in need of blood transfusion. Blood is a scarce resource, because it does not have any alternatives and the only source of blood is the volunteer donors. Inequality between blood supply and demand is a common problem faced by many countries. In addition to its significant effect on the success of the medical operations, it also has an important role in health economics.

Therefore, developing strategies for effective and efficient management of blood supply chain is a critical and important issue for most of the countries.

There are several studies focusing on different blood supply chain designs with the aim of achieving both economies of scale and high service quality. Regionalization of blood banking systems is one of the popular discussion topics in this context. Alternative structures for regionalizing blood banking systems and alternative job descriptions for different kinds of blood establishments are investigated. Real life applications have evolved in parallel with the improvements in the literature, and regionalized blood management systems have been established in most of the developed countries.

1.2. Blood Supply Chain in Turkey: Past and Present

The first blood law of the Republic of Turkey was issued in 1983 (Law No: 2857) and updated in 2007 (Law No: 5624). The first blood law defined the types of blood centers as A and B, and blood stations as well. These establishments were independent of each other. According to the first blood law, hospital blood banks (transfusion centers) were authorized to collect, test, and store blood and its components. However, this task description of hospital blood banks was not appropriate to sustain safe and reliable blood supply. The main problems about this system can be summarized as follows:

- Blood donations in hospital blood banks were made by patients' relatives. However, collecting blood from volunteer donors is one of the most important requirements according to field standards and best practices to provide safe blood. It is also important for long term self-sufficiency in blood banking and for achieving economies of scale (Popovsky, 1997).
- Diseases such as HIV and Hepatitis, which can be transmitted through blood transfusion, have a time window during which traditional methods cannot detect them. This duration can be shortened from 3 to 5 months to 2 to 4 weeks by using new generation test methods, such as PCR (Polymerase Chain Reaction).

However, these new generation test methods are very costly for a hospital blood bank with a blood collection activity at a very low level. Therefore, hospital blood banks had to use the traditional test methods.

- Managing blood banking activities compatible with the regulations and quality requirements results in high operating costs for the blood establishments with a low collection activity level. As a result, most of the hospital blood banks in Turkey were not able to satisfy the requirements to achieve and sustain safe blood supply.

In the early 2000s, authorities in Turkey started to work on developing a blood and blood products law so as to organize the functioning of blood establishments. The aim of this law was to eliminate the main deficiencies (incompatibility with blood safety requirements, economies of scale problems, gap between blood demand and supply, low service quality) observed in the blood supply chain. A draft of Blood and Blood Products bill was prepared by the Turkish Ministry of Health in 2005. The Turkish parliament approved this bill in 2007 and the new Blood and Blood Products law was published. This new law necessitates a blood banking system which centralizes blood collection, processing and testing activities, and this centralized system is composed of the following blood establishments:

- *Regional Blood Center (RBC):* RBC is the main unit responsible for coordinating blood collection activities, processing and testing blood components, and supplying them to the transfusion centers within its responsibility area. RBC separates blood into its components, carries out blood tests, and distributes the components to transfusion centers based on their needs.
- *Donation Center (DC):* DC operates under the coordination of RBC both in technical and administrative operations. Its main responsibility is carrying out the blood collection activities within its responsibility area.
- *Transfusion Center (TC):* TC is the unit located within the hospital. Except for the emergency situations, TC is not allowed to collect blood. TC carries out pre-transfusion tests, acquires and reserves blood components, and sends them to the

demanding hospital units for transfusion. TC is also responsible for following up the effects of transfusion on patients during and after the transfusion.

Turkish Red Crescent Society (TRCS) is assigned to be the responsible organization for supplying safe and reliable blood and blood products throughout the country. Therefore, TRCS reorganized its blood services to be compatible with the structure as stated in the new law. TRCS' national blood services are divided into 19 regions and only one RBC is established for each region. TRCS has so far established 62 DCs throughout the country. These 19 RBCs and 62 DCs of TRCS are licensed by the Ministry of Health (MoH). Within the framework of the reorganization activities; the existing buildings, devices, equipment, and material-related aspects of all RBCs and DCs of TRCS have been upgraded. Central laboratories (CLs) have been established for undertaking the blood safety tests. The personnel of the blood services of the TRCS have participated in various training programs and received training certificates. The TRCS has signed protocols on the blood supply with almost 1600 TCs across the country. In parallel to these activities, a well-designed public relations policy has been put in place by the TRCS, which helps secure public support and raise public awareness on the importance of voluntary blood donation. The dramatic rise in the voluntary donation rate over a short span of time is the most notable indicator of the success of the public relations activities. Levels of blood donation by TRCS between years 2004 and 2015 are illustrated in Figure 1.

Although the blood supply system in Turkey has been strengthened to a certain extent, some problems still hurt the overall functionality. The top issue in this respect is the inability to maintain the nationwide voluntary blood donations at sufficient levels. The forecasted need for 2017 to achieve self-sufficiency in terms blood and blood components throughout the country is 2.475 million blood donations. As an important step towards sustaining the current system within the transition period, the MoH has granted licences to the temporary RBCs that adopt replacement donation, but did not fulfill the requirements expected from a decent blood facility in terms of voluntary donation, and laboratory and logistics capacities. This course of action has contributed to the prevention of probable blood shortages, sustaining the current functions of the system as well as raising the awareness of the blood center personnel on restructuring and service quality issues. However, the inability of these centers to fulfill the requirements expected from an RBC has resulted in gaps between the existing legal framework and the real-life practices. Despite the fact that the new blood law came into force already in 2007, a large proportion of blood is still donated at the hospital based blood banks or at temporary RBCs. However, the share of blood donations made at TRCS facilities seems to rise gradually, to 82% of the total amount in 2015, while this figure was around 24%, 40%, and 60% in years 2007, 2010 and 2012, respectively.

Another setback observed in the blood supply chain is the inefficient use of blood and blood components accompanied with the inefficient operational activities in the blood supply chain system. The negative impact of the inefficient use of blood and blood components increases with the insufficient level of voluntary blood donations. One of the basic factors for a successful centralized blood system is the availability of blood in TCs at a level that would not stall medical interventions. However, given that blood is a perishable product, this can only be possible with the establishment of a solid infrastructure that would allow for effective inventory control and an effective management system that would be operational at both regional and national levels.

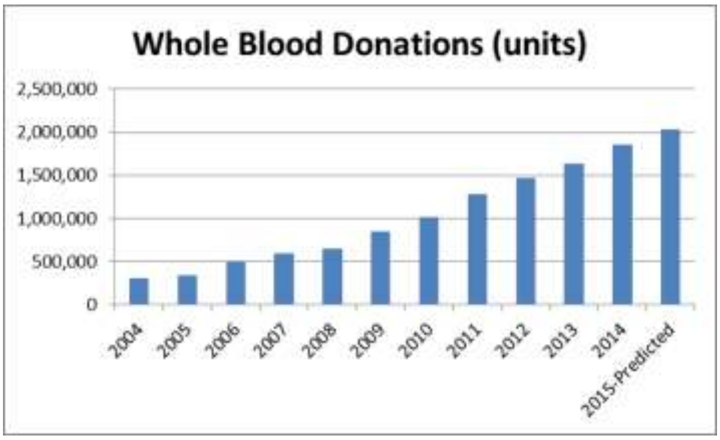


Figure 1. Levels of Blood Donation by TRCS

Source: Turkish Red Crescent Blood Services Report, 2014

Administrative and technical management of the scattered TCs poses another setback. In addition to this, RBCs cannot work in full capacity due to the insufficient voluntary blood donation rate; hence, economies of scale cannot be maintained and with the resulting operational inefficiencies, the cost of acquiring safe blood increases. A systematic mechanism capable of reporting the untoward and unexpected events that may emerge throughout the blood banking and transfusion processes has not yet been set up in Turkey. Lack of such a mechanism results in inability to measure the effectiveness of strategies adopted by the national health authority, inability to identify probable sources of error, and inability to carefully measure the performance of the blood supply chain. Therefore, a systematic feedback mechanism is needed for continuous improvement of the blood supply chain system. Another problem observed in the Turkish blood supply chain is that a common quality standard has not been reached in the countrywide service provision. For example, an RBC or a university hospital in Ankara may offer a service quality even higher than that in European countries, whereas centers in the eastern Turkey may offer much lower levels of service quality. While differences in the infrastructure play an important role in the emergence of such discrepancies among different regions, differences in the knowledge levels of the blood centers' personnel also remain to be one of the basic factors. A SWOT diagram displaying the strong and weak characteristics of the blood supply system and a fishbone diagram displaying the causes of problems observed in the Turkish blood supply system are given in Figures 2 and 3, respectively.

The main reason of most of the problems described above is the lack of organization due to the transition period, which is expected to be completed by 2017 when TRCS is expected to be able to secure voluntary blood donations sufficient at the national level and temporary RBCs will be closed. In order to overcome these problems, new projects have been started in order to improve the blood supply chain. Main objectives of these projects can be summarized as follows:

- Executing a comprehensive survey of the current blood supply chain that will highlight the problems in the chain. Identifying the gaps between the current system and the one proposed by international regulations and standards, and developing a roadmap including strategic planning.

- Revising the national blood policy of the country and establishing a regional organization together with the needed legal and regulatory adjustments.
- Executing two levels of capacity building, managerial and technical, aiming at enabling Ministry of Health to perform its regulatory, inspection and licensing roles on one side, and enabling the blood banking and transfusion professionals to operate in a standardized way harmonized with the EU Directives.
- Establishment of a national information system which will provide real time data that will allow decision makers to analyze the trends in the blood system and to develop necessary corrective and preventive actions.

One of the motivations of our study stems from these projects aiming to solve problems observed in the Turkish blood supply chain. In our study, we will focus on the decisions in the blood supply chain at strategic and tactical levels. We try to develop an integrated approach including three main decisions in a supply chain: inventory management, facility locations-allocations, and distribution and routing. Our aim is to propose a framework which will support decision makers in the strategic planning process. It is expected that outputs of our study will provide a roadmap to solve some of the problems at least observed in the Turkish blood supply system especially the ones about efficiency and service quality. Outputs of the study aim to constitute a general framework which may also be a useful tool for other countries facing with similar problems while managing their blood supply chains.

The thesis includes eight chapters. Previous studies on blood supply chain management and location-inventory-routing problems are summarized, and the unique features of our study are discussed in Chapter 2. The problem environment and the proposed approach in our study to address the problem are defined in Chapter 3. In Chapter 4, the mathematical formulation of the problem under consideration and its special cases are presented. Proposed solution methods and their implementations are explained in Chapters 5 and 6, respectively. Computational results are presented in Chapter 7, and the thesis is concluded in Chapter 8.

Figure 2. The SWOT Diagram of the Blood Supply System in Turkey

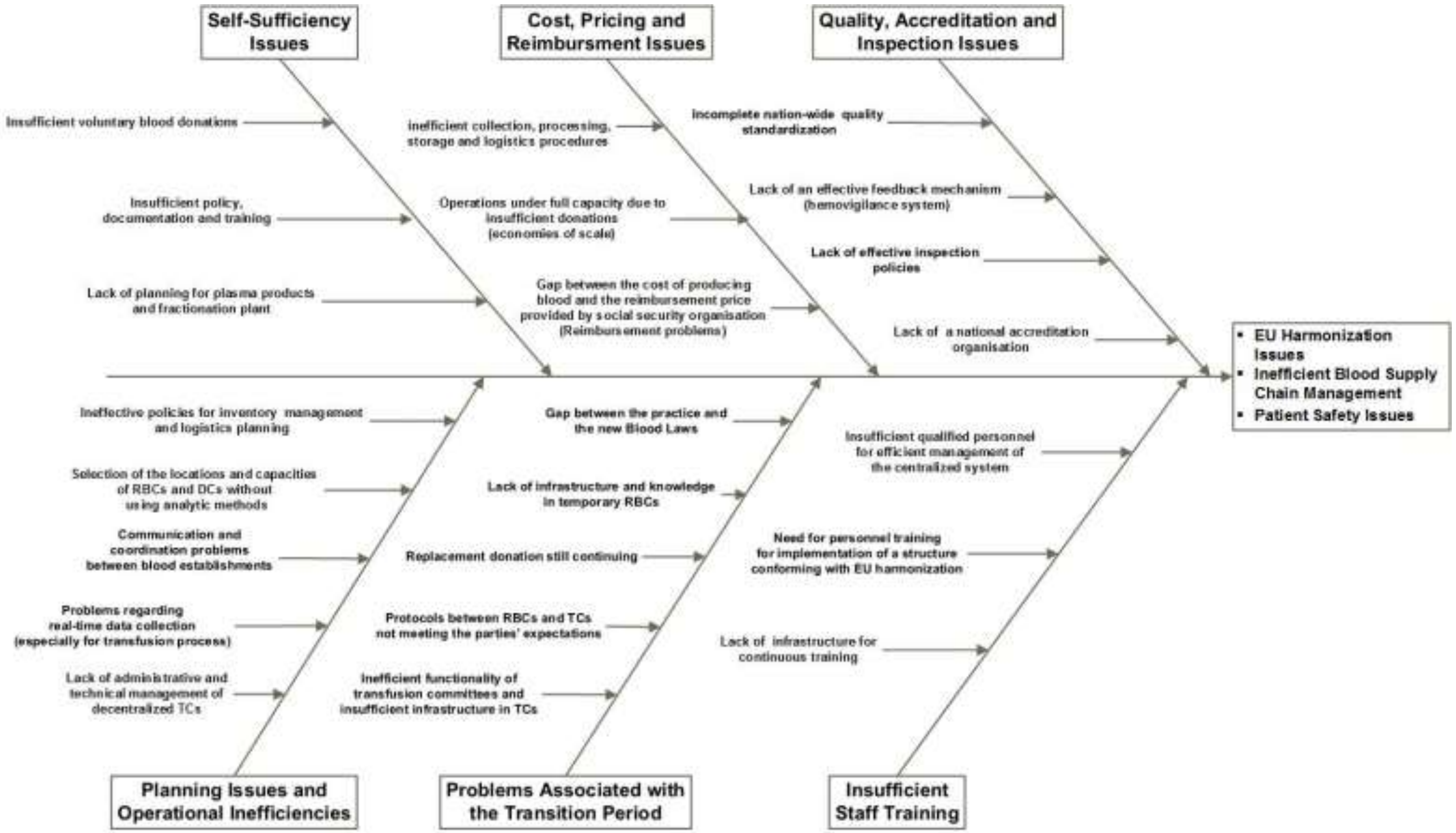


Figure 3. Fishbone Diagram

CHAPTER 2

LITERATURE REVIEW

In this chapter, we first provide a general review of the previous studies on blood supply chain management and location-inventory-routing problems. Then we present a comparison of our study with the previous ones in the literature.

2.1. Blood Supply Chain Management

One of the most vital parts of the health services is blood banking, proper implementations of which carry a great value in the success of medical treatment procedures. During the 70s and 80s, this subject attracted a vast amount of attention from both operations researchers and health professionals; later, the same subject has become a hot topic again during 2000s.

Belien and Force (2012) presented a review of the literature for blood supply chain management and inventory issues of blood products. Different perspectives to classify the existing literature were identified in this review as follows:

- Type of blood product (red blood cells, blood platelets, plasma, whole blood, frozen blood)
- Solution method (simulation, queuing models, stochastic dynamic programming, integer programming, linear programming, statistical analysis, cost analysis, heuristics, mathematical derivations, what-if scenario analysis, custom spreadsheets)
- Hierarchical level (hospital level, regional blood center level, supply chain level)

- Type of problem (Inbound problems, Outbound problems)
- Type of approach (Stochastic, deterministic)
- Exact versus heuristic
- Performance measures (Outdates/Outdate Rates/Wastage, Shortages/Shortage Rates/Backorders, Deliveries/Transportation Costs, Availability/Inventory Level/Service Level/Days of Supply, Safety/Age of Blood at Transfusion/Quality, Processing Times (donors)/Donation Frequency)
- Practical implementation/case studies (Practical Implementation/Case Study, No Practical Implementation/No Case Study)

In our study, we present the literature using the classification category of "hierarchical level". Studies are further classified under sub-categories such as "individual hospital level", "RBC level", and "supply chain level". Studies dealing with hospital blood banks and decisions at this level are discussed under "individual hospital level" category. Studies dealing with the decision problems at the regional level or the comparison of centralized and decentralized structure or distribution policies among hospitals are discussed under "RBC level" category, while the studies focusing on the whole supply chain are discussed under "supply chain level" category.

2.1.1. Individual Hospital Level

Elston and Pickrel (1965) studied blood demand and usage data from a hospital in North Carolina with excessive simulations. Main objective of their study was to determine desirable inventory levels and to test a policy on inventory management.

Jennings (1968) evaluated hospital blood bank performance by using simulation with the data of a hospital in Massachusetts. In this study, trade-off curves showing outdates vs. shortages as functions of inventory level were derived for the first time.

Rabinowitz (1973) evaluated policies for blood bank inventory by computer simulations in which data from New York Hospital was used as input. A similar study dealing with the simulation of the inventory system in a hospital blood bank was carried out by Vrat and Khan (1976).

Pegels et al. (1977) and Cumming (1976b) conducted comprehensive simulations for analyzing effects of blood freezing policies on the behavior of the hospital's blood inventory. These studies asserted that blood freezing policies affect the stability of the operation of the Hospital Blood Bank by keeping outdating blood level approximately constant.

Dumas and Rabinowitz (1977) analyzed "negative-to-positive" policy which was a new cross-matching policy at that time. In this policy, under certain blood-age conditions it is allowed to use Rh (-) blood units for Rh (+) patients. They evaluated the performance of three different policies (double cross-matching, negative-to-positive, and simultaneous usage of both) over a range of demand levels and blood types. The main finding was that, with some additional cross-matching effort, double cross-matching is effective in reducing the wastage of Rh (+) and Rh (-) blood products. Another finding was that with some additional usage of negative blood, the negative-to-positive policy can result in a substantial reduction in negative blood waste, meanwhile keeping cross-matching work and positive waste unaffected. The end result of their study showed that the most effective reduction in Rh (+) and Rh (-) blood waste could be accomplished by the combined usage of these policies.

Friedman et al. (1982) used simulation for setting inventory levels of red blood cells with the assumption of a 35-day shelf-life span. They described blood management policies from the clinicians' perspective. Their argument was against setting common shortage rates in operations research literature and their suggestion was focusing on an empirical approach constructed around reducing safety stocks.

Sirelson and Brodheim (1991) tested platelet ordering policies for a blood bank using simulation based on a fixed base stock level and mean daily demand. The study resulted in a finding which indicates a base stock level definition by using mean demand and a safety stock level that can be used to reduce the outdate and shortage rates. Their study also points out that a reduction in outdate and shortage rates can be reached at the regional level. On the other hand such a reduction is a far more difficult goal at the hospital level. Similar findings are reported in the study by Katz el al. (1983).

A simulation model to determine outdates and shortages for cross-matched blood using broadly accepted parameters (cross-match to transfusion ratio, cross-match release period, etc.) was developed by Jagannathan and Sen (1991). The model is capable of providing a method to determine the desired free inventory levels.

Haijema et al. (2007) dealt with platelet production and inventory management problem and presented a method combining Markov Dynamic Programming (MDP) and simulation. The method was applied in a Dutch blood bank which was a real life case. A number of useful observations were obtained: (1) The ‘optimal’ production rule for platelets is complicated, therefore, it is not practical for implementation, (2) However, ‘nearly optimal’ results can be achieved by applying simple order-up-to rules, (3) Both single level and double level order-up-to rules may perform well, but the latter provides further improvements.

Erickson et al. (2008) developed a spreadsheet-based prediction model for managing the use of frozen red blood cells in times of disasters, using several emergency scenarios. The study indicates that storing frozen red blood cell in the inventory can only be useful for eliminating shortages in a short term, when the main supply coming from the blood center is disrupted, like in case of natural disasters. The frozen red blood cell reserves are proven to be inadequate sources for high transfusion demands in cases of big or long term disasters.

Heddle et al. (2009) presented an approach for establishing benchmarking targets for outdated red blood cells units at hospital blood banks. They analyzed 156 hospitals to identify factors affecting red blood cell outdates. They categorized the hospitals according to the factors affecting wastage. The study indicates that with such a categorization, a benchmarking target can be identified for each individual category of hospitals.

2.1.2. Regional Blood Center Level

Jennings (1973) investigated the regional performance as the number of hospitals in a territory is changed, and the ratio of supply to demand in the territory stays consistent. He compared two different territories both including identical hospitals, but the numbers of hospitals in the territories differ. The study demonstrated that between the two territories, the one having a larger number of hospitals performs better, since it can handle the day-by-day fluctuations of demand better among hospitals in its boundary.

Frankfurther et al. (1974) utilized a positive exponential function in a model to fit the relationship between outdates and past blood collection data. They built up a user interface for the blood bank staff to enter expected daily blood collections into the software. They utilized an exponential smoothing model including a weekly cycling feature to forecast day-by-day transfusions. They implemented the proposed system in a Regional Blood Center in New York. They made a benefit/cost analysis of the proposed system using the outcomes acquired from the pilot implementation in New York. Their results showed that the proposed forecasting model has the capability of delivering a higher benefit/cost ratio.

Cumming et al. (1976a) considered a blood collection planning model, aiming to improve blood collection operations at the regional level. Main motivation behind their study was to help the regional blood suppliers in smoothing out seasonal imbalances between the demand and supply of blood.

Brodheim and Prastacos (1979) discussed the Long Island blood supply system as a model for any Regional Blood Center and the affiliated hospital blood banks. They reported on a blood supply management software implemented in that region. This software uses the results concerning the optimal allocation strategies described in Prastacos (1978).

Or and Pierskella (1979) considered location, allocation, and transportation decisions in a regionalized setting for blood supply management. They proposed a transportation-allocation model, and developed heuristic solution methods for the model. They tested the proposed methods using the data obtained from Chicago area and reported successful results in terms of both total system cost and solution time.

Kendall (1980) formulated a model to assist regional blood managers in planning blood collection operations and in determining the size of inventory. In this study, main focus was the planning of the blood collection and inventory management activities of a regional blood system on an annual basis, rather than just concentrating on daily inventory control. They mentioned that developing annual plans is crucial for blood service establishments.

Kendall and Lee (1980) considered blood rotation policies. They proposed a goal programming model which includes goal constraints related to the age of blood, the cost of blood collections, the blood inventory levels, the count of outdated blood units, and the availability of fresh blood. They applied the philosophy to a vast area. Their results showed that the blood collection need can be reduced by 5% in the region where they applied their methodology.

A literature review was composed by Nahmias (1982) that deals with inventory problems about perishable products instead of considering the entire supply chain. The study includes a brief review of the application of the models related with blood bank management.

Melnyk et al. (1995) worked with survival analysis using data related with blood donation process. The main focus of their study was to identify the processing time differences among different blood donor classes. Donor classes under consideration were regular, autologous, and directed donors. Donors were further separated into categories as repeat and first-time donors. They reached out to the conclusion that the distinction between first-time and repeat donor had no effect on processing time distribution; and that the distinction between first-regular, autologous, and directed donors had no effect on processing times, except the health history stage of donation process.

Custer et al. (2005) considered the cost issues of blood supply. They calculated unit and total production costs related to the main stages of blood supply such as donation collection, donor screening and processing, donor recruitment and selection, and distribution of blood.

Denesiuk et al. (2006) proposed a redistribution method for the red blood cells which are near-outdate in order to reduce overall blood disposal rate in a specific region. The method is based on transporting red blood cell units that are about to outdate from a hospital with a low blood usage rate to a high-utilization rate hospital. The main idea behind the method is delivering the near-outdate units to the hospitals where they would have a more noteworthy possibility of being utilized before they become outdated.

Katsaliaki and Brailsford (2007) examined policies for managing the blood inventory of a hospital. The main target of the study was to improve the management policies of the hospital by modelling the whole supply chain. Only a part of the blood supply chain including a transfusion center and a regional blood center was considered. They utilized discrete-event simulation to identify ordering policies which will result in better outcomes in terms of shortage and outdate rates, service levels, and system costs.

Kopach (2008) developed a red blood cell inventory framework with two different demand rates. The principle technique of the study was using a queuing model which recognizes urgent and non-urgent demand. He compared the efficiency of the model and current inventory control techniques using simulations. He presented comparisons based on the data of the Canadian Blood Services.

Schreiber et al. (2005) proposed the hypothesis that the first-time donors with a high donation frequency during the first year are more likely to become regular donors in the following years, and used logistic regression analysis to verify this. The results of the analysis supported their hypothesis. They concluded that encouraging first-time donors for donating again in the first year will be more efficient for blood bankers to recruit regular blood donors.

Çetin and Sarul (2009) considered a mathematical programming model for location of the blood banks. The model under consideration was a combination of a set covering model and a center of gravity method. The objectives of the model were minimizing the total distance travelled between the hospitals and blood banks, fixed cost of locating blood banks, and an inequality index as a fairness mechanism for the distances. A numerical example was solved using and results were presented.

AuBuchon et al. (2011) considered the idea of centralized transfusion services and presented the centralized transfusion model implemented in Seattle. They expressed that the centralized model encourages more extensive utilization of the occupational capabilities of the blood center's physicians. Triulzi (1997) discussed the applicability of outsourcing the transfusion services of hospitals. He supported the centralized transfusion service model and concluded that if an outsourcing model for transfusion services is properly implemented by hospitals, it can result in reduced costs and improved patient care.

2.1.3. Supply Chain Level

The literature review of Pierskalla (2004) concentrated on supply chain management of blood banks. His study incorporates an outline of the blood supply chain and a review of various operational and tactical decision issues within the chain.

Şahin et al. (2007) presented mathematical models dealing with the location-allocation decisions faced with in a regionalized blood banking structure. They formulated a *pq*-median location model with the objective of minimizing the total population-weighted distances in the chain. The solution of this model determines the locations of *q* Regional Blood Centers that supply *p* blood centers. Moreover, they developed a set-covering model to determine the minimum number of blood stations required. They also developed an integer programming model to determine the fleet size of the vehicles for the regions. They reported computational results based on real data.

Yegül (2007) analyzed policies for managing a unique blood supply chain network, as defined in the new Blood and Blood Products Law of the Republic of Turkey. The main objective of the study was to obtain a better understanding of the system, and to find improved policies to manage it more efficiently. A discrete event simulation model was developed to analyze the blood supply chain. Effects of different management policies on the supply chain performance were analyzed. Important improvements are achieved in terms of the selected performance measures such as outdate, mismatch, and shortage rates of the region.

Fontaine et al. (2009) considered the platelet (PLT) supply chain and proposed a new approach for platelet inventory management. They mentioned the importance of the joint effort of blood centers and hospital transfusion administrations in improving the chain. They exhibited a case study which demonstrates the advantage of joining powers of blood centers and transfusion centers as a reduction in the PLT outdate rate.

Kamp et al. (2010) formulated a mathematical model and developed computer simulations to mimic the spread of influenza. They analyzed the case scenarios in regards to the accessibility of blood products in case of an influenza epidemic event. Their results showed that identifying the fraction of transfusions that cannot be delayed has a crucial importance. They mentioned the importance of epidemic readiness by proposing the usage of a prioritization plan for the utilization and release of blood products.

Nagurney and Masoumi (2011) considered network design/redesign model for a complex blood supply chain structure. In particular, they considered the design of a blood supply chain including demand points, distribution centers, testing and processing labs, collection sites, and blood centers. They demonstrated that the proposed network design is general and flexible enough to handle various different supply chain configurations by conducting numerical studies.

2.2. Facility Location, Inventory Management and Distribution Decisions

Three main decisions of supply chain management are inventory management, facility locations, and distribution and routing of products. Initially, these problems were handled separately. Location decisions have been studied extensively (see, for example, Jayaraman, 1998; Hindi and Pienkosz, 1999; Melkote and Daskin, 2001; Melo et al., 2006; Drezner and Scott, 2010). There are also several papers on inventory management decisions (see, for example, Chen et al., 2001; Axsater et al., 2007). Routing decisions are formulated in different ways by researchers. A recent taxonomic review of vehicle routing problems can be found in Ekşioğlu et al. (2009).

Considering the benefits of an integrated approach, researchers integrated two or three of the above problems based on the previous work. In our study, we try to extend this integrated approach (Location-Inventory-Routing) for a specific problem environment which also includes location of different types of facilities at the same time. Therefore, in this section we will focus on studies which either propose an integrated approach or deal with the location of more than one facility at the same time.

2.2.1. Location Problems with Multiple Location Layers

There are several studies in the literature which deal with the location of more than one type of facility at the same time. We will present some relevant examples of this category here; for further information we refer readers to Melo et. al. (2009).

Kaufman et al. (1977) developed a model in which warehouses and plants are located simultaneously with the objective of minimizing total cost. In their supply chain configuration, each demand point can be supplied directly by a warehouse or a plant. In addition to that, their model also handles a configuration including two levels of distribution centers. They proposed a branch-and-bound algorithm to solve the mathematical model, and also reported their computational results.

Hinojosa et al. (2000) considered a facility location problem where facilities can be established with two different distribution levels by time period selections. Their model aims to minimize the total cost for satisfying the demands for all goods over the planning horizon at different demand points while meeting the capacity requirements of intermediate warehouses and plants. They formulated the model as a mixed-integer programming model and developed a Lagrangian relaxation based solution procedure, together with a heuristic method that builds feasible solutions to the original problem from the solutions at the lower bounds obtained by the relaxed problem. Their results demonstrated that the proposed solution method performs better for an extensive variety of problems.

Jayaraman and Pirkul (2001) considered an integrated logistics model that locates both distribution and production facilities in a multi-echelon environment, and concentrates on two main decisions; one strategic decision (the location of plants and warehouses) and the other operational decision (appropriate strategy for distributing goods from plants to demand points through warehouses). The distribution strategy is affected by the shipments of materials from vendors to plants, the product mix at every plant, and the distribution of products from plants to different demand points through warehouses. They formulated a mixed-integer programming model and presented a Lagrangian based heuristic solution method that utilizes the solution obtained by the relaxed problem. Their experiments showed that the proposed solution procedure is both efficient and effective.

Melo et al. (2005) proposed a modelling framework that handles different aspects of network design, such as external supply of materials, distribution of commodities, generic supply chain network structure, inventory opportunities for products, different facility configurations, storage limitations, and availability of capital for investments. They discussed the connection of the proposed modelling structure with the current models. They reported computational results obtained by using test problems of reasonable sizes that were solved using a standard mathematical programming software. Although the modelling approach considers much more complex supply chain configurations, sample problems only include location of facilities single of a type. The study is not based on an algorithmic methodology; the primary point is setting up a general modelling structure.

2.2.2. Location-Inventory Problems

Nozick and Turnquist (2001) proposed a method with the aim of optimizing the inventory locations for individual commodities in a multi-commodity two-echelon inventory system, and integrating those choices into the distribution centers' location analysis. They presented a method to figure out which commodities should be stocked at the distribution centers based on the trade-off between cost and service quality, as well as customer preferences. In order to optimize the number and location of distribution centers, a fixed-charge facility location model is presented and the proposed model is linked with the method developed for determining the inventory locations.

Shen et al. (2003) dealt with a joint location-inventory problem including a single supplier and multiple retailers having variable demands. They focused on advantages of risk-pooling by allowing a few retailers to serve as distribution centers for other retailers. Their problem was to determine the retailers which will serve as distribution centers and the allocations of these retailers to distribution centers. The problem was formulated as a nonlinear integer programming model which was transformed to a set-covering integer programming model. They demonstrated that the problem could be solved effectiently in general.

Daskin et al. (2002) developed a Lagrangian relaxation solution algorithm for the model discussed in Shen et al. (2003). They identified a number of heuristics to achieve good feasible solutions. Additionally, they depicted two variable-forcing rules that are effective in forcing candidate sites out of and into the solution. They tested the algorithms on problems of different sizes. Their results indicated that their method performs better than the proposed approach of Shen et al. (2003) in terms of computational times.

Synder et al. (2007) presented a stochastic version of the model presented by Daskin et al. (2002). The objective of their model was to find solutions minimizing the expected total cost, consisting of location, transportation, and inventory costs over all scenarios. The model developed explicitly handles the risk-pooling impacts and economies of scale resulting from merging the stocking points. They introduced an exact algorithm based on a Lagrangian-relaxation of the location model.

Sadjady and Davoudpour (2012) considered a two-echelon network design problem in a multi-commodity, single-period, deterministic setting. The problem encapsulated decisions both at tactical and strategical levels, including locations and capacities of plants and warehouses, warehouse-retailer allocations and also transportation mode selections. The problem was formulated as a mixed-integer programming model, which aimed to minimize total cost of the network including opening costs for facilities, inventory holding, and transportation costs for products. A Lagrangian based heuristic solution algorithm was also presented which solves the real size problems successfully in reasonable computational times.

2.2.3. Location-Routing Problems (LRP)

There are several examples of location-routing problems in the literature (e.g. Chao, 2002; Melechovský et al., 2005) and a detailed survey of LRPs can be found in Nagy and Salhi (2007), and Prodhon and Prins (2014). We will only present some of them which are more relevant to our study, namely multi-level LRPs.

2.2.3.1. Multi-Level Location-Routing Problem and Its Extensions

Jacobsen and Madsen (1980), and Madsen (1983) presented a problem where newspapers are transported from the plant to transfer points and from transfer points to the clients. The problem comprises of; (i) determining the locations of transfer points, (ii) allocating clients to transfer points (or to the plant), (iii) designing a vehicle route through transfer points, and (iv) designing vehicle routes for each of the client clusters.

Semet and Taillard (1993) presented the road-train routing problem which concerns constructing a route for a vehicle composed of two parts, a trailer and a truck. The vehicle (trailer+truck) does not have access to some of the customers. Therefore, the trailer is detached and left at a customer location while a subset of the customers are visited by the truck, which then returns to pick up the trailer. The route of the vehicle with the trailer corresponds to the primary tour, while the routes run by the truck alone are the secondary tours.

Lin and Lei (2009) considered a problem including a set of plants, two sets of clients (a set of smaller clients and a set of larger clients). The aim was to determine the locations of the uncapacitated distribution centers, the subset of larger clients that will be served in the first routing level, and to construct the vehicle routes for both levels. They developed a genetic algorithm in which a chromosome specifies just the open distribution centers and the big clients that will be served in the first level. They also proposed a cluster-based routing heuristic combined with a local search in order to decode this indirect solution and construct the routes for two levels.

Boccia et al. (2010) considered the two echelon LRP with several plants and proposed a tabu search which handles the problem as two capacitated LRPs, one for each echelon. Decomposition was applied to each capacitated LRP resulting in a capacitated facility location problem, and a multi-depot vehicle routing problem with specific neighborhoods. In each echelon, whenever an improvement was obtained in the capacitated facility location problem, the multi-depot vehicle routing problem module was called to obtain the new location configuration. The link between two echelons was established by re-optimizing the capacitated facility location problem, whenever a modification in the satellites of some customers was obtained in the second echelon.

Nguyen et al. (2012) studied a two echelon LRP that includes an already located central warehouse and a set of potential satellites having capacity restrictions. They proposed four constructive heuristics, and two metaheuristics based on greedy randomized adaptive search procedure for solving the problem. Their results showed that metaheuristics outperforms the constructive ones, and all heuristics provides acceptable CPU times even for large-sized instances.

Contartdo et al. (2012) also studied a two echelon LRP including a plant, second level facilities, and customers. They developed a branch-and-cut algorithm based on a two-index vehicle flow formulation which is strengthened by some valid inequalities. Their results demonstrated that the proposed algorithm is able to solve the problems with up to 50 customers and 10 second level facilities optimally. For larger instances the proposed algorithm achieved small and hence acceptable gaps.

2.2.4. Inventory-Routing Problems

Inventory-routing decisions have been studied extensively in the literature. Baita et al. (1998), Moin and Salhi (2006), and Andersson et al. (2010) present detailed literature surveys of inventory-routing problems. We will only present some examples of inventory-routing problems which are more relevant to our study, namely multi-depot inventory routing problems (MDIRP).

2.2.4.1. Multi-Depot Inventory Routing Problems (MDIRP)

MDIRPs discussed in the literature are mainly based on the maritime industry. In maritime industry applications, the supply chain mainly consists of several ports and several customers, and have many-to-many topology. However, applications in maritime industry are not so relevant to our study due to the differences in supply chain configurations. Therefore, we focus on the studies considering road-based transportation.

Ramkumar et al. (2012) dealt with multi-commodity MDIRP under a vendor managed inventory setting. They modelled the problem as a mixed-integer linear program. They conducted numerical studies on test data sets and a real life case. However, their computational studies showed that the approach had limitations mainly in terms of solution time. They reported 8 hours of CPU time usage for small-sized problem instances, still not reaching the optimal solution.

Razavi and Nik (2013) studied MDIRP with backlog orders. They presented a mixed-integer programming model for the problem. They proposed a solution method based on a parallel genetic algorithm for solving large-sized instances. They conducted computational experiments and compared their results with the lower bounds obtained by an optimization software package for large sized-instances. Their results showed that the proposed algorithm is efficient.

Lmariouh et al. (2016) considered MDIRP for a multi-product setting. They dealt with a real life problem faced by a food company. They developed a mixed-integer linear program for the problem. They conducted numerical studies on four real-life based problems and compared their solution with the ones proposed by the planner of the company. Their results showed that their method performs better than the one proposed by the planner.

2.2.5. Location-Inventory-Routing Problems

Liu and Lee (2003) considered the multi-depot LRP for a single product setting. They presented a mathematical model for the problem which also takes inventory control decisions into consideration. They proposed a two-stage heuristic method to solve the problem. In the first stage, they used a route-first, location-allocation-second approach aiming to minimize the total cost (inventory, transportation and location costs). At the end of the first stage, an initial solution was obtained. In the second stage, an improvement heuristic search was used to improve the initial solution. Using simulation, they evaluated the performance of the proposed method. Computational results showed that the proposed method performs better than the existing ones which do not take inventory control decisions into consideration.

Liu and Lin (2005) dealt with the same location-inventory-routing problem. They decomposed the problem into a depot location-allocation problem and an inventory routing problem, and then solved the sub-problems independently. They also presented an alternative hybrid heuristic based on the combination of simulated annealing and tabu search techniques. Their computational results showed that the proposed heuristic outperforms the solution method previously presented by Liu and Lee (2003).

Ma and Davidrajuh (2005) dealt with a supply chain structure which include retailers with random demands, potential wholesalers, and a central depot. Inventories are managed at the upstream two layers in the chain. They presented a model with the objective of minimizing the transportation costs, the opening costs of wholesalers, and the inventory holding costs for the wholesalers and the depot. An algorithm iterating between a tactical and a strategic model was proposed. However, the study was primarily a methodological one and did not include any computational results.

Ambrossino and Scutella (2005) considered distribution network design problems including warehousing, facility location, inventory, and transportation decisions. They investigated various realistic scenarios. They proposed two different formulations for mathematical modelling of the problems, together with their proofs.

Shen and Qi (2007) studied a supply chain design problem where the location and number of the distribution centers should be determined. Their aim was to minimize the systemwide cost that involves costs of opening distribution centers, inventory costs at the distribution centers, and transportation costs in the chain. The problem was formulated as a nonlinear integer programming model and a solution algorithm based on a Lagrangian relaxation was proposed. Their results demonstrated the benefits of the proposed integrated modelling approach.

Xuefeng (2010) studied a location-inventory-routing problem. Supply chain structure considered in the study was composed of retail stores, potential distribution centers, and a central warehouse. The aim of the study was to minimize the total cost including transportation costs, inventory costs, and facility location costs. The problem was formulated as a nonlinear mixed-integer programming model, and a solution algorithm based on a nested Lagrangian relaxation was proposed. Their computational results based on some example problems demonstrated that the proposed algorithm performs well in terms of both solution quality and run time.

Hiassat and Diabat (2011) studied a supply chain structure which includes a supplier, multiple distribution centers, and multiple retailers having deterministic demand. Distribution of a single perishable product was in consideration. The objective of their problem was to determine the number and location of warehouses to open, and allocation of customers to warehouses so as to minimize the total cost. They proposed a mathematical model for the inventory-location problem with routing costs, and solved small test problems using GAMS. Their results showed the advantages of integrating the decisions at the strategic and tactical levels.

Javid and Azad (2010) studied a stochastic supply chain system consisting of several customers and several potential distribution centers. They proposed a model aiming to optimize location, allocation, routing, and inventory decisions. They developed both an exact method and a heuristic solution method. Heuristic solution method was based on a combination of simulated annealing and tabu search. Their numerical studies showed that the heuristic solution method performs well for different sized problems.

Guerrero et al. (2013) studied a supply chain structure consisting of multiple depots with storage capacity and multiple retailers with deterministic demand. They considered a location-inventory-routing problem. Their objective was to determine the depots to open, the amounts of product transfers between depots and retailers, and also between suppliers and depots per period, and the vehicle routes. They formulated the problem as a mixed-integer linear programming model, and strengthened the model by two sets of valid inequalities. They presented a hybrid solution method. This method was based on embedding an exact approach within a heuristic scheme. They presented numerical studies using three sets of instances for inventory-routing, location-routing, and location-inventory-routing problems.

Zhang et al. (2014) considered a supply chain network including multiple depots and multiple customers facing with dynamic demand over a discrete planning horizon. The objective was to determine the depots to open, the amounts of transfers to customers per period and vehicle routes so as to minimize the total cost of the system. A mixed-integer programming model was constructed, and a hybrid metaheuristic was proposed.

Nekooghadirli et al. (2014) presented a bi-objective location-inventory-routing model that considers a multi-product and multi-period system. Two objectives of the model are (i) minimizing the total cost and (ii) minimizing the maximum average time for delivering products to customers. Four different multi-objective meta-heuristic algorithms were proposed, and their performances were evaluated using the results obtained from numerical studies.

2.2.6. Special Cases of Location-Inventory-Routing Problem with Multiple Location Layers

As it will be discussed in the following sections, special cases of Location-Inventory-Routing Problem with Multiple Location Layers under the predetermined parameter settings, are equivalent to the well-known problems such as Multi-Depot Vehicle Routing Problem – MDVRP, Single Source Capacitated Facility Location Problem – SSCFLP, and Capacitated Vehicle Routing Problem – CVRP. There are also articles papers on MDVRP, SSCFLP, and CVRP.

2.2.6.1. Multi-Depot Vehicle Routing Problem (MDVRP) and Its Extensions

Sumichrast and Markham (1995) proposed a heuristic to solve MDVRP where a fleet of trucks is used to transfer different raw materials from multiple sources to multiple plants. At the first step of the heuristic, an initial feasible solution is obtained by determining the least costly way for supplying each plant with the material demanded by one plant at a time. Then, for each truck, routes are exchanged to check if a net cost savings can be achieved, while maintaining feasibility. In order to evaluate the performance of the proposed heuristic, they compared the results of the heuristic with the lower bound obtained from a relaxed binary formulation. Comparisons on the results of experiments applied on various different sized test problems (from 52 to 609 nodes) demonstrated that the proposed heuristic performs well.

Wu et al. (2002) developed a different solution method for the MDVRP. They divided the problem into two sub-problems; the general vehicle routing problem and the location-allocation problem. Sub-problems are solved in a sequential and iterative manner using the simulated annealing algorithm. Results of their numerical studies indicated that the performance of the proposed method is both effective and efficient.

Mirabi et al. (2010) studied the problem of MDVRP aiming to minimize the delivery times of vehicles. Three hybrid heuristics were developed to solve the problem. Proposed hybrid heuristics were based on different combinations of constructive heuristic search and improvement techniques. They presented results of various experiments applied on randomly generated different sized test problems. Their results showed that the proposed hybrid heuristics perform better than one of the best-known existing heuristic, method developed by Giosa et al. (2002).

Gulczynski et al. (2011) combined the MDVRP and the split delivery VRP. The resulting problem was named as the multi-depot split delivery VRP. A heuristic based on integer programming was developed to solve the problem. They also applied the proposed heuristic to 30 instances in order to identify the reduction in distance travelled which can be obtained by allowing split deliveries among vehicles based at different depots and vehicles based at the same depot.

Kuo and Wang (2012) developed a variable neighborhood search (VNS) model to solve the MDVRP with loading cost which is a combination of vehicle routing problem with loading cost and MDVRP. The proposed VNS was composed of three main stages. First stage is using a stochastic method to obtain the initial solution. The second stage is randomly selecting one of four operators (node insertion, node exchange, section exchange, arc exchange) which will be used to search neighborhood solutions. Final stage is using a criterion for neighborhood solution acceptance. Their experimental results showed that the method is capable of providing an improvement in total transportation cost, around 23.77% on the average, over the best known results.

Contartdo and Martinelli (2015) studied the MDVRP under route length and capacity constraints. An exact solution method was developed for the problem. The capacitated VRP was also considered as a general case of the MDVRP, and numerical experiments were conducted on various instances from the literature. Their results showed that the proposed method is competitive against the state-of-the-art methods.

Li et al. (2015) were the first to develop a metaheuristic approach for MDVRP along with simultaneous deliveries and pickups. Their approach was based on an iterated local searching algorithm. They embedded an adaptive neighborhood selection mechanism into the perturbation steps of the iterated local search and improvement steps in order to strengthen the search. New perturbation operators were also proposed to diversify the search. Their results showed that the proposed heuristic outperforms the previously developed methods for the problem.

2.2.6.2. Single Source Capacitated Facility Location Problem (SSCFLP) and Its Extensions

Tragantalerngsak et al. (1997) considered the two-echelon SSCFLP problem. A mathematical model was proposed, and six heuristics based on Lagrangian relaxation were developed for its solution. A sub-gradient optimization process was utilized to solve the dual problem. They presented computational results which showed that the proposed method provides better solutions than the ones from the traditional linear programming relaxation.

Tragantalerngsak et al. (2000) studied the two-echelon SSCFLP developing another approach. This time they proposed a branch and bound algorithm based on Lagrangian relaxation to solve the SSCFLP. Their results indicated that the method is efficient for a large suite of test problems of practical and realistic size.

Rönnqvist et al. (1999) described a new solution approach for SSCFLP based on the repeated matching algorithm. This algorithm solves a series of matching problems until the defined convergence criteria are met, and at each iteration, generates a feasible solution. Their numerical results showed that the solution obtained by using the proposed method are often better than the ones obtained by using the best Lagrangian heuristics.

Cortinhal and Captivo (2003) studied the SSCFLP and proposed a Lagrangian relaxation in order to get lower bounds for the problem. An upper bound was obtained by the Lagrangian heuristics followed by a local search or a tabu search metaheuristic. The numerical studies indicated that tabu search metaheuristic performs better than local search.

Rahmani and MirHassani (2014) proposed a new hybrid optimization method to solve the capacitated facility location problem. The proposed method is a combination of the standard genetic algorithm and the discrete firefly algorithm. Numerical studies were conducted on different sized problems. For small-sized problems they compared the results with CPLEX results and for large ones with Particle Swarm Optimization Algorithm. Their results showed that the proposed algorithm is applicable for small, medium, and large-sized problems.

Ho (2015) also studied SSCFLP and developed a heuristic based on iterated tabu search. The heuristic incorporates tabu search with perturbation operators in order to eliminate the risk of getting stuck in local optima. Experimental results showed that the proposed heuristic generates high quality solutions and it is competitive with other metaheuristics proposed for solving the SSCFLP.

2.2.6.3. Capacitated Vehicle Routing Problem (CVRP) and Its Extensions

Moghaddam et al. (2006) proposed a linear integer model for CVRP. The objectives of the model are maximizing the capacity usage and minimizing the heterogeneous fleet cost. In their model there is a hard time window over depot and fleet cost is independent of the route length. A hybrid simulated annealing solution method based on the nearest neighborhood search is proposed to solve the problem. Their results showed that good solutions can be obtained by the proposed method in reasonable times.

Christiansen and Lysgaard (2007) proposed an exact algorithm for the CVRP with stochastic demands. They formulated the problem as a set partitioning problem. They also showed that, using a dynamic programming scheme, the associated column generation sub-problem can be solved. Results of the study indicated that their algorithm complements the L-shaped method and a broad range of problems could be solved using the proposed method.

Juan et al. (2010) also studied CVRP and presented a hybrid algorithm that combines a classical CVRP heuristic with Monte Carlo simulation. A comparison is presented with some well-known benchmarks. Their results showed that the proposed algorithm is able to compete or even outperform more complex algorithms in most of the cases.

Szeto et al. (2011) developed an artificial bee colony heuristic to solve CVRP. An enhanced version of the heuristic is also proposed in order to improve the solution quality. The performance of the enhanced version of the heuristic is evaluated on two sets of problems, and compared with the original one. Their computational results showed that the enhanced version of the heuristic outperforms the original version, and can perform better than the existing heuristics.

Bortfeldt (2012) considered the CVRP with three-dimensional loading constraints. They proposed a hybrid algorithm that combines a tree search algorithm for loading and a tabu search algorithm for routing. Numerical studies were also conducted using all public test instances. Results showed that the proposed method improves most of the best solutions previously published with drastically reduced computational efforts.

Jin et al. (2014) also studied CVRP and presented a cooperative parallel metaheuristic. Results of their computational studies indicated that the developed method provides new best solutions to most of the large-scale benchmark instances previously studied in the literature, therefore, it is highly competitive.

2.3. Comparison of Our Study with the Previous Ones in the Literature

Our problem lies in the intersection of "Location-Inventory-Routing Problems" and "Location Problems with Multiple Location Layers". In other words, we extend the previously mentioned integrated approach (Location-Inventory-Routing) for a specific problem environment which includes the following distinctive characteristics:

- A highly complex hierarchical structure to be considered (Blood supply chain under our consideration includes DCs, CLs, RBCs, RTCs, and TCs. Previous studies adopting an integrated approach deal with a supply chain structure which only includes three different types of facilities, i.e. plant(s), distribution centers, and customers which correspond to RBCs, RTCs, and TCs in the context of blood supply chain).
- Different types of facilities to be located (RBCs and RTCs).
- Both inbound (blood collection) and outbound (blood distribution) transportation costs to be considered.
- A solution approach to be presented (rather than just presenting a general modeling framework).

In order to make this distinction more clear, we compare our study with the recent similar studies, i.e. selected examples of the ones adopting an integrated approach, or dealing with location of facilities at multiple layers. Comparison given in Table 1 is mainly based on the supply chain structure, types of material flows, time horizon, cost components considered, routing decisions, and solution approaches.

Table 1. Comparison of Our Study with the Similar Ones in the Literature

Problem Features		Our Study	Pirkul and Jayaraman (1997)	Jayaraman and Pirkul (2001)	Javid and Azad (2010)	Shen et. al. (2003)	Sadjay and Davoudpoor (2011)	Badri et. al. (2013)	Xuefeng (2010)	Hiassat and Diabat (2011)	Daskin and Coullard (2002)	Shen and Qi (2007)	Liu and Lee (2003)	Melo et. al. (2005)
Supply Chain Structure	Facility Topology	Multi Type	Multi Type	Multi Type	Single Type	Single Type	Multi Type	Multi Type	Single Type	Single Type	Single Type	Single Type	Single Type	Multi Type
	Vendor	Multiple	X	Multiple	X	X	X	Multiple	X	X	X	X	X	Multiple
		Capacitated		Capacitated				Capacitated						Capacitated
		Known Locations		Known Locations				Known Locations						Unknown Locations
	Production Plant	Multiple	Multiple	Multiple	Single	Single	Multiple	Multiple	Single (as center warehouse)	Single	One or more	Single	Single	Multiple
		Capacitated	Capacitated	Capacitated	Uncapacitated	Uncapacitated	Capacitated	Capacitated	Uncapacitated	Uncapacitated	Uncapacitated	Uncapacitated	Uncapacitated	Capacitated
		Unknown Locations	Unknown Locations	Unknown Locations	Known Location	Known Location	Unknown Locations	Unknown Locations	Known Location	Known Location	Known Location	Known Location	Known Location	Unknown Locations
	Warehouse	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple
		Capacitated	Capacitated	Capacitated	Capacitated	Capacitated	Capacitated	Capacitated	Uncapacitated	Uncapacitated	Uncapacitated	Uncapacitated	Uncapacitated	Capacitated
		Unknown Locations	Unknown Locations	Unknown Locations	Unknown Locations	Unknown Locations	Unknown Locations	Unknown Locations	Unknown Locations	Unknown Locations	Unknown Locations	Unknown Locations	Unknown Locations	Unknown Locations
	Customer	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple	Multiple
		Normal Demand	Known Deterministic Demand	Known Deterministic Demand	Normal Demand	Normal Demand	Known Deterministic Demand	Known Deterministic Demand	Normal Demand	Known Deterministic Demand	Normal Demand	Normal Demand	Stochastic Demand	Known Deterministic Demand
		Known Locations	Known Locations	Known Locations	Known Locations	Known Locations	Known Locations	Known Locations	Known Locations	Known Locations	Known Locations	Known Locations	Known Locations	Unknown Locations
Material Flow	Multi Product/Single Product	Single Product	Multi Product	Multi Product	Single Product	Single Product	Multi Product	Multi Product	Single Product	Single Product	Single Product	Single Product	Single Product	Multiple Product

Table 1. (Continued)

Problem Features		Our Study	Pirkul and Jayaraman (1997)	Jayaraman and Pirkul (2001)	Javid and Azad (2010)	Shen et. al. (2003)	Sadjay and Davoudpoor (2011)	Badri et. al. (2013)	Xuefeng (2010)	Hiassat and Diabat (2011)	Daskin and Coullard (2002)	Shen and Qi (2007)	Liu and Lee (2003)	Melo et. al. (2005)
Time Horizon	Single Period /Multi Period	Single	Single	Single	Single	Single	Single	Multiple	Single	Multiple	Single	Single	Single	Multiple
COST COMPONENTS	Fixed Cost Associated with Production Plants	✔ Several capacity levels	✔ Different capacity levels not considered	✔ Different capacity levels not considered	X	X	✔ Several capacity levels	✔ Several capacity levels	X	X	X	X	X	✔
	Fixed Cost Associated with Warehouses	✔ Several capacity levels	✔ Different capacity levels not considered	✔ Different capacity levels not considered	✔ Several capacity levels	✔	✔ Several capacity levels	✔ Several capacity levels	✔ Different capacity levels not considered	✔	✔	✔	✔	✔
	Variable Cost Associated with Production Plant	X	X	✔	X	X	✔	✔	✔	X	X	X	X	✔
	Variable Cost Associated with Warehouses	X	X	✔	✔	X	✔	✔	X	X	X	X	X	✔
	Fixed Cost of Distributing Finished Products (plant-warehouse)	✔	X	✔	✔	✔	X	✔	✔	X	Partially	✔	X	✔

Table 1. (Continued)

Problem Features		Our Study	Pirkul and Jayaraman (1997)	Jayaraman and Pirkul (2001)	Javid and Azad (2010)	Shen et. al. (2003)	Sadjay and Davoudpoor (2011)	Badri et. al. (2013)	Xuefeng (2010)	Hiassat and Diabat (2011)	Daskin and Coullard (2002)	Shen and Qi (2007)	Liu and Lee (2003)	Melo et. al. (2005)
COST COMPONENTS	Variable Cost of Distributing Finished Products (plant-warehouse)	✔	✔	✔	✔	✔	✔ (allows different transportation modes)	✔	✔	X	X	✔	X	✔
	Cost of Transporting Raw Materials from Vendors to Production Plant	✔	X	✔	X	X	X	✔	X	X	X	X	X	✔
	Inventory Costs for Warehouses	✔	X	X	✔	✔	✔	✔	✔	X	✔	✔	✔	✔
	Inventory Costs for Production Plants	X	X	X	X	X	✔	✔	X	X	X	X	X	✔
	Inventory Costs for Vendors	X	X	X	X	X	X	X	✔	✔	X	X	X	✔
	Costs for transfers From warehouses to customer	✔	✔	✔	✔	✔	✔ (allows different transportation modes)	✔	✔	✔	✔	✔	✔	✔

Table 1. (Continued)

Problem Features		Our Study	Pirkul and Jayaraman (1997)	Jayaraman and Pirkul (2001)	Javid and Azad (2010)	Shen et. al. (2003)	Sadjay and Davoudpoor (2011)	Badri et. al. (2013)	Xuefeng (2010)	Hiassat and Diabat (2011)	Daskin and Coullard (2002)	Shen and Qi (2007)	Liu and Lee (2003)	Melo et. al. (2005)
ROUTING DECISION	Routing Decisions	✔	X	X	✔	X	X	X	✔	✔	X	✔ (routing costs included by approxima-tion but routing decisions are not considered)	✔	X
MODEL	Model Formulation (*)	MINLP	MIP	MIP	MINLP	MINLP	MIP	MIP	MINLP	MIP	NIP	NIP	NIP	MIP
SOLUTION	Solution Technique	Optimal Solution Method + Heuristics Based On Decomposition And Simulated Annealing	Heuristic Solution Procedure Utilizing Lagrangian Relaxation	Heuristic Solution Procedure Utilizing Lagrangian Relaxation	Exact Solution Method + Heuristic Based On Tabu Search And Simulated Annealing	Restructure The Model Into a Set Covering IP Model Pricing Problem Solved by Using Column Generation Algorithm	Heuristic Solution Procedure Utilizing Lagrangian Relaxation	Heuristic Solution Procedure Utilizing Lagrangian Relaxation	Lagrangian Relaxation Based Solution Algorithm	GAMS CPLEX MIP Solver for Small Sized Problems (2 Warehouses and 4 Customers)	Lagrangian Relaxation Based Solution Algorithm	Lagrangian Relaxation Based Solution Algorithm	Two-phase Heuristic	Paper is not Based On Algorithmic Approach, Main Aim Is Establishing A General Modeling Framework. Sample Problems Only Includes Location of DCs

(*) MIP: Mixed Integer Programming, MINLP: Mixed Integer Non-Linear Programming, NIP: Non-linear Integer Programming, IP: Integer Programming

CHAPTER 3

THE PROBLEM DEFINITION

In this chapter, we first define the existing Turkish blood supply chain and the one that is planned to be established in the very near future by 2017. Then we define the problem that is addressed in this study.

3.1. The Problem Environment

In most of the countries in the world, blood banking operations are managed in a regionalized manner. In the regionalized structure, an RBC is in charge of coordination and management of blood banking operations within its responsibility area. In other words, this structure constitutes the centralization of blood banking operations at the regional level. Centralization of blood banking activities has several advantages in terms of economies of scale and service quality. However, these advantages can only be acquired by the effective management of the complex blood supply chain. Additionally, for the success of medical operations, availability of blood and blood components should be guaranteed at the transfusion centers (hospitals), in some areas even hundreds of kilometers away from an RBC.

In Turkey, as a result of the collaboration of TRCS and the Ministry of Health, regionalization of blood services throughout the country has been started which is compatible with the structure defined in the new blood and blood products law published in 2007. However, the reorganization of blood services is still in the transition period, and it is expected to be over by 2017. A schematic view of the current structure of the Turkish Blood Supply Chain is illustrated in Figure 4.

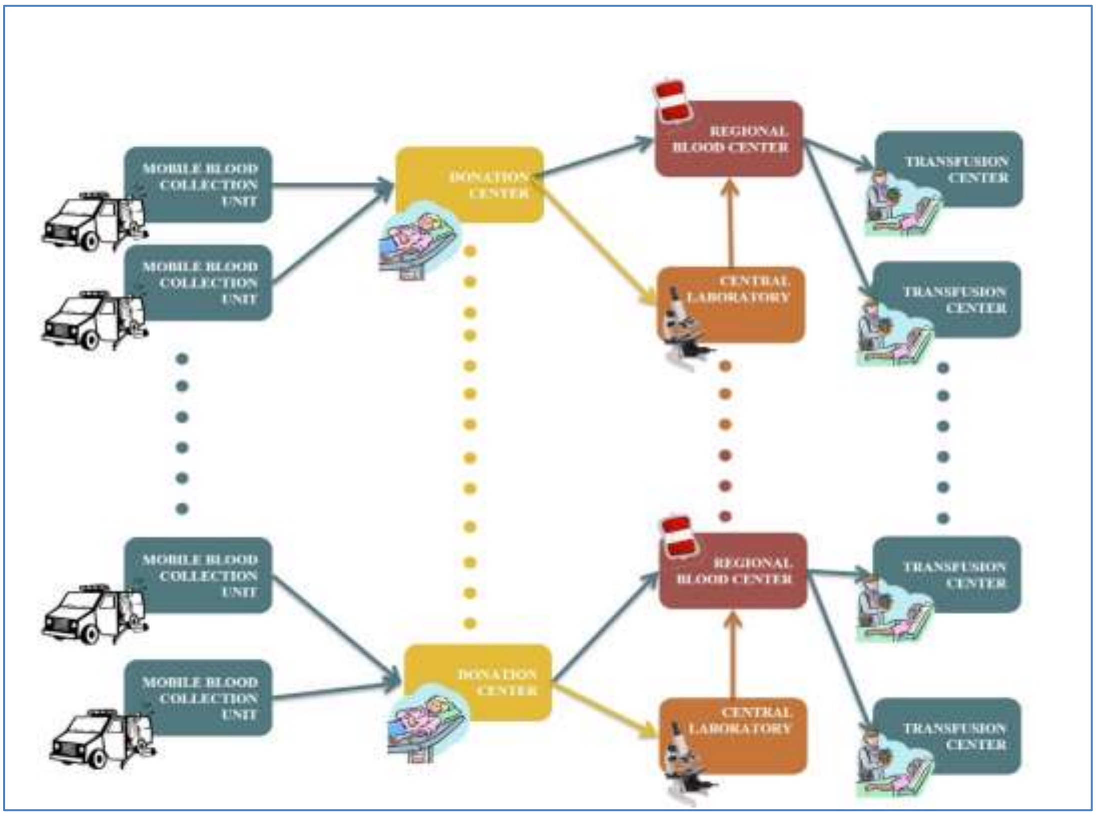


Figure 4. Current Structure of the Turkish Blood Supply Chain

As depicted in the figure, there are several mobile blood collection units (or temporary units) responsible for collecting blood from volunteer blood donors in some predetermined sites. These mobile units are assigned to a Donation Center (DC). DCs manage blood and blood components collection activities within their area of responsibility. As DCs are permanent donation sites, they are the main sources of repeated and regular donors. Blood and blood components donated by the repeated and regular donors are considered to be safer than the ones donated by the first time or irregular donors. Whole blood collected by either mobile units or DCs are sent to their associated responsible Regional Blood Center (RBC). Blood samples taken from donors are sent to the responsible Central Laboratory (CL) to be tested, which is either located in the RBC or nearby.

CL is the unit that carries out serological tests on all blood samples taken from donors within its area of responsibility. After tests are finalized, the responsible RBC is informed about the test results using an online software.

RBC is the unit that coordinates and administrates the blood services within its area of responsibility with its lower level units, which are the DCs and mobile units. Whole blood units sent by DCs are divided into blood components in the component laboratories located within the RBC. Then blood components are stored in quarantine inventory until the serological test results are known. If positive test results are declared by the CL, then the corresponding blood units are discarded, otherwise the components with negative test results are carried to the available inventory which includes ready-to-use products. If needed, special processes such as filtering, pooling etc. are applied in the processing laboratory also located in the RBC. Ready-to-use blood and blood components are supplied by the RBC to all transfusion centers within its area of responsibility according to their demands. RBC may also include a DC and a CL. However, these facilities can also be located separately.

Transfusion centers (TCs) are the units located in the hospitals. They manage their blood and blood components inventory, and when needed, they demand blood and blood components from their associated responsible RBC. These centers are also responsible for carrying out compatibility tests before transfusion, and following up the patient status after transfusion. These centers are not allowed to collect blood with the exception of emergency cases.

All facilities in the chain are owned and operated by the TRCS, except the TCs and temporary RBCs. Transfusion centers are owned by either public hospitals, or university hospitals, or private hospitals. Temporary RBCs are the facilities at hospitals which have adopted replacement donation, hence, do not fulfill the requirements expected from a decent blood facility in terms of voluntary donation, and laboratory and logistics capacities. These centers are actually the transfusion centers in large hospitals and authorized for meeting their own demands for blood and blood components only during the transition period. As stated before, transition period is expected to be over by 2017, when TRCS is expected to be able to secure voluntary blood donations sufficient at the national level, and hence temporary RBCs will have been closed by then.

The numbers of the facilities in the current Turkish blood supply chain are as follows:

- 19 RBCs owned and operated by the TRCS
- 62 DCs owned and operated by the TRCS
- Approximately 140 mobile blood collection units owned and operated by the TRCS
- 4 CLs owned and operated by the TRCS
- 35 temporary RBCs
- Approximately 1600 TCs

In addition to the efforts spent to overcome the problems associated with the transition period, and to ensure proper and full functioning of the centralized blood services structure, authorities are developing new strategies to further improve the blood supply chain. One of these new strategies is to centralize the transfusion services, by the incorporation of a new type of facility, called the Regional Transfusion Center (RTC), to the blood supply chain, similar to the current centralized blood banking operations (volunteer donor recruitment, blood collection, processing and testing, etc.). RTC is a facility that is responsible for centrally managing pre-transfusion tests, providing consultancy services to the TCs with highly qualified staff, and storing blood and blood components for supplying ready-to-use blood and blood components to all transfusion centers within its area of responsibility. In other words, RTC operates as a central transfusion laboratory and a distribution center as well. Furthermore, RTC also provides consultancy services to the transfusion centers within its area of responsibility.

There are several studies in the literature focusing on the idea of centralized transfusion services (see, for example, Triulzi, 1997; AuBuchon et al., 2011). These studies point out the several economic, medical, and quality benefits of centralized transfusion services, and demonstrate the models that show the feasibility of the idea.

The benefits expected from the centralized transfusion services can be summarized as follows:

- Increased safety with centralized testing performed by experienced transfusion service staff utilizing standardized and efficient testing procedures.
- Improved patient outcomes at lower costs through improved blood component utilization and reduction in the Crossmatch-to-Transfusion ratio.
- Enhanced transfusion medicine knowledge for the clinical and medical staff of the transfusion centers (other hospitals) when transfusion medicine and technical expertise of the RTC is shared.
- Increased efficiency in the delivery of services and logistics. Adding a new level to the supply chain which acts as a distribution center, thus improving inventory and logistics performance.
- Potential cost savings for the hospital by a reduction in unnecessary and duplicate testing, product consumption, and labor costs, and elimination of reagent and supply costs to the hospital.

In the presence of RTCs, RTCs form an additional echelon in the blood supply chain. Hence, RBCs do not directly supply TCs anymore. Instead, TCs are supplied by RTCs that are in turn supplied by RBCs. This situation will change the structure of the blood supply chain. The proposed new structure is illustrated in Figure 5, in case regionalized transfusion services are realized.

Figure 5 depicts the proposed new structure which can be realized after the transition period is over. At the end of the transition period, annual blood donation obtained by TRCS is expected to increase, and also temporary RBCs are to be closed. Therefore, the numbers and the locations of RBCs are subject to change in the near future. These expected changes in the chain bring in the following decisions to be made by the decision makers: "how many RTCs and RBCs are needed", "Where to locate the RTCs and RBCs", “What should be the capacities of RTCs and RBCs in the chain”, and "How to allocate the responsibility regions of RBCs and RTCs". In our study, we intend to propose an approach aiming to answer these questions by simultaneously taking into account also the other main decisions of the blood supply chain, such as inventory management at the RTCs , and distribution and routing of blood and blood components to the TCs.

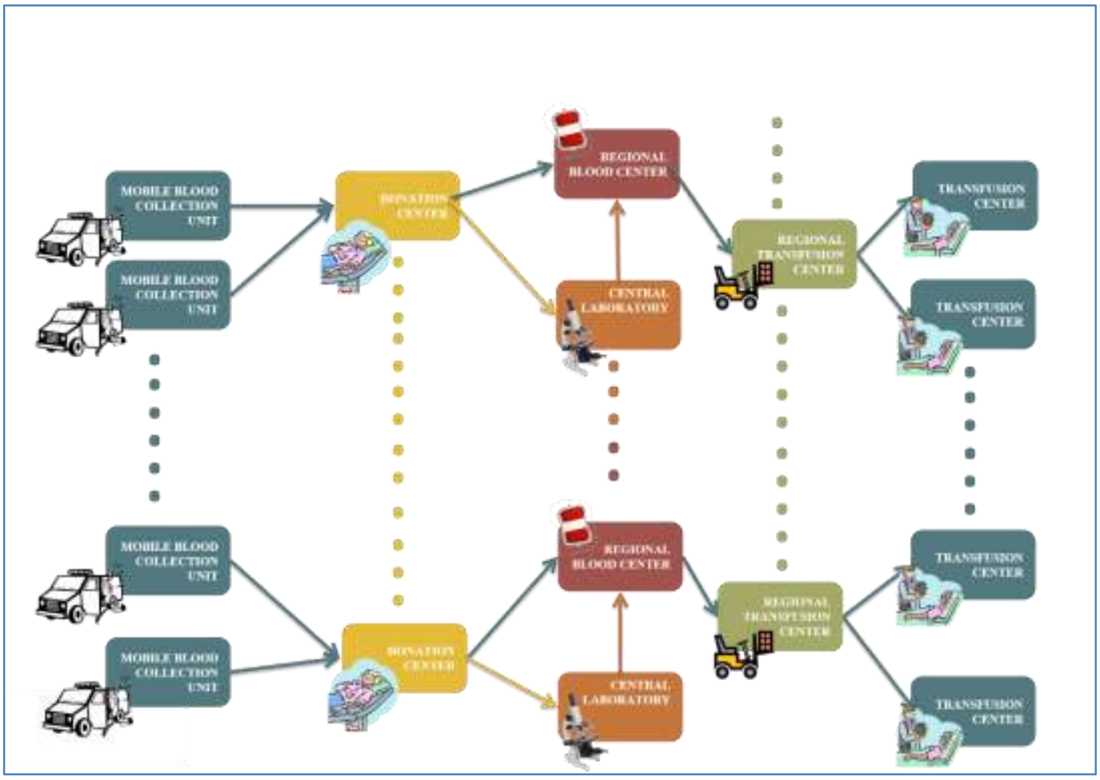


Figure 5. The Proposed New Structure of the Turkish Blood Supply Chain

3.2. The Problem Definition

In our study, we will consider a joint location-inventory-routing problem with multiple location layers. The problem involves multiple DCs, multiple RBCs (suppliers), multiple RTCs (distribution centers), multiple CLs and multiple TCs (retailers). Basic assumptions made in advance before modelling the supply chain described above are as follows:

- As the decision makers declare that changing the location of DCs, TCs and CLs is not an option, we will assume that these locations are known and cannot be changed.
- The transportation of blood samples is free of charge (there is a protocol between an air carrier and the owner of CLs). Hence, we do not model the CLs explicitly in the model. Costs associated with the CLs and the transfers between CLs and other facilities are ignored.
- Inventory costs at DCs, RBCs and TCs are ignored.
    - As the whole blood units obtained from the volunteer donors are sent to the associated RBC immediately in order to make this valuable source ready-to-use as soon as possible, DCs hold inventory at most for one day only. Therefore, inventory costs associated with DCs are negligible.
    - We assume that the TCs maintain only a minimal amount of inventory. In our problem environment, the safety stock for all TCs served by the same RTC is maintained at the RTC. In this case, due to the risk pooling effect, less safety stock is required at the RTC than in the case in which every TC maintains its own safety stock. Therefore, we can safely ignore the inventory costs at the TCs.
    - In Turkey, self-sufficiency in terms of blood components has not been achieved yet. Therefore, RBCs send the blood components to TCs immediately as soon as they become ready-to-use. Under current conditions, RBCs hold inventory for a limited time period and therefore

we can assume that inventory costs at RBCs are also negligible. However, this assumption may not be realistic in the future. For instance, when self-sufficiency is achieved. In this case RBCs will be holding a considerable amount of inventory. Nevertheless, inventory costs associated with RBCs will be ignored for simplicity only.

- We assume that demand at each TC follows a normal distribution, and the TCs' demands are independent (see Eppen, 1979; Daskin et al., 2002; and Shen et al., 2003; for the same assumption in their studies).
- Although 8 different blood groups and 3 different blood components are available, in our problem we aggregate them all, and hence consider blood as a single product.
- Lead time between any RTC and RBC is assumed to be the same and deterministic for each RTC-RBC pair.
- It is assumed that each RTC uses a (Q,R) inventory policy, and that each RTC holds a safety stock to cope with the variation in blood demand of TCs. Inventory at RTCs is assumed to be depleted over time at a constant rate.
- We assume that shipments between DCs and RBCs, and between RBCs and RTCs are direct shipments. However, in reality, shipments between RTCs and TCs will be in the form of milk runs.
- We assume that all vehicles have the same capacity, and that they are homogeneous.

In the light of the explanations above, our problem is stated as: Given a set of DCs, and TCs (with uncertain product demand), determine how many RBCs and RTCs to locate, where to locate them, which TCs to assign to each RTC, which RTCs to assign to each RBC, which DCs to assign to each RBC, what should be the reorder frequency and size at RTCs, what should be the level of safety stock at RTCs, how to construct the vehicles' routes between opened RTCs and their affiliated TCs to minimize the total expected cost including the cost items listed below:

- Fixed cost of opening RBCs
- Fixed cost of opening RTCs
- Routing cost from the opened RTCs to the TCs
- Transportation cost from RBCs to RTCs
- Transportation cost from DCs to RBCs
- Cycle inventory costs (cost of ordering and cost of carrying inventory) and costs of safety stock (to maintain a target service level) of RTCs

We formulate the problem defined above as a mixed-integer nonlinear programming model in the following section. Then we present alternative solution approaches for the problem, and evaluate their performances through computational results for several different-sized problems, in the following sections.

It should be noted that the proposed approach may not simultaneously optimize location, allocation, inventory, and routing decisions in the chain, due to the simplifying assumptions about inventory and routing issues. Inventory and routing decisions will be open to further improvements. However, determining the locations and allocations of the facilities by taking into consideration the inventory and distribution aspects is expected to provide a better solution than the case when these aspects are not considered. Hence, the proposed approach allows us to consider also the tactical aspects, while making a decision at the strategic level. The solutions obtained are expected to provide an improved base, since strategic location decisions have a big impact on inventory and shipment costs. Once the location and allocation decisions are made using the proposed approach, one can elaborate more on inventory and routing issues in detail to achieve further improvements in the solutions.

CHAPTER 4

MODEL FORMULATION AND SPECIAL CASES OF THE MODEL

In this chapter, we formulate the problem addressed in the previous section as a nonlinear mixed-integer programming model and demonstrate the special cases of the model.

4.1. Model Formulation

Index Sets

K Set of Transfusion Centers (TCs)

J Set of potential Regional Transfusion Centers (RTCs)

H Set of potential Regional Blood Centers (RBCs)

T Set of Donation Centers (DCs)

M_j Set of capacity levels for RTC j $(j \in J)$

N_h Set of capacity levels for RBC h $(h \in H)$

V Set of vehicles

Parameters and Notation

B Number of TCs in set K, i.e. $B = |K|$

μ_k Mean annual demand at TC k $(\forall k \in K)$

σ_k^2 Variance of annual demand at TC k $(\forall k \in K)$

f_j^n Fixed annual cost of opening and operating RTC j with capacity level n $(\forall j \in J, \forall n \in M_j)$

g_h^n Fixed annual cost of opening and operating RBC h with capacity level n $(\forall h \in H, \forall n \in N_h)$

w_j^n Capacity of RTC j at capacity level n $\left(\forall j \in J, \forall n \in M_j\right)$

u_h^n Capacity RBC h at capacity level n for $(\forall h \in H, \forall n \in N_h)$

CAP_t Capacity for DC t $(\forall t \in T)$

d_{kl} Transportation cost from k to l $(\forall\ (l,k) \in (JxK)\ \cup\ (KxK)\ \cup\ Kx\ J)$

vc Annual delivery capacity of a vehicle (q x capacity of truck)

q Annual number of visits of each vehicle from an RTC to a TC

h_j Annual inventory holding cost per unit of blood at RTC j $(\forall j \in J)$

p_j Fixed cost of placing an order to the RBC by RTC j $(\forall j \in J)$

lt Lead time (in years) of RTC j $(\forall j \in J)$ for procurement of blood from RBC

α Targeted percentage of customer orders which should be satisfied on time (fill rate), $\alpha > 0.5$

z_α α-percentile of standard normal distribution

DRR Blood disposal (due to positive test results and unexpected errors in production processes) rate at RBCs

BigM Big number (or highest capacity level associated with the facility type)

c_{th} Cost-weighted distance between DC t and RBC h $(\forall h \in H, \forall t \in T)$

e_{hj} Cost-weighted distance between RTC j and RBC h $(\forall j \in J, \forall h \in H)$

Decision Variables

$$R_{klv} = \begin{cases} 1 \text{ if } k \text{ precedes } l \text{ in route of vehicle } v \\ 0 \text{ otherwise} \end{cases}$$
$$\forall\ (l,k) \in (JxK)\ \cup\ (KxK)\ \{(k,k)\colon k \in K\}\ \cup\ (K\text{x}J)$$

$$Z_{jk} = \begin{cases} 1 \text{ if TC } k \text{ is assigned to RTC } j \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall k \in K)$$

$$Y_{hj} = \begin{cases} 1 \text{ if RTC } j \text{ is assigned to RBC } h \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall h \in H)$$

$$X_{th} = \begin{cases} 1 \text{ if DC } t \text{ is assigned to RBC } h \\ 0 \text{ otherwise} \end{cases} \qquad (\forall t \in T, \forall h \in H)$$

$$W_j^n = \begin{cases} 1 \text{ if RTC } j \text{ is opened with capacity level } n \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall n \in M_j)$$

$$U_h^n = \begin{cases} 1 \text{ if RBC } h \text{ is opened with capacity level } n \\ 0 \text{ otherwise} \end{cases} \qquad (\forall h \in H, \forall n \in N_h)$$

C_{th} : Amount sent from DC t to RBC h $(\forall t \in T, \forall h \in H)$

D_{hj} : Amount sent from RBC h to RTC j $(\forall h \in H, \forall j \in J)$

Q_j : Order size at RTC j $(\forall j \in J)$

m_{kv} : Variable defined for subtour elimination $(\forall k \in K, \forall v \in V)$

(P) Minimize

$$\sum_{j \in J} \sum_{n \in Mj} f_j^n W_j^n + \sum_{h \in H} \sum_{n \in N_h} g_h^n U_h^n + q \sum_{v \in V} \sum_{j \in J} \sum_{k \in K} d_{jk} R_{jkv} + q \sum_{v \in V} \sum_{k \in K} \sum_{j \in J \cup K \{k\}} d_{kj} R_{kjv} + \sum_{t \in T} \sum_{h \in H} c_{th} C_{th} + \sum_{h \in H} \sum_{j \in J} e_{hj} D_{hj} + \sum_{j \in J} (p_j) \frac{\sum_{k \in K} \mu_k Z_{jk}}{Q_j} + \sum_{j \in J} \frac{h_j Q_j}{2} + \sum_{j \in J} h_j z_\alpha \sqrt{lt \sum_{k \in K} \sigma_k^2 Z_{jk}} \quad (1)$$

Subject to;

$$\sum_{v \in V} \sum_{l \in J \cup K (K \setminus \{k\})} R_{klv} = 1 \ (\forall k \in K) \quad (2)$$

$$\sum_{k \in K} \mu_k \sum_{l \in J \cup K (K \setminus \{k\})} R_{klv} \leq vc \ (\forall v \in V) \quad (3)$$

$$m_{kv} - m_{lv} + (B \times R_{klv}) \leq B - 1 \ (\forall k, l \in K, \forall v \in V) \quad (4)$$

$$\sum_{l \in K \cup J (K \setminus \{k\})} R_{klv} - \sum_{l \in K \cup J (K \setminus \{k\})} R_{lkv} = 0 \ (\forall k \in K, \forall v \in V) \quad (5)$$

$$\sum_{l \in K} R_{jlv} - \sum_{l \in K} R_{ljv} = 0 \ (\forall j \in J, \forall v \in V) \quad (6)$$

$$\sum_{j \in J} \sum_{k \in K} R_{jkv} \leq 1 \ (\forall v \in V) \quad (7)$$

$$\sum_{l \in J \cup K (K \setminus \{k\})} R_{klv} + \sum_{l \in K} R_{jlv} - Z_{jk} \leq 1 \ (\forall j \in J, \forall k \in K, \forall v \in V) \quad (8)$$

$$\sum_{n \in M_j} W_j^n \leq 1 \; (\forall j \in J) \tag{9}$$

$$\sum_{n \in N_h} U_h^n \leq 1 \; (\forall h \in H) \tag{10}$$

$$\sum_{k \in K} \mu_k Z_{jk} \leq \sum_{n \in Mj} w_j^n W_j^n \; (\forall j \in J) \tag{11}$$

$$\sum_{k \in K} \mu_k Z_{jk} \leq \sum_{h \in H} D_{hj} \; (\forall j \in J) \tag{12}$$

$$\sum_{h \in H} Y_{hj} = \sum_{n \in M_j} W_j^n \; (\forall j \in J) \tag{13}$$

$$\sum_{h \in H} X_{th} = 1 \; (\forall t \in T) \tag{14}$$

$$\sum_{h \in H} D_{hj} \leq \sum_{n \in Mj} w_j^n W_j^n \; (\forall j \in J) \tag{15}$$

$$\sum_{t \in T} C_{th} \leq \sum_{n \in N_h} u_h^n U_h^n \; (\forall h \in H) \tag{16}$$

$$\sum_{h \in H} C_{th} \leq CAP_t \quad (\forall t \in T) \tag{17}$$

$$D_{hj} \leq BigM \, Y_{hj} \; (\forall h \in H, \forall j \in J) \tag{18}$$

$$C_{th} \leq BigM \, X_{th} \; (\forall h \in H, \forall t \in T) \tag{19}$$

$$\sum_{t \in T} C_{th} \geq (1 + DRR) \sum_{j \in J} D_{hj} \quad (\forall h \in H) \tag{20}$$

$$Y_{hj} \leq \sum_{n \in M_j} W_j^n \; (\forall h \in H, \forall j \in J) \tag{21}$$

$$X_{th} \leq \sum_{n \in N_h} U_h^n \; (\forall h \in H, \forall t \in T) \tag{22}$$

$$Z_{jk} \in \{0,1\} \quad (\forall j \in J, \forall k \in K) \tag{23}$$

$$X_{th} \in \{0,1\} \quad (\forall t \in T, \forall h \in H) \tag{24}$$

$$Y_{hj} \in \{0,1\} \quad (\forall j \in J, \forall h \in H) \tag{25}$$

$$W_j^n \in \{0,1\} \quad (\forall j \in J, \forall n \in M_j) \tag{26}$$

$$U_h^n \in \{0,1\} \quad (\forall h \in H, \forall n \in N_h) \tag{27}$$

$R_{klv} \in \{0,1\}$ $(\forall\ (l,k) \in (JxK)\ \cup\ (KxK) \setminus \{(k,k):\ k \in K\} \cup\ (K\text{x}J))$ (28)

$m_{kv}\ \geq 0$ $(\forall k \in K, \forall v \in V)$ (29)

$C_{th}\ \geq 0$ $(\forall t \in T, \forall h \in H)$ (30)

$D_{hj}\ \geq 0$ $(\forall h \in H, \forall j \in J)$ (31)

$Q_j \geq 0\ (\forall j \in J)$ (32)

Objective Function Terms

(1) Includes the following costs:

- Fixed cost of opening and operating RTCs, given as $\sum_{j\,\in\,J} \sum_{n\,\in\,Mj}\ f_j^n\, W_j^n$.
- Fixed cost of opening and operating RBCs, given as $\sum_{h\,\in\,H} \sum_{n\,\in\,N_h} g_h^n\, U_h^n$.
- Routing cost from the opened RTCs to the TCs, given as $q \sum_{v\,\in\,V}\ \sum_{j\,\in\,J} \sum_{k\,\in\,K} d_{jk} R_{jkv}\ +$ $q\ \sum_{v\,\in\,V}\ \sum_{k\,\in\,K} \sum_{j\,\in\,J\,\cup K\,\{k\}} d_{kj} R_{kjv}$.
- Transportation cost from RBCs to RTCs, given as $\sum_{h\,\in\,H} \sum_{j\,\in\,\text{J}}\ e_{hj} D_{hj}$.
- Transportation cost from DCs to RBCs, given as $\sum_{t\,\in\,T} \sum_{h\,\in\,H} c_{th} C_{th}$.
- Cycle inventory costs at RTCs, given as $\sum_{j\,\in\,J}\ \frac{h_j Q_j}{2}$.
- Costs of safety stock at RTCs, given as $\sum_{j\,\in\,J}\ \ h_j z_\alpha \sqrt{lt\ \sum_{k\,\in\,K} \sigma_k^2 Z_{jk}}$.

Constraints

(2) Each TC is included on exactly one vehicle route.

(3) Capacity of a vehicle is not exceeded.

(4) Subtours of vehicles are avoided.

(5)-(6) Conservation of flow is guaranteed at each RTC and each TC node.

(7) Each route includes only one RTC.

(8) If the route of vehicle v visiting the TC k starts its route from RTC j, then TC k is assigned to RTC j.

(9)	Each RTC can be assigned to only one capacity level.
(10)	Each RBC can be assigned to only one capacity level.
(11)	Capacity of an RTC should not be exceeded.
(12)	Demand at RTCs are satisfied.
(13)	Each RTC can be assigned to only one opened RBC.
(14)	Each DC can be assigned to only one RBC.
(15)	If an RTC is not opened, no products can be sent to that RTC, and capacity of an RTC should not be exceeded.
(16)	If an RBC is not opened, no products can be sent to that RBC, and capacity of an RBC should not be exceeded.
(17)	Capacity of a DC should not be exceeded.
(18)	If RTC j is not assigned to RBC h , no products can be sent from RBC h to RTC j.
(19)	If DC t is not assigned to RBC h, no products can be sent from DC t to RBC h.
(20)	Amount sent from an RBC to RTCs cannot exceed the amount received by that RBC from the DCs (considering the disposal rate).
(21)	If an RTC is not opened, it cannot be assigned to any RBC.
(22)	If an RBC is not opened, no DCs can be assigned to that RBC.
(23)-(28)	Integrality constraints on the binary variables.
(29)-(32)	Non-negativity constraints on other decision variables.

Problem (P) is NP-Hard, since location-routing problems are NP-Hard (Perl and Daskin, 1985). However, in the following subsections, we also show in detail that subcases of problem P, under the predetermined parameter settings, are equivalent to the well-known problems in the literature which are shown to be NP-hard as well. These problems are as follows:

- Multi-Depot Vehicle Routing Problem – MDVRP
- Single-Source Capacitated Facility Location Problem – SSCFLP
- Capacitated Vehicle Routing Problem – CVRP

4.2. Special Cases of the Model

4.2.1. NP-Hardness Proof 1 (Multi-Depot Vehicle Routing Problem – MDVRP)

4.2.1.1. Multi-Depot Vehicle Routing Problem

The following problem is a version of MDVRP which is known to be NP-Hard (Surekha and Sumathi, 2011):

Minimize

$$\sum_{v \in V} \sum_{j \in J} \sum_{k \in K} d_{jk} R_{jkv} + \sum_{v \in V} \sum_{k \in K} \sum_{j \in J \cup K \setminus \{k\}} d_{kj} R_{kjv} \tag{1'}$$

Subject to;

$$\sum_{v \in V} \sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} = 1 \ \ (\forall k \in K) \tag{2'}$$

$$\sum_{k \in K} \mu_k \sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} \le vc \ \ (\forall v \in V) \tag{3'}$$

$$m_{kv} - m_{lv} + (B \times R_{klv}) \le B - 1 \ \ (\forall k, l \in K, \forall v \in V) \tag{4'}$$

$$\sum_{l \in K \cup J\ (K \setminus \{k\})} R_{klv} - \sum_{l \in K \cup J\ (K \setminus \{k\})} R_{lkv} = 0 \ \ (\forall k \in K, \forall v \in V) \tag{5'}$$

$$\sum_{l \in K} R_{jlv} - \sum_{l \in K} R_{ljv} = 0 \ \ (\forall j \in J, \forall v \in V) \tag{6'}$$

$$\sum_{j \in J} \sum_{k \in K} R_{jkv} \le 1 \ \ (\forall v \in V) \tag{7'}$$

$$\sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} + \sum_{l \in K} R_{jlv} - Z_{jk} \le 1 \ \ (\forall j \in J, \forall k \in K, \forall v \in V) \tag{8'}$$

$$\sum_{k \in K} \mu_k Z_{jk} \le w_j \ (\forall j \in J) \tag{9'}$$

$$R_{klv} \in \{0,1\} \quad (\forall\ (l,k) \in (JxK) \cup (\text{KxK}) \setminus \{(k,k) : k \in K\} \cup (KxJ)) \tag{10'}$$

$$Z_{jk} \in \{0,1\} \quad (\forall j \in J, \forall k \in K) \tag{11'}$$

$$m_{kv} \ge 0 \ \ (\forall k \in K, \forall v \in V) \tag{12'}$$

4.2.1.2. Parameter Settings

We set values for parameters in our original problem (*P*) in order to show that under these parameter settings, our problem is equivalent to the MDVRP above.

$T = \{1\}$,	$f_1^1 = 0$,	$lt = 0$,
$H = \{1\}$,	$g_1^1 = 0$,	$q = 1$,
$N_1 = \{1\}$,	$h_1 = 0$,	$u_1^1 = (1+DRR) \sum_{j \in J} w_j^1$,
$M_j = \{1\}$ $(\forall j \in J)$,	$e_{11} = 0$,	$DRR = 0$,
$p_1 = 0$,	$c_{11} = 0$,	$BigM = \sum_{k \in K} \mu_k$,
μ_k given $(\forall k \in K)$,	$\sigma_k = 0$ $(\forall k \in K)$,	$V = \{1, \ldots.., \|V\|\}$
$CAP_1 = \sum_{k \in K} \mu_k$,	$K = \{2, \ldots.., \|K\|+1\}$	

4.2.1.3. Stating Our Problem with Parameter Settings for MDVRP (P-Subcase 1)

Minimize

$$\sum_{v \in V} \sum_{j \in J} \sum_{k \in K} d_{jk} R_{jkv} + \sum_{v \in V} \sum_{k \in K} \sum_{j \in J \cup K \setminus \{k\}} d_{kj} R_{kjv} \tag{1*}$$

Subject to;

$$\sum_{v \in V} \sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} = 1 \ \ (\forall k \in K) \tag{2*}$$

$$\sum_{k \in K} \mu_k \sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} \le vc \ \ (\forall v \in V) \tag{3*}$$

$$m_{kv} - m_{lv} + (B \times R_{klv}) \le B - 1 \ \ (\forall k, l \in K, \forall v \in V) \tag{4*}$$

$$\sum_{l \in K \cup J\ (K \setminus \{k\})} R_{klv} - \sum_{l \in K \cup J\ (K \setminus \{k\})} R_{lkv} = 0 \ \ (\forall k \in K, \forall v \in V) \tag{5*}$$

$$\sum_{l \in K} R_{jlv} - \sum_{l \in K} R_{ljv} = 0 \ \ (\forall j \in J, \forall v \in V) \tag{6*}$$

$$\sum_{j \in J} \sum_{k \in K} R_{jkv} \le 1 \ \ (\forall v \in V) \tag{7*}$$

$$\sum_{l \in J \cup K\ (K\ \{k\})} R_{klv} + \sum_{l \in K} R_{jlv} - Z_{jk} \ \leq 1 \ \ (\forall j \in J, \forall k \in K, \forall v \in V) \tag{8*}$$

$$W_j^1 \leq 1 \ \ (\forall j \in J) \tag{9*}$$

$$U_1^1 \leq 1 \tag{10*}$$

$$\sum_{k \in K} \mu_k Z_{jk} \ \leq \ w_j^1 W_j^1 \ (\forall j \in J) \tag{11*}$$

$$\sum_{k \in K} \mu_k Z_{jk} \ \leq \ D_{1j} \ \ (\forall j \in J) \tag{12*}$$

$$Y_{1j} = W_j^1 \ \ (\forall j \in \mathrm{J}) \tag{13*}$$

$$X_{11} = 1 \tag{14*}$$

$$D_{1j} \ \leq \ w_j^1 W_j^1 \ (\forall j \in J) \tag{15*}$$

$$C_{11} \ \leq \ u_1^1 U_1^1 \tag{16*}$$

$$C_{11} \ \leq \sum_{k \in K} \mu_k \tag{17*}$$

$$D_{1j} \ \leq \ Y_{1j} \sum_{k \in K} \mu_k \ (\forall j \in J) \tag{18*}$$

$$C_{11} \ \leq \ X_{11} \sum_{k \in K} \mu_k \tag{19*}$$

$$C_{11} \ \geq \ \sum_{\mathrm{j} \in \mathrm{J}} D_{1j} \tag{20*}$$

$$Y_{1j} \ \leq \ W_j^1 \ (\forall j \in J) \tag{21*}$$

$$X_{11} \ \leq \ U_1^1 \tag{22*}$$

$$Z_{jk} \in \{0,1\} \quad (\forall j \in \mathrm{J}, \forall k \in K) \tag{23*}$$

$$X_{1j} \in \{0,1\} \tag{24*}$$

$$Y_{1j} \in \{0,1\} \tag{25*}$$

$$W_j^1 \in \{0,1\} \ \ (\forall j \in \mathrm{J}) \tag{26*}$$

$$U_1^1 \in \{0,1\} \tag{27*}$$

$$R_{lkv} \in \{0,1\} \ \ (\forall\ (l,k) \in (JxK) \ \cup \ (KxK) \ \cup \ (KxJ) \setminus (k,k){:}\ k \in K, \forall v \in V\ ) \tag{28*}$$

$$m_{kv} \geq 0 \ \ (\forall k \in K, \forall v \in V) \tag{29*}$$

$$C_{11} \geq 0 \tag{30*}$$

$D_{1j} \geq 0 \ (\forall j \in J)$ (31*)

$Q_j \geq 0 \ (\forall j \in J)$ (32*)

Noting this, and the equality of the objective functions of (MDVRP) and (P-Subcase 1), we will show that the two problems are equivalent.

Let $\overline{\Delta}$ and Δ be the (feasible) solution spaces of (MDVRP) and (P-Subcase 1), respectively;

Let F = {(R, Z): (R, X, U, Y, Z, C, D, W, Q) $\in \Delta$} and let $(\overline{R}, \overline{Z}) \in \overline{\Delta}$. Note that ($\overline{R}$, $\overline{Z}$) satisfies (2*) – (8*);

Let ($\overline{X}$, $\overline{U}, \overline{Y}, \overline{C}$, $\overline{D}, \overline{W}, \overline{Q}$) be fixed as the following values which are feasible to (P-Subcase 1):

$\bar{X}_{11} = 1$

$\bar{U}_1^1 = 1$

$\bar{C}_{11} = \sum_{k \in K} \mu_k$

$\bar{Q}_j = 1 \ (\forall j \in J)$

$\bar{D}_{1j} = \sum_{k \in K} \mu_k \bar{Z}_{jk} \ (\forall j \in J)$

$\bar{W}_j^1 = \sum_{k \in K} \bar{Z}_{jk} \ (\forall j \in J)$

$\bar{Y}_{1j} = \bar{W}_j^1$

Then $(\overline{R}, \overline{X}, \overline{Y}, \overline{Z}, \overline{C}, \overline{D}, \overline{W}, \overline{Q}) \in \Delta$, since (2*)-(32*) is satisfied.

$(\overline{R}, \overline{X}, \overline{Y}, \overline{Z}, \overline{C}, \overline{D}, \overline{W}, \overline{Q}) \in \Delta \Rightarrow (\overline{R}, \overline{Z}) \in F$.

We proved $(\overline{R}, \overline{Z}) \in \overline{\Delta} \Rightarrow (\overline{R}, \overline{Z}) \in F$. i.e, $\overline{\Delta} \subset F$

Now $F \subseteq \overline{\Delta}$.

Take now, $(\overline{R},\ \overline{Z}\ ) \in F$ => then there exists $(\overline{R}, \overline{X}, \overline{Y}, \overline{Z}, \overline{C}, \overline{D}, \overline{W}, \overline{Q}) \in \Delta$. Then $\overline{R}$ satisfies (2*) - (8*) and (11*) in both (MDVRP) and (P-Subcase 1), hence $\overline{R} \in \Delta$, $F \ \subseteq \ \overline{\Delta}$.

Objective functions of (MDVRP) and (P-Subcase 1) are equal, and we show that solution spaces of these two problems are equivalent. Therefore, the two problems with the corresponding parameter settings are equivalent. Solving (P-Subcase 1) also solves (MDVRP), hence (MDVRP) is a subcase of *(P)*. *(P)* is NP-hard since (MDVRP) is known to be NP-hard (Bodin et. al., 1983; Lenstra and Kan, 1981).

4.2.2. NP-Hardness Proof 2 (Single Source Capacitated Facility Location Problem – SSCFLP)

Lemma1: Given an instance of (P) with $|V| \geq |K|, q > 0,\ d_{kj}\ \geq 0, d_{jk} \geq 0, \forall j \in J, \forall k \in K,$ and $d_{k1k2} > 4. \max\{d_{jk}: j \in J, k \in K \text{ or } k \in J, j \in K\ \} = \overline{d}\ ,\ \forall k_1 \in \mathrm{K}, \forall k_2 \in K \backslash \{k_1\}$ then in an optimal solution of (P), no vehicle $v \in V$ visits two different demand points (TCs), i.e., every demand point $k \in K$ is served by a dedicated vehicle $v_k\ \epsilon\ V$, that only traverses back and forth from j_k (the RTC serving TC *k*) to *k*.

Proof: Assume that, in a solution of (P), a certain vehicle $v_1 \in V$ serves a subset of TCs $S\ \subseteq K$ with $|S|\ \geq 2$. We will show that this solution is suboptimal by modifying the values of only some R_{lkv} variables, and attaining a better objective value.

Since $|V|\ \geq |K|$ and $|S|$ TCs are served by a single vehicle in the current solution, there are at least $|V| - (\ |K| - |S| + 1) \geq |S| - 1$ trucks idle. Along with v_1, we have $|S|$ available trucks $\ \bar{V} = \left\{\ v_1, \dots\dots v_{|S|}\right\}$ to serve TCs in S, without changing the routes of any other trucks $R_{lkv}, v\ \epsilon\ \mathrm{V}\ \backslash \bar{V}$.

Let $S = \{k, \dots \dots . . , k_{ISI}\} \subseteq K$. Let the RTC serving S have index $\ j \in J$.

Let $\bar{R}_{jk_iv_i} = \bar{R}_{k_ijv_i} = 1$ for $i \in \{1, \ldots\ldots, |S|\}$, all other $\bar{R}_{jkv_i}$ variables having value 0, $i \in \{1, \ldots\ldots, |S|\}$, and for $v \in V \setminus \bar{V}$ $\bar{R}_{lkv} = R_{lkv}$. Note that all other variables remain unchanged, which can be observed by checking that Z_{jk} is unchanged, since RTC-TC assignments are unchanged. Then, the change in the objective function is:

$$q \sum_{v \in \bar{V}} \sum_{j \in J} \sum_{k \in K} d_{jk} \bar{R}_{jkv} + q \sum_{v \in \bar{V}} \sum_{k \in K} \sum_{j \in J \cup K \setminus \{k\}} d_{kj} \bar{R}_{kjv}$$
$$- q \sum_{v \in \bar{V}} \sum_{j \in J} \sum_{k \in K} d_{jk} R_{jkv} - q \sum_{v \in \bar{V}} \sum_{k \in K} \sum_{j \in J \cup K \setminus \{k\}} d_{kj} R_{kjv}$$

$$\leq$$

$$q \sum_{v \in \bar{V}} \sum_{j \in J} \sum_{k \in K} \bar{d} \bar{R}_{jkv} + q \sum_{v \in \bar{V}} \sum_{k \in K} \sum_{j \in J \cup K \setminus \{k\}} \bar{d} \bar{R}_{kjv}$$
$$- q \sum_{v \in \bar{V}} \sum_{k_1 \in K} \sum_{k_2 \in K \setminus \{k\}} d_{k_1k_2} R_{k_1k_2v}$$
$$<$$
$$2q|S|\bar{d} - q \sum_{v \in \bar{V}} \sum_{k_1 \in K} \sum_{k_2 \in K \{k\}} 4\bar{d} R_{k_1k_2v}$$
$$= q|S|2\bar{d} - q\,(|S| - 1)4\bar{d}$$

the inequalities above hold, since in $R_{k_1k_2v}$ $v \in \bar{V}$ only for v_1 there are non-negative values, corresponding to $|S| - 1$ arcs traversing $k_1, \ldots\ldots, k_{ISI}$ TCs.

$= q\bar{d}\,(2\,|S| - 4\,|S| + 4) = q\bar{d}\,(4 - 2\,|S|) \leq 0$ since $|S| \leq 2$

Hence, we attain a solution with a less cost, and initial solution is suboptimal.

4.2.2.1. Parameter Settings

We set values for parameters in our original problem (P) in order to show that, under these parameter settings, our problem is equivalent to the SSCFLP above.

$T = \{1\}$,	$u_1^1 = \sum_{k \in K} \mu_k$,	$lt = 0$,
$H = \{1\}$,	$CAP_1 = \sum_{k \in K} \mu_k$,	$DRR = 0$,
$N_1 = \{1\}$,	$vc = \max_{k}\{\mu_k\}$	$c_{11} = 0$
$M_j = \{1\}$, $(\forall j \in J)$,	$q = 1$,	$e_{1j} = 0$, $(\forall j \in J)$,
$\sigma_k = 0$ $(\forall k \in K)$,	$h_j = 0$, $(\forall j \in J)$,	$DL =$ bigM
$g_1^1 = 0$,	$p_j = 0$, $(\forall j \in J)$,	$\lvert V \rvert = \lvert K \rvert$

$d_{jk} = d_{kj} = \frac{\delta_{jk}}{2}$ $(\forall j \in J)$, $(\forall k \in K)$,

$d_{k1k2} = 4 \max_{j \in J, k \in K} d_{jk} + 1 \quad (\forall\, k1, k2 \in K)$

4.2.2.2. Stating Our Problem with Parameter Settings for SSCFLP (P-Subcase 2)

By Lemma 1 and the above parameter settings, the model will be as follows:

Minimize

$$\sum_{j \in J} f_j^1 W_j^1 + \sum_{v \in V} \sum_{j \in J} \sum_{k \in K} d_{jk} R_{jkv} + \sum_{v \in V} \sum_{k \in K} \sum_{j \in J \cup K \setminus \{k\}} d_{kj} R_{kjv} \qquad (1^{**})$$

Subject to;

$$\sum_{v \in V} \sum_{l \in J} R_{klv} = 1 \quad (\forall k \in K) \qquad (2^{**})$$

$$\sum_{k \in K} \mu_k \sum_{l \in J} R_{klv} \leq vc \quad (\forall v \in V) \qquad (3^{**})$$

$$m_{kv} - m_{lv} + (B \times R_{klv}) \leq B - 1 \quad (\forall k, l \in K, \forall v \in V) \qquad (4^{**})$$

$$\sum_{l \in J} R_{klv} - \sum_{l \in J} R_{lkv} = 0 \quad (\forall k \in K, \forall v \in V) \qquad (5^{**})$$

$$\sum_{l \in K} R_{jlv} - \sum_{l \in K} R_{ljv} = 0 \quad (\forall j \in J, \forall v \in V) \qquad (6^{**})$$

$$\sum_{j \in J} \sum_{k \in K} R_{jkv} \leq 1 \quad (\forall v \in V) \qquad (7^{**})$$

$$\sum_{l \in J} R_{klv} + \sum_{l \in K} R_{jlv} - Z_{1k} \leq 1 \quad (\forall j \in J, \forall k \in K, \forall v \in V) \qquad (8^{**})$$

$$W_1^1 \leq 1 \quad (9^{**})$$

$$U_1^1 \leq 1 \quad (10^{**})$$

$$\sum_{k \in K} \mu_k Z_{1k} \ \leq \ w_j^1 W_j^1 \ \ (\forall j \in J) \quad (11^{**})$$

$$\sum_{k \in K} \mu_k Z_{jk} \ \leq \ D_{1j} \ \ (\forall j \in J) \quad (12^{**})$$

$$Y_j = W_j^1 \ (\forall j \in J) \quad (13^{**})$$

$$X_{11} = 1 \quad (14^{**})$$

$$D_{1j} \ \leq \ w_j^1 W_j^1 \ (\forall j \in J) \quad (15^{**})$$

$$C_{11} \ \leq U_1^1 \ \textstyle\sum_{k \in K} \mu_k \quad (16^{**})$$

$$C_{11} \ \leq \sum_{k \in K} \mu_k \quad (17^{**})$$

$$D_{1j} \ \leq \ Big\ M\ Y_{1j} \ (\forall j \in J) \quad (18^{**})$$

$$C_{11} \ \leq \ Big\ M\ X_{11} \quad (19^{**})$$

$$C_{11} \ \geq \ \sum_{j \in J} D_{1j} \quad (20^{**})$$

$$Y_{11} \ \leq \ W_1^1 \quad (21^{**})$$

$$X_{11} \ \leq \ U_1^1 \quad (22^{**})$$

$$Z_{jk} \in \{0,1\} \quad (\forall j \in J, \forall k \in K) \quad (23^{**})$$

$$X_{11} \in \{0,1\} \quad (24^{**})$$

$$Y_{1j} \in \{0,1\} \quad (\forall j \in J) \quad (25^{**})$$

$$W_1^1 \in \{0,1\} \quad (26^{**})$$

$$U_1^1 \in \{0,1\} \quad (27^{**})$$

$$R_{klv} \in \{0,1\} \ \ (\forall \ (l,k) \in (JxK) \ \cup \ (KxK) \setminus \{(k,k) : \ k \in K \} \cup \ (K\text{x}J)) \quad (28^{**})$$

$$m_{kv} \geq \ \ 0 \qquad (\forall k \in K, \forall v \in V) \quad (29^{**})$$

$$C_{11} \ \geq \ 0 \quad (30^{**})$$

$$D_{1j} \ \geq 0 \qquad (\forall j \in J) \quad (31^{**})$$

$$Q_j \geq 0 \qquad (\forall j \in J) \quad (32^{**})$$

4.2.2.3. Inspection of Values of All Variables and Rewriting the Problem (P-Subcase 2)

$(2 **) \Rightarrow \exists_{j_k}^{v_k}\ s.t. R_{kj_kv_k} = 1\ \forall k \in K$ (33 **)

$(33 **)\ and\ (5 **)$

$\Rightarrow \sum_{j \in J} R_{jkv_k} = 1,$ by $(6 **)$ and Lemma 1 note that $R_{j_kkv_k} = 1$ $(34 **)$

since a truck does not visit multiple demand points.

$(8 **), (33 **) and\ (34 **)$

$\Rightarrow Z_{j_kk} = 1\ \forall k \in K.$

Now, we know that in an optimal solution of (P subcase 2):

$\forall k \in K\ \exists j_k\ \ s.t.\ Z_{j_kk} = 1.$

Let's assume $\exists \bar{k}\ \in K\ s.t. Z_{\bar{j}\bar{k}} = 1, \bar{j} \neq j_k.$ Then,

$$\sum_{k \in K} \mu_k \geq U_1^1 \sum_{k \in K} \mu_k \geq C_{11} \geq \sum_{j \in J} D_{1j} \qquad \text{from } (16 **) \text{ and } (20 **)$$

$$\sum_{k \in K} \mu_k Z_{jk} \leq D_{1j}\ \ (\forall j \in J) \qquad \text{from } (11 **)$$

$$\sum_{j \in j} D_{1j} \geq \sum_{j \in j} \sum_{k \in K} \mu_k Z_{jk} = \sum_{k \in K} \sum_{j \in J} \mu_k Z_{jk} = \sum_{k \in K} \mu_k Z_{j_kk} + \sum_{k \in K} \sum_{j \in J, j \neq j_k} \mu_k Z_{jk}$$

$$= \sum_{k \in K} \mu_k + \mu_{\bar{k}} Z_{\bar{j}\bar{k}} = \sum_{k \in K} \mu_k + \mu_{\bar{k}} \ \rightarrow \text{Contradiction}$$

By contradiction, we prove $Z_{jk} = 0$ for $\forall j \neq j_k\ \forall\ k\ \in K.$

All above

$$\Rightarrow \sum_{j \in J} Z_{jk} = 1 = \sum_{j \in J} \sum_{v \in V} R_{jkv} = \sum_{j \in J\ U\ K\{k\}} \sum_{v \in V} R_{kjv} = R_{j_kkv_k}\ (\forall k \in K)(35 **)$$

Then we can rewrite the objective function of (P-Subcase 2) as follows:

$$\sum_{j \in J} f_j^1 W_j^1 + \sum_{v \in V} \sum_{j \in J} \sum_{k \in K} d_{jk} R_{jkv} + \sum_{v \in V} \sum_{k \in K} \sum_{j \in J \cup K \setminus \{k\}} d_{kj} R_{kjv}$$

$$= \sum_{j \in J} f_j^1 W_j^1 + \sum_{k \in K} d_{j_k k} R_{j_k k v_k} + \sum_{k \in K} d_{k j_k} R_{k j_k v_k}$$

$$= \sum_{j \in J} f_j^1 W_j^1 + \sum_{k \in K} d_{j_k k} Z_{j_k k} + \sum_{k \in K} d_{k j_k} Z_{j_k k} = \sum_{j \in J} f_j^1 W_j^1 + \sum_{k \in K} \delta_{j_k k} Z_{j_k k}$$

$$= \sum_{j \in J} f_j^1 W_j^1 + \sum_{j \in J} \sum_{k \in K} \delta_{j_k} Z_{j_k}$$

Therefore, the objective functions are equivalent for all solutions of SSCFLP and all solutions of P-Subcase 2 in which each city is served by a dedicated truck (by Lemma 1, these contain all optimal solutions). Along with 11** and 35** we can conclude that P-Subcase 2 is a valid formulation for SSCLFP. *(P)* is NP-hard since SSCFLP is known to be NP-hard. A formulation of SSCFLP can be found below (Silva and Figuera, 2007).

4.2.2.4. Single-Source Capacitated Facility Location Problem (SSCFLP)

The following problem is a version of SSCFLP which is known to be NP-Hard.

Minimize

$$\sum_{j \in J} W_j f_j + \sum_{j \in J} \sum_{k \in K} \delta_{j_k} Z_{j_k}$$

Subject to;

$$\sum_{j \in J} Z_{jk} = 1 \quad (\forall k \in K)$$

$$\sum_{k \in K} \mu_k Z_{jk} \leq w_j W_j \quad (\forall j \in J)$$

$$Z_{jk} \in \{0,1\} \ , (\forall k \in K) \ (\forall j \in J)$$

$$W_j \in \{0,1\} \ , (\forall j \in J)$$

4.2.3. NP-Hardness Proof 3 (Capacitated Vehicle Routing Problem – CVRP)

4.2.3.1. Capacitated Vehicle Routing Problem

The following problem is a version of CVRP which is known to be NP-Hard.

Minimize

$$\sum_{v \in V} \sum_{j \in J} \sum_{k \in K} d_{jk} R_{jkv} + \sum_{v \in V} \sum_{k \in K} \sum_{j \in J \cup K \setminus \{k\}} d_{kj} R_{kjv} \qquad (1'')$$

Subject to;

$$\sum_{v \in V} \sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} = 1 \ \ (\forall k \in K) \qquad (2'')$$

$$\sum_{k \in K} \mu_k \sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} \le vc \ \ (\forall v \in V) \qquad (3'')$$

$$m_{kv} - m_{lv} + (B \times R_{klv}) \le B - 1 \ \ (\forall k, l \in K, \forall v \in V) \qquad (4'')$$

$$\sum_{l \in K \cup J\ (K \setminus \{k\})} R_{klv} - \sum_{l \in K \cup J\ (K \setminus \{k\})} R_{lkv} = 0 \ \ (\forall k \in K, \forall v \in V) \qquad (5'')$$

$$\sum_{l \in K} R_{jlv} - \sum_{l \in K} R_{ljv} = 0 \ \ (\forall j \in J, \forall v \in V) \qquad (6'')$$

$$\sum_{j \in J} \sum_{k \in K} R_{jkv} \le 1 \ \ (\forall v \in V) \qquad (7'')$$

$$m_{kv} \ge 0 \qquad (\forall k \in K, \forall v \in V) \qquad (8'')$$

$$R_{jkv} \in \{0,1\} \ (\forall j \in J, \forall k \in K, \forall v \in V) \qquad (9'')$$

$$R_{klv} \in \{0,1\} \ \ (\forall\ (l,k) \in (JxK)\ \cup\ (KxK) \setminus \{(k,k) :\ k \in K\} \cup\ (K\text{x}J)) \qquad (10'')$$

J denotes the set of depots, $J = \{1\}$, K denotes the set of retailers, $K = \{2, \ldots\ldots, |K| + 1\}$, V denotes the set of vehicles, $V = \{1, \ldots\ldots, |V|\}$.

4.2.3.2. Parameter Settings

We set values for parameters in our original problem (*P*) in order to show that under these parameter settings our problem is equivalent to the CVRP above.

$T = \{1\}$,	$f_1^1 = 0$,	$lt = 0$,
$H = \{1\}$,	$g_1^1 = 0$,	$q = 1$,
$J = \{1\}$,	$h_1 = 0$,	$w_1^1 = \sum_{k \in K} \mu_k$,
$N_1 = \{1\}$,	$e_{11} = 0$,	$u_1^1 = (1+DRR)\, w_1^1$,
$M_1 = \{1\}$,	$c_{11} = 0$,	$DRR = 0$,
$p_1 = 0$,	$\sigma_k = 0 \ (\forall k \in K)$,	$bigM = \sum_{k \in K} \mu_k$,
μ_k given $(\forall k \in K)$,	$K = \{2, \ldots, \vert K\vert+1\}$	$V = \{1, \ldots, \vert V\vert\}$
$CAP_1 = \sum_{k \in K} \mu_k$,		

4.2.3.3. Stating Our Problem with Parameter Settings for CVRP (P-Subcase 3)

Min

$$\sum_{v \in V} \sum_{j \in J} \sum_{k \in K} d_{jk} R_{jkv} + \sum_{v \in V} \sum_{k \in K} \sum_{j \in J \cup K \setminus \{k\}} d_{kj} R_{kjv} \tag{1***}$$

S.t.

$$\sum_{v \in V} \sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} = 1 \ \ (\forall k \in K) \tag{2***}$$

$$\sum_{k \in K} \mu_k \sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} \leq vc \ \ (\forall v \in V) \tag{3***}$$

$$m_{kv} - m_{lv} + (B \times R_{klv}) \leq B - 1 \ \ (\forall k, l \in K, \forall v \in V) \tag{4***}$$

$$\sum_{l \in K \cup J\ (K \setminus \{k\})} R_{klv} - \sum_{l \in K \cup J\ (K \setminus \{k\})} R_{lkv} = 0 \ \ (\forall k \in K, \forall v \in V) \tag{5***}$$

$$\sum_{l \in K} R_{jlv} - \sum_{l \in K} R_{ljv} = 0 \ \ (\forall j \in J, \forall v \in V) \tag{6***}$$

$$\sum_{j \in J} \sum_{k \in K} R_{jkv} \leq 1 \ \ (\forall v \in V) \tag{7***}$$

$$\sum_{l \in J \cup K\ (K\ \{k\})} R_{klv} + \sum_{l \in K} R_{jlv} - Z_{1k} \leq 1 \quad (\forall j \in J, \forall k \in K, \forall v \in V) \tag{8***}$$

$$W_1^1 \leq 1 \tag{9***}$$

$$U_1^1 \leq 1 \tag{10***}$$

$$\sum_{k \in K} \mu_k Z_{1k} \leq w_1^1 W_1^1 \tag{11***}$$

$$\sum_{k \in K} \mu_k Z_{1k} \leq D_{11} \tag{12***}$$

$$Y_{11} = W_1^1 \tag{13***}$$

$$X_{11} = 1 \tag{14***}$$

$$D_{11} \leq w_1^1 W_1^1 \tag{15***}$$

$$C_{11} \leq u_1^1 U_1^1 \tag{16***}$$

$$C_{11} \leq \sum_{k \in K} \mu_k \tag{17***}$$

$$D_{11} \leq Y_{11} \sum_{k \in K} \mu_k \tag{18***}$$

$$C_{11} \leq X_{11} \sum_{k \in K} \mu_k \tag{19***}$$

$$C_{11} \geq D_{11} \tag{20***}$$

$$Y_{11} \leq W_1^1 \tag{21***}$$

$$X_{11} \leq U_1^1 \tag{22***}$$

$$Z_{1k} \in \{0,1\} \ (\forall k \in K) \tag{23***}$$

$$X_{11} \in \{0,1\} \tag{24***}$$

$$Y_{11} \in \{0,1\} \tag{25***}$$

$$W_1^1 \in \{0,1\} \tag{26***}$$

$$U_1^1 \in \{0,1\} \tag{27***}$$

$$R_{klv} \in \{0,1\} \ (\forall\ (l,k) \in (JxK) \cup (KxK) \setminus \{(k,k) :\ k \in K\} \cup (K\mathrm{x}J)) \tag{28***}$$

$$m_{kv} \geq 0 \qquad (\forall k \in K, \forall v \in V) \tag{29***}$$

$$C_{11} \geq 0 \tag{30***}$$

$$D_{11} \geq 0 \tag{31***}$$

$$Q_1 \geq 0 \tag{32***}$$

4.2.3.4. Inspection of Values of All Variables

$X_{11} = 1$ from (14***),

$X_{11} = 1$ and (22***) and (27***) => $U_1^1 = 1$,

(2*) implies that for exactly one $\overline{v}_k \in$ V ;

$$\sum_{l \in J \cup (K \setminus \{k\})} R_{kl\overline{v}_k} = 1 \quad (\forall k \in K)$$

(4*) assures that $R_{1\bar{k}\overline{v}_k} = 1$ for some $\bar{k} \in K$ (otherwise truck $\overline{v}_k$ makes a subtour in K).

$\forall k \in$ K, $\exists \overline{v}_k$ st

$$\sum_{l \in J \cup (K \setminus \{k\})} R_{kl\overline{v}_k} + \sum_{l \in K} R_{1l\overline{v}_k} = 2$$

and together with $(8 ***) \Longrightarrow \ Z_{1k} = 1 \quad (\forall k \in K)$.

W_1^1 = 1 from (11***), $Y_{11} = 1$ from (13***),

Then, $(12 ***)$ implies $\sum_{k \in K} \mu_k \leq D_{11}$,

$(15 ***)$ implies $D_{11} \leq \sum_{k \in K} \mu_k$, $D_{11} = \sum_{k \in K} \mu_k$.

Similarly by $(20 ***)$ and $(17 ***)$ implies $C_{11} = \sum_{k \in K} \mu_k$.

To sum up, in a feasible solution of P-Subcase 3, all variables except R_{lkv}, have the above mentioned fixed values.

Noting this, and that the equality objective functions of CVRP and P-Subcase 3 we now show that the two problems are equivalent.

Let $\prod$ and $\overline{\prod}$ be the (feasible) solution spaces of CVRP and P-Subcase 3, respectively;

Let $S = \{R: (R, X, U\ Y, Z, C, D, W\ Q) \in \overline{\prod}\}$, Let $\overline{R} \in \prod$. Note that $\overline{R}$ satisfies (2***) – (7***),

Let ($\overline{X}, \overline{U}, \overline{Y}, \overline{Z}, \overline{C}, \overline{D}, \overline{Q}$, $\overline{W}$) be fixed as the only feasible values to P-Subcase 3, then ($\overline{X}, \overline{U}, \overline{Y}, \overline{Z}, \overline{C}, \overline{D}, \overline{Q}$, $\overline{W}$) $\in \overline{\prod}$, since $\overline{R}$ is not involved in (8***) – (12***), and these are satisfied by the other variables, similarly $\overline{R}$ satisfies (2***) – (7***). (8***) is satisfied by ($\overline{R}$, $\overline{X}, \overline{U}, \overline{Y}, \overline{Z}, \overline{C}, \overline{D}, \overline{Q}$, $\overline{W}$) since $\overline{Z}$ = 1, hence (8***) turns into:

$$\sum_{l \in J \cup K\ (K\ \{k\})} \overline{R}_{klv} + \sum_{l \in K} \overline{R}_{1lv} \le 2 \ \ (\forall k \in K)(\forall v \in V).$$

(2’’) $\equiv$ (2***) implies the summation

$$\sum_{l \in J \cup K\ (K\ \{k\})} \overline{R}_{klv} \le 1 \ \ (\forall k \in K).$$

(6’’) $\equiv$ (6***) implies that,

$\sum_{l \in K} \overline{R}_{1lv} \le 1$ $(\forall\, v \in V)$ hence,

($\overline{R}, \overline{Z}$) (i.e.,) ($\overline{R}$, $\overline{X}, \overline{U}, \overline{Y}, \overline{Z}, \overline{C}, \overline{D}, \overline{Q}$, $\overline{W}$) satisfies (8***) $(\forall k \in K)(\forall v \in V)$

($\overline{R}$, $\overline{X}, \overline{U}, \overline{Y}, \overline{Z}, \overline{C}, \overline{D}, \overline{Q}$, $\overline{W}$) $\in \overline{\prod}$ => $\overline{R} \in S$.

We proved $\overline{R} \in \prod$ => $\overline{R} \in S$. i.e, $\prod \subset S$.

Now $S \subseteq \prod i$.

Take now, $\overline{R} \in S$ => ($\overline{R}$, $\overline{X}, \overline{U}, \overline{Y}, \overline{Z}, \overline{C}, \overline{D}, \overline{Q}$, $\overline{W}$) $\in \overline{\prod}$. Then $\overline{R}$ satisfies (2***) – (7***) in both CVRP and P-Subcase 3, hence $\overline{R} \in \prod$, $S \subseteq \prod i$.

The two problems with the corresponding parameter settings are equivalent. Solving P-Subcase 3 also solves CVRP, hence CVRP is a subcase of *(P). (P)* is NP-hard, since CVRP is known to be NP-hard (Laporte 1992).

CHAPTER 5

THE PROPOSED SOLUTION APPROACHES

In this section we present two different types of solution approaches:

- Optimal solution finding approaches
- Heuristic approaches

In the optimal solution approach, the problem is transformed into a mixed-integer convex program. In this case, small-sized instances of the problem can be optimally solved by using branch-and-bound methods, but solving medium and large-sized ones for the optimal solution turns out to be impractical. Therefore, we present heuristic solution approaches as alternative solution approaches, especially for the medium to large-sized problem instances.

5.1. Optimal Solution Approach

In the process of transforming the original problem into a mixed-integer convex program, we follow the analysis of Javid and Azad (2010):

Note that $Q_j > 0,\ j \epsilon J$ is the only constraint posed on the order quantity variable Q_j. There are two terms in the objective function including Q_j, one increasing and the other one decreasing with Q_j. Since there are no constraints relating Q_j's to each other, or to other variables, we can select an optimal Q_j by optimizing each Q_j, independently over the objective term:

$$f_j(Q_j) = \frac{a_j}{Q_j} + b_j Q_j$$

where

$$a_{j=}p_j \sum_{k \,\epsilon\, K} \mu_k Z_{jk} \text{ and } b_j = \frac{h_j}{2}$$

We equate the first derivative of f_j to zero:

$f_j'(Q_j) = -a_j(Q_j)^{-2} + b_j = 0,$ which implies

$$Q_j = \sqrt{\frac{a_j}{b_j}}$$

Noting that $a_j > 0$ ($Z_{jk} > 0$ for some $k \,\varepsilon\, K$ in a feasible solution) and f_j is a convex function (of Q_j):

$$f_j''(Q_j) = 2a_j(Q_j)^{-3} > 0.$$

We find the optimal value of Q_j for any feasible solution Z_{jk} as:

$$Q_j^* = \sqrt{\frac{a_j}{b_j}} = \sqrt{\frac{2\, p_j\, \sum_{k \,\epsilon\, K} \mu_k Z_{jk}}{h_j}}$$

When we substitute Q_j^* in the objective function, we have:

(P2) Minimize

$$\sum_{j \,\epsilon\, J} \sum_{n \,\epsilon\, \mathrm{Mj}} f_j^n W_j^n + \sum_{h \,\epsilon\, H} \sum_{n \,\epsilon\, N_h} g_h^n U_h^n$$
$$+ q \sum_{v \,\epsilon\, V} \sum_{j \,\epsilon\, J} \sum_{k \,\epsilon\, K} d_{jk} R_{jkv} + q \sum_{v \,\epsilon\, V} \sum_{k \,\epsilon\, K} \sum_{j \,\epsilon\, J \,\cup K \setminus\{k\}} d_{kj} R_{kjv}$$
$$+ \sum_{t \,\epsilon\, T} \sum_{h \,\epsilon\, H} c_{th} C_{th} + \sum_{h \,\epsilon\, H} \sum_{j \,\epsilon\, \mathrm{J}} D_{hj}\, e_{hj}$$
$$+ \sum_{j \,\epsilon\, J} \sqrt{2 h_j p_j \sum_{k \,\epsilon\, K} \mu_k Z_{jk}} + \sum_{j \,\epsilon\, J} h_j z_\alpha \sqrt{lt \sum_{k \,\epsilon\, K} \sigma_k^2 Z_{jk}}$$

In the above objective function, all terms, except $\sum_{j \epsilon J} \sqrt{2h_j p_j \sum_{k \epsilon K} \mu_k Z_{jk}}$ and $\sum_{j \epsilon J} h_j z_\alpha \sqrt{lt \sum_{k \epsilon K} \sigma_k^2 Z_{jk}}$, are linear functions of variables, but with these two terms, the above objective function is concave.

To show this, Let

$$g_j(Z_{j1}, \dots \dots, Z_{jIKI}) = \sqrt{\sum_{k=1}^{IKI} u_k Z_{jk}}$$

for $u_k \geq 0, k \in K$. The first derivative of g_j is as follows:

$$\frac{\partial\, g_j(\dots)}{\partial\, Z_{jk}} = \frac{1}{2}\left(\sum_{l=1}^{IKI} u_l Z_{jl}\right)^{-1/2} u_k\,,$$

$$Dg_j\,(\dots) = \tfrac{1}{2}\left(u^T Z_j\right)^{-1/2} u \quad \text{where } Z_j = \begin{bmatrix} Z_{1k} \\ \vdots \\ Z_{1IKI} \end{bmatrix}.$$

and its Hessian matrix is:

$$\frac{\partial^2\, g_j(\dots)}{\partial\, Z_{jl} \partial\, Z_{js}} = -\frac{1}{4}\left(u^T Z_j\right)^{-3/2} u_l u_s\,,$$

$$Hg_j(\dots) = -\tfrac{1}{4}\left(u^T Z_j\right)^{-3/2} u\, u^T.$$

To show $Hg_j(\dots)$ is Negative Semi-definite (NGS), take any $x \epsilon \mathbb{R}^{|K|}$:

$$x^T Hg_j x = -\frac{1}{4}\left(u^T Z_j\right)^{-3/2} (x^T u)^2$$

which is non-positive, since $u \geq 0,\ z \geq 0$ and $u^T z \neq 0$ in the interior of the feasible region of our problem based on the parameter settings. Note that $\sum_j g_j$ is a finite sum of concave functions, hence it is concave.

We define the problem as NLMIP with the convex feasible region for the continuous relaxation, but the objective function is concave. Introducing Z_{jk}^2 instead of Z_{jk} in the objective function, we have an equivalent NLMIP formulation as follows, but now the objective function is convex.

(P3) Minimize

$$\sum_{j\,\epsilon\,J}\sum_{n\,\epsilon\,\mathrm{Mj}} f_j^n\,W_j^n + \sum_{h\,\epsilon\,H}\sum_{n\,\epsilon\,N_h} g_h^n\,U_h^n +$$

$$q\sum_{v\,\epsilon\,V}\sum_{j\,\epsilon\,J}\sum_{k\,\epsilon\,K} d_{jk}R_{jkv} + q\sum_{v\,\epsilon\,V}\sum_{k\,\epsilon\,K}\sum_{j\,\epsilon\,J\,\cup K\,\backslash\{k\}} d_{kj}R_{kjv}$$

$$+\sum_{t\,\epsilon\,T}\sum_{h\,\epsilon\,H} c_{th}C_{th} + \sum_{h\,\epsilon\,H}\sum_{j\,\epsilon\,\mathrm{J}} D_{hj}\,e_{hj}$$

$$+\sum_{j\,\epsilon\,J}\sqrt{2h_jp_j}\sqrt{\sum_{k\,\epsilon\,K}\mu_k Z_{jk}^2} + \sum_{j\,\epsilon\,J} h_j z_\alpha\sqrt{lt\sum_{k\,\epsilon\,K}\sigma_k^2 Z_{jk}^2}$$

Subject to;

$$\sum_{v\,\in\,\mathrm{V}}\sum_{l\,\in J\,\cup\,K\,(K\backslash\,\{k\})} R_{klv} = 1\ \ (\forall k\,\epsilon\,K) \tag{2^}$$

$$\sum_{k\,\in\,K}\mu_k\sum_{l\,\in J\,\cup\,K\,(K\backslash\,\{k\})} R_{klv} \le vc\ \ (\forall v\,\epsilon\,V) \tag{3^}$$

$$m_{kv} - m_{lv} + (B\times R_{klv}) \le B - 1\ \ (\forall k,l\,\epsilon\,K,\forall v\,\epsilon\,V) \tag{4^}$$

$$\sum_{l\,\in K\,\cup\,J\,(K\backslash\,\{k\})} R_{klv} - \sum_{l\,\in K\,\cup\,J\,(K\backslash\,\{k\})} R_{lkv} = 0\ \ (\forall k\,\epsilon\,K,\forall v\,\epsilon\,V) \tag{5^}$$

$$\sum_{l\,\in K} R_{jlv} - \sum_{l\,\in K} R_{ljv} = 0\ \ (\forall j\,\epsilon\,J,\forall v\,\epsilon\,V) \tag{6^}$$

$$\sum_{j\,\in J}\sum_{k\,\in K} R_{jkv} \le 1\ \ (\forall v\,\epsilon\,V) \tag{7^}$$

$$\sum_{l\,\in J\,\cup\,K\,(K\backslash\,\{k\})} R_{klv} + \sum_{l\,\in K} R_{jlv} - Z_{jk}^2 \le 1\ \ (\forall j\,\epsilon\,J,\forall k\,\epsilon\,K,\forall v\,\epsilon\,V) \tag{8^}$$

$$\sum_{n\,\in\,M_j} W_j^n \le 1\ (\forall j\,\epsilon\,J) \tag{9^}$$

$$\sum_{n\,\in\,N_h} U_h^n \le 1\ (\forall h\,\epsilon\,H) \tag{10^}$$

$$\sum_{k \in K} \mu_k Z_{jk}^2 \leq \sum_{n \in Mj} w_j^n W_j^n \ (\forall j \in J) \quad (11^\wedge)$$

$$\sum_{k \in K} \mu_k Z_{jk}^2 \leq \sum_{h \in H} D_{hj} \ (\forall j \in J) \quad (12^\wedge)$$

$$\sum_{h \in H} Y_{hj} = \sum_{n \in \mathrm{M}_j} W_j^n \ (\forall j \in J) \quad (13^\wedge)$$

$$\sum_{h \in H} X_{th} = 1 \ (\forall t \in T) \quad (14^\wedge)$$

$$\sum_{h \in H} D_{hj} \leq \sum_{n \in \mathrm{Mj}} w_j^n W_j^n \ (\forall j \in J) \quad (15^\wedge)$$

$$\sum_{t \in T} C_{th} \leq \sum_{n \in N_h} u_h^n U_h^n \ (\forall h \in H) \quad (16^\wedge)$$

$$\sum_{h \in H} C_{th} \leq CAP_t \quad (\forall t \in T) \quad (17^\wedge)$$

$$D_{hj} \leq BigM\ Y_{hj} \ (\forall h \in H, \forall j \in J) \quad (18^\wedge)$$

$$C_{th} \leq BigM\ X_{th} \ (\forall h \in H, \forall t \in T) \quad (19^\wedge)$$

$$\sum_{t \in T} C_{th} \geq (1 + DRR) \sum_{j \in J} D_{hj} \quad (\forall h \in H) \quad (20^\wedge)$$

$$Y_{hj} \leq \sum_{n \in M_j} W_j^n \ (\forall h \in H, \forall j \in J) \quad (21^\wedge)$$

$$X_{th} \leq \sum_{n \in N_h} U_h^n \ (\forall h \in H, \forall t \in T) \quad (22^\wedge)$$

$$Z_{jk}^2 \in \{0,1\} \quad (\forall j \in J, \forall k \in K) \quad (23^\wedge)$$

$$X_{th} \in \{0,1\} \quad (\forall t \in T, \forall h \in H) \quad (24^\wedge)$$

$$Y_{hj} \in \{0,1\} \quad (\forall j \in J, \forall h \in H) \quad (25^\wedge)$$

$$W_j^n \in \{0,1\} \quad (\forall j \in J, \forall n \in M_j) \quad (26^\wedge)$$

$$U_h^n \in \{0,1\} \quad (\forall h \in H, \forall n \in N_h) \quad (27^\wedge)$$

$$R_{lkv} \in \{0,1\} \quad (\forall\ (l,k) \in (JxK) \cup (KxK) \setminus \{(k,k) :\ k \in K\} \cup (KxJ)) \quad (28^\wedge)$$

$$m_{kv} \geq 0 \ (\forall k \in K, \forall v \in V) \quad (29^\wedge)$$

$$C_{th} \geq 0 \quad (\forall t \in T, \forall h \in H) \quad (30^\wedge)$$

$$D_{hj} \geq 0 \ (\forall h \in H, \forall\ j \in J) \quad (31^\wedge)$$

Again we will investigate the non-linear terms to check if *(P3)* is convex. Note that the continuous relaxation of $\sum_{k \in K} \mu_k Z_{jk}^2$ is a quadratic convex function. The two nonlinear terms $\sum_{j \in J} \sqrt{2h_j p_j \sum_{k \in K} \mu_k Z_{jk}^2}$ and $\sum_{j \in J} h_j z_\alpha \sqrt{lt \sum_{k \in K} \sigma_k^2 Z_{jk}^2}$] in the objective function are convex by the following theorem.

Theorem: let f: $\mathbb{R}^N \to \mathbb{R}$, $f(z) = \sqrt{z^T U z} = \sqrt{\sum_{i=1}^N u_i Z_i^2}$ for some $U \in \mathbb{R}^{nxn}$,

$$U = \begin{pmatrix} u_1 & & 0 \\ & \ddots & \\ 0 & & u_n \end{pmatrix}$$

s.t. $u = \begin{bmatrix} u_i \\ \vdots \\ u_n \end{bmatrix} \geq 0$, then f is convex.

$$\frac{\partial f(z)}{\partial z_i} = \frac{1}{2} (z^T U z)^{-1/2}\, 2\, u_i z_i = (z^T U z)^{-1/2}\, u_i z_i$$

$$Df(z) = (z^T U z)^{-1/2}\, Uz$$

$$\frac{\partial^2 f(z)}{\partial z_i \partial z_j} = -(z^T U z)^{-3/2}\, u_j z_j\, u_i z_i \quad \text{for } i, j \in \{1, \dots N\} \quad i \neq j$$

$$\frac{\partial^2 f(z)}{\partial z_i^2} = (-1)(z^T U z)^{-3/2} (u_i z_i)^2 + (z^T U z)^{-1/2} u_i$$

$$H f(z) = (z^T U z)^{-1/2} [U - (z^T U z)^{-1} U z z^T U]$$

Note that $z^T U z > 0$ in the interior of the feasible region,
for $U - (z^T U z)^{-1} [U z z^T U]$ we can take arbitrary $x \in \mathbb{R}^N$ to show the positive semi definiteness (PSD) property:

$$x^T [u - (z^T U z)^{-1} (U z z^T U)]\, x = x^T U\, x - z^T U\, z\, (x^T U z)^2.$$

If we let $C = \begin{pmatrix} \sqrt{u_1} & & 0 \\ & \ddots & \\ 0 & & \sqrt{u_n} \end{pmatrix} = C^T$ (possible since $u \geq 0$),

$x^T U\, x - (z^T Uz)^{-1}\, (x^T Uz)^2 \geq 0$

$$\Updownarrow$$

$(x^T U\, x) - (z^T Uz) \geq (x^T Uz)^2$

$$\Updownarrow$$

$(\bar{x}^T\, \bar{x}) - (\bar{z}^T \bar{z}) \geq (\bar{x}^T \bar{z})^2$ where $\bar{x} = Cx$ and $\bar{z} = Cz$, and the final inequality is true by the Cauchy-Schwarz inequality.

$\sum_{k \in K} \mu_k Z_{jk}^2$ is a quadratic convex function and the two nonlinear terms $\sum_{j \in J} \sqrt{2h_j p_j \sum_{k \in K} \mu_k Z_{jk}^2}$ and $\sum_{j \in J} h_j z_\alpha \sqrt{lt \sum_{k \in K} \sigma_k^2 Z_{jk}^2}$ are convex, consequently, the continuous relaxation of *(P3)* is a convex program. After this transformation, the resulting model *(P3)* is a mixed-integer convex program. Hence small-sized instances of the problem can be solved optimally.

5.2. Heuristic Solution Approaches

There are many heuristic methods (decomposition methods, inductive methods, reduction methods, constructive methods, local search methods, problem specific methods, etc.) that are very different in nature. Silver (2007) proposes a classification for heuristic methods as follows:

- Randomly Generated Solutions
- Problem Decomposition / Partitioning
- Inductive Methods
- Methods that Reduce the Solution Space
- Approximation Methods
- Constructive Methods
- Local Improvement (Neighborhood Search) Methods
- Metaheuristics: There are several metaheuristic methods presented in the literature, some examples of mainly used metaheuristic methods are as follows:
    - Beam Search
    - Tabu Search

- Simulated Annealing
- Multi-Start Constructive Approaches
- Genetic algorithms
- Neural networks

The main decision to be made at this point of our study is to decide which heuristic solution method is to be applied. When we try to evaluate the performances of possible heuristic solution methods on our specific problem, based on previous studies in the literature, it is seen that there are no other models considering the same supply chain structure. However, as shown in the previous sections, subcases of our problem (Location-Inventory-Routing Problem with Multiple Location Layers) under the predetermined parameter settings, are equivalent to the well-known problems such as Multi-Depot Vehicle Routing Problem –MDVRP, Single-Source Capacitated Facility Location Problem – SSCFLP, Capacitated Vehicle Routing Problem – CVRP. MDVRP structure is relatively more similar to our problem environment. Therefore, observation of the previously applied techniques on MDVRP may give us an insight about the performances of alternative heuristic solution methods. Researchers use different techniques as hybrid genetic algorithms, decomposition heuristics, metaheuristics such as simulated annealing, multi-objective scatter search, etc. to solve the MDVRP in the literature. Since decomposition (Perl and Daskin, 1985; Hansen et al., 1994; Contartdo and Martinelli, 2015) and simulated annealing methods (Mirabi, Ghomi and Jolai, 2010; Wu et al. 2002) have been applied to different variants of MDVRP with fairly good results, we select these techniques as the basis for our heuristic method development efforts.

5.2.1. Decomposition Heuristics

In any decomposition heuristic method, the first step is defining the subproblems. After they are defined, one or more of the three general solution approaches listed below can be applied:

1. Solving the subproblems independently and consolidating their solutions.
2. Solving the subproblems sequentially.

3. Solving the subproblems iteratively.

First two of the four decomposition heuristic methods proposed in our study are based on the second solution approach listed above, and solves the subproblems in a sequential manner, while the last two decomposition heuristics use both the sequential and iterative solution approaches.

In the first two decomposition heuristics using sequential solution approach, the original problem (Location-Inventory-Routing Problem with Multiple Location Layers) is decomposed into three subproblems; two different location-allocation problems and one vehicle routing problem. The first of the two location-allocation problems aims to determine RTCs to be opened, their capacity levels, and allocation of TCs to RTCs; while the second one aims to determine RBCs to be opened, their capacity levels, allocation of RTCs to RBCs, allocation of DCs to RBCs, and transfer amounts between DCs and RBCs. The third subproblem aims to generate the vehicle routes between the opened RTCs and their affiliated TCs. The solution of the first subproblem is used as an input for the second and the third subproblems.

In the last two decomposition heuristics using sequential and iterative solution approaches together, the original problem is decomposed into four subproblems; three different location-allocation problems and one vehicle routing problem. The first of the three location-allocation problems aims to determine RTCs to be opened, their capacity levels, and allocation of TCs to RTCs without knowing the locations of RBCs. Using the solution obtained from the first subproblem as an input, the second location-allocation problem aims to determine RBCs to be opened, their capacity levels, allocation of RTCs to RBCs, allocation of DCs to RBCs, and transfer amounts between DCs and RBCs. The third subproblem is an extended version of the first one. It aims to decide RBC-RTC assignments, transfer amounts between those facilities in addition to the decisions (RTCs to be opened, their capacity levels, and allocation of TCs to RTCs) tried to be achieved in the first subproblem. When compared with the first subproblem, the third one uses additional information, i.e., locations of RBCs, obtained from the second subproblem. It also considers the inbound transportation, i.e., transfers between RBCs and RTCs. In these two decomposition heuristics, the second and the third subproblems are solved iteratively until the stopping criterion is met. The fourth subproblem aims to generate the vehicle routes between the opened RTCs and their affiliated TCs. The final solution obtained from the iterative cycle is used as an input for the fourth subproblem.

Two different sequences, which can be used while solving the subproblems sequentially, are identified based on the sequence of the location decisions:

- Sequence 1: First locate RTCs, then locate RBCs, and then develop vehicle routes
- Sequence 2: First locate RBCs, then locate RTCs, and then develop vehicle routes

In the first two decomposition heuristics, subproblems are solved using Sequence 1 listed above. Although the same decomposition approach and the same solution sequence is used in both of the heuristics, they differ in modelling approaches used for the first subproblem. The rest of the subproblems (subproblems 2 and 3) are the same for the first two decomposition heuristics using the sequential solution approach.

In the last two decomposition heuristics, both solution sequences are used. Heuristics start solving subproblems based on sequence 1, but within the iterative cycle both sequence 1 and sequence 2 are used while deciding the locations of RBCs and RTCs, iteratively. The iterative decomposition heuristics only differ in their modelling approaches for the first subproblem.

5.2.1.1. Decomposition Heuristic 1 (DH1)

5.2.1.1.1. Decomposition Approach and Decomposition Scheme

DH1 belongs to the first sequence group (First locate RTCs, then locate RBCs, then develop vehicle routes). Three subproblems (in sequence), and interactions between them are described below.

Subproblem 1 (DH1SP1)

We consider a location-allocation problem which is stated as:

- Given a set of TCs with deterministic product demand;
- Determine: the number of RTCs to locate, their capacity levels, their location sites and TCs to assign to each RTC,
- To minimize the total expected cost including the cost items listed below:
    - Fixed cost of opening RTCs,
    - Transportation cost directly from RTCs to TCs.

Changes or additional assumptions, compared to the structure of the supply chain described in the original problem that are made before modelling Subproblem 1 are as follows:

- We do not consider DCs, RBCs in the chain, nor the interactions of RTCs and DCs with these facilities,
- Shipments between RTCs and TCs are direct shipments,
- Inventory costs at RTCs are ignored.

Subproblem 2 (DH1SP2)

We consider a location-allocation problem which is stated as:

- Given a set of DCs and RTCs with deterministic product demand;
- Determine: the number of RBCs to locate, their capacity levels, their location sites and RTCs to assign to each RBC, DCs to assign to each RBC, the amount of transfers between DCs and the opened RBCs,
- To minimize the total expected cost including the cost items listed below:
    - Fixed cost of opening RBCs,
    - Transportation cost directly from DCs to RBCs,
    - Transportation cost directly from RBCs to RTCs.

Changes or additional assumptions, compared to the structure of the supply chain described in the original problem that are made before modelling Subproblem 2 are as follows:

- We do not consider TCs, and interactions of RTCs,
- Inventory costs at RTCs are ignored.

<u>Subproblem 3 (DH1SP3)</u>

We consider a vehicle routing problem which is stated as:

- Given a set of RTCs with known capacity levels and TCs with deterministic product demand, vehicles with known capacities, and allocation of TCs to RTCs;
- Determine the vehicle routes,
- To minimize the total expected cost including the cost items listed below
    - Routing cost from the opened RTCs to TCs.

Changes or additional assumptions, compared to the structure of the supply chain described in the original problem that are made before modelling Subproblem 3 are as follows:

- Inventory costs at RTCs are ignored.

<u>Merging the Solutions of the Subproblems to Obtain a Feasible Solution to the Original Problem</u>

While obtaining a feasible solution to the original problem, the decisions listed below (with the corresponding decision variables) under each subproblem are consolidated, and used as the input for the objective function of the original problem.

Subproblem 1 (DH1SP1)

- Opened RTCs and their capacity levels (W_j^n),
- RTC-TC Assignments (Z_{jk})

Subproblem 2 (DH1SP2)

- Opened RBCs and their capacity levels (U_h^n)
- RBC-RTC Assignments (Y_{hj})
- DC-RBC Assignments (X_{th})
- Amount of Transfers between DCs and opened RBCs (C_{th})
- Amount of Transfers between opened RBCs and RTCs (D_{hj})

Subproblem 3 (DH1SP3)

- Vehicle Routes (R_{lkv})

The decomposition scheme of DH1 is summarized in Figure 6.

5.2.1.1.2. Mathematical Representations of the Subproblems

5.2.1.1.2.1. Model Formulation of DH1 Subproblem 1 (DH1SP1 - RTC Location Problem)

Index Sets

K Set of Transfusion Centers (TCs)

J Set of potential Regional Transfusion Centers (RTCs)

M_j Set of capacity levels for RTC j ($j \in J$)

Parameters and Notation

μ_k Mean annual demand at TC k ($\forall k \in K$)

f_j^n fixed annual cost of opening and operating RTC j at capacity level n $\left(\forall j \in J, \forall n \in M_j\right)$

w_j^n capacity of RTC j at capacity level n $\left(\forall j \in J, \forall n \in M_j\right)$

r_{jk} weighted distance between RTC j and TC k ($\forall j \in J, \forall\ k \in K$)

q annual number of visits of each vehicle

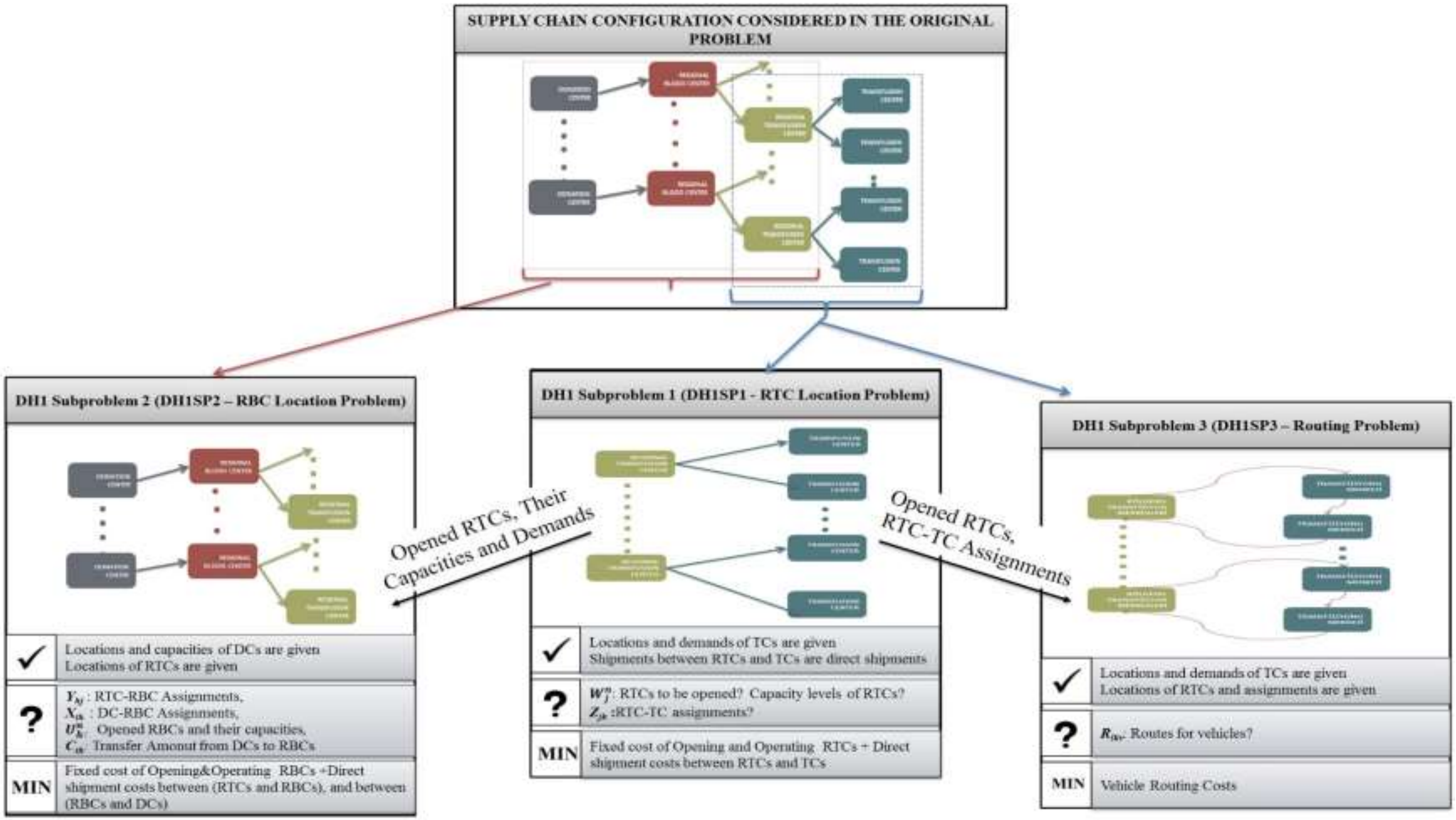


Figure 6. Decomposition Scheme of DH1

Decision Variables

$$Z_{jk} = \begin{cases} 1 \text{ if TC } k \text{ is assigned to RTC } j \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall k \in K)$$

$$W_j^n = \begin{cases} 1 \text{ if RTC } j \text{ is opened with capacity level } n \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall n \in M_j)$$

DH1SP1 - RTC Location Problem

Minimize

$$\sum_{j \in J} \sum_{n \in M_j} f_j^n W_j^n + q \sum_{j \in J} \sum_{k \in K} Z_{jk} r_{jk}$$

Subject to;

$$\sum_{k \in K} \mu_k Z_{jk} \leq \sum_{n \in M_j} w_j^n W_j^n \; (\forall j \in J) \qquad \text{(DH1SP1-1)}$$

$$\sum_{n \in M_j} W_j^n \leq 1 \; (\forall j \in J) \qquad \text{(DH1SP1-2)}$$

$$\sum_{j \in J} Z_{jk} = 1 \; (\forall k \in K) \qquad \text{(DH1SP1-3)}$$

$$Z_{jk} \in \{0,1\} \quad (\forall j \in J, \forall k \in K) \qquad \text{(DH1SP1-4)}$$

$$W_j^n \in \{0,1\} \quad (\forall j \in J, \forall n \in M_j) \qquad \text{(DH1SP1-5)}$$

Constraints

(DH1SP1-1)	Capacity constraint associated with RTC
(DH1SP1-2)	Each RTC can be assigned to only one capacity level
(DH1SP1-3)	Each TC can be assigned to only one opened RTC
(DH1SP1-4) and (DH1SP1-5)	Integrality constraints on the binary variables

5.2.1.1.2.2. Model Formulation of DH1 Subproblem 2 (DH1SP2 - RBC Location Problem)

Index Sets

J Set of Regional Transfusion Centers (RTCs) (Input from the solution of the subproblem DH1SP1)

H Set of potential Regional Blood Centers (RBCs)

T Set of Donation Centers (DCs)

N_h Set of capacity levels for RBC h $(h \in H)$

Parameters and Notation

g_h^n fixed annual cost of opening and operating RBC h at capacity level *n* $(\forall h \in H, \forall n \in N_h)$

u_h^n capacity of RBC h at capacity level n $(\forall h \in H, \forall n \in N_h)$

CAP_t capacity for DC t $(\forall t \in T)$

DRR blood disposal rate at RBCs

BigM big number

c_{th} weighted distance between DC t and RBC h $(\forall h \in H, \forall t \in T)$

e_{hj} weighted distance between RTC j and RBC h $(\forall j \in J, \forall h \in H)$

r_j Mean annual demand at RTC; Total amount sent from RTC j to all its assigned TCs in the solution of the DH1SP1 $(\sum_{k \in K} Z_{jk}\, \mu_k)$ value found from the solution of the subproblem DH1SP1)

Decision Variables

$$Y_{hj} = \begin{cases} 1 \text{ if RTC } j \text{ is assigned to RBC } h \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall h \in H)$$

$$X_{th} = \begin{cases} 1 \text{ if DC } t \text{ is assigned to RBC } h \\ 0 \text{ otherwise} \end{cases} \qquad (\forall t \in T, \forall h \in H)$$

$$U_h^n = \begin{cases} 1 \text{ if RBC } h \text{ is opened with capacity level } n \\ 0 \text{ otherwise} \end{cases} \qquad (\forall h \in H, \forall n \in N_h)$$

C_{th} : Amount sent from DC t to RBC h $(\forall t \in T, \forall h \in H)$

D_{hj} : Amount sent from RBC h to RTC j $(\forall h \in H, \forall j \in J)$

DH1SP2 - RBC Location Problem

Minimize

$$\sum_{h \in H} \sum_{n \in N_h} g_h^n U_h^n + \sum_{t \in T} \sum_{h \in H} c_{th} C_{th} + \sum_{h \in H} \sum_{j \in J} e_{hj} D_{hj}$$

Subject to;

$$\sum_{h \in H} C_{th} \leq CAP_t \quad (\forall t \in T) \tag{DH1SP2-1}$$

$$\sum_{t \in T} C_{th} \leq \sum_{n \in N_h} u_h^n U_h^n \ (\forall h \in H) \tag{DH1SP2-2}$$

$$C_{th} \leq BigM\ X_{th}\ (\forall h \in H, \forall t \in T) \tag{DH1SP2-3}$$

$$\sum_{t \in T} C_{th} \geq (1 + DRR) \sum_{j \in J} Y_{hj}\, r_j \quad (\forall h \in H) \tag{DH1SP2-4}$$

$$\sum_{n \in N_h} U_h^n \leq 1\ (\forall h \in H) \tag{DH1SP2-5}$$

$$\sum_{h \in H} X_{th} = 1\ (\forall t \in T) \tag{DH1SP2-6}$$

$$X_{th} \leq \sum_{n \in N_h} U_h^n\ (\forall h \in H, \forall t \in T) \tag{DH1SP2-7}$$

$$\sum_{h \in H} Y_{hj} = 1\ (\forall j \in J) \tag{DH1SP2-8}$$

$$Y_{hj}\ r_j = D_{hj}\ (\forall h \in H, \forall j \in J) \tag{DH1SP2-9}$$

$$X_{th} \in \{0,1\} \quad (\forall t \in T, \forall h \in H) \tag{DH1SP2-10}$$

$$Y_{hj} \in \{0,1\} \quad (\forall j \in J, \forall h \in H) \tag{DH1SP2-11}$$

$$U_h^n \in \{0,1\} \quad (\forall h \in H, \forall n \in N_h) \tag{DH1SP2-12}$$

$$D_{hj} \geq 0 \qquad (\forall h \in H, \forall j \in J) \tag{DH1SP2-13}$$

$$C_{th} \geq 0 \qquad (\forall t \in T, \forall h \in H) \tag{DH1SP2-14}$$

Constraints

(DH1SP2-1)	Capacity of any DC is not exceeded.
(DH1SP2-2)	If an RBC is not opened, no products can be sent to that RBC; and capacity of any RBC is not exceeded.
(DH1SP2-3)	If DC *t* is not assigned to RBC *h*, no products can be sent from DC *t* to RBC *h*.
(DH1SP2-4)	Amount sent from an RBC to RTCs cannot exceed the amount received by that RBC from the DCs (considering the disposal rate).
(DH1SP2-5)	Each RBC can be assigned to only one capacity level.
(DH1SP2-6)	Each DC can be assigned to only one RBC.
(DH1SP2-7)	If an RBC is not opened, no DCs can be assigned to that RBC.
(DH1SP2-8)	Each RTC can be assigned to only one opened RBC.
(DH1SP2-9)	Amount sent from an RBC to an RTC should be equal to the total demand of that RTC.
(DH1SP2-10) to (DH1SP2-12)	Integrality constraints on the binary variables.
(DH1SP2-13) to (DH1SP2-14)	Non-negativity constraints on other decision variables.

5.2.1.1.2.3. Model Formulation of DH1 Subproblem 3 (DH1SP3 - Routing Problem)

Index Sets

K Set of Transfusion Centers (TCs)

J Set of Regional Transfusion Centers (RTCs) (Input from the solution of the problem DH1SP1)

V Set of vehicles

Parameters and Notation

B Number of TCs in set K, i.e. $B = |K|$

μ_k Mean annual demand at TC k $(\forall k \in K)$

d_{kl} Transportation cost from node k to node l

$(\forall\ (l,k) \in (JxK)\ \cup\ (KxK)\ \cup\ Kx\ J)$

vc Annual delivery capacity of a vehicle (q x capacity of truck)

q Annual number of visits of each vehicle from an RTC to a TC

Decision Variables

$$R_{klv} = \begin{cases} 1 \text{ if } k \text{ precedes } l \text{ in route of vehicle } v \\ 0 \text{ otherwise} \end{cases}$$

$\forall\ (l,k) \in (JxK) \cup\ (KxK)\ \{(k,k): k \in K\} \cup\ (KxJ)$

m_{kv} : Variable defined for subtour elimination $(\forall k \in K, \forall v \in V)$

DH1SP3 - Routing Problem

Minimize

$$q \sum_{v \in V} \sum_{j \in J} \sum_{k \in K} d_{jk} R_{jkv} + q \sum_{v \in V} \sum_{k \in K} \sum_{j \in J \cup K \setminus \{k\}} d_{kj} R_{kjv}$$

Subject to

$$\sum_{v \in V} \sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} = 1\ \ (\forall k \in K) \tag{DH1SP3-1}$$

$$\sum_{k \in K} \mu_k \sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} \leq vc\ \ (\forall v \in V) \tag{DH1SP3-2}$$

$$m_{kv} - m_{lv} + (B \times R_{klv}) \leq B - 1\ \ (\forall k, l \in K, \forall v \in V) \tag{DH1SP3-3}$$

$$\sum_{l \in K \cup J\ (K \setminus \{k\})} R_{klv} - \sum_{l \in K \cup J\ (K \setminus \{k\})} R_{lkv} = 0\ \ (\forall k \in K, \forall v \in V) \tag{DH1SP3-4}$$

$$\sum_{l \in K} R_{jlv} - \sum_{l \in K} R_{ljv} = 0\ \ (\forall j \in J, \forall v \in V) \tag{DH1SP3-5}$$

$$\sum_{j \in J} \sum_{k \in K} R_{jkv} \leq 1\ \ (\forall v \in V) \tag{DH1SP3-6}$$

$$\sum_{l \in J \cup K\ (K \setminus \{k\})} R_{klv} + \sum_{l \in K} R_{jlv} - Z_{jk} \leq 1\ \ (\forall j \in J, \forall k \in K, \forall v \in V) \tag{DH1SP3-7}$$

$R_{klv} \in \{0,1\}$ $(\forall(l,k) \in (JxK) \cup (KxK) \setminus \{(k,k) : k \in K\} \cup (K\text{x}J))$ (DH1SP3-8)

$m_{kv} \geq 0$ $(\forall k \in K, \forall v \in V)$ (DH1SP3-9)

Constraints

(DH1SP3-1)	Each TC is included on exactly one vehicle route.
(DH1SP3-2)	Capacity of each vehicle is not exceeded.
(DH1SP3-3)	Subtours of vehicles are avoided.
(DH1SP3-4) and (DH1SP3-5)	Conservation of flow is guaranteed at each node.
(DH1SP3-6)	Vehicle starts from only one RTC.
(DH1SP3-7)	If the route of vehicle v visiting TC k starts its route from RTC j, then TC k is assigned to RTC j.
(DH1SP3-8) and (DH1SP3-9)	Non-negativity constraints on decision variables.

5.2.1.2. Decomposition Heuristic 2 (DH2)

5.2.1.2.1. Decomposition Approach and Decomposition Scheme

DH2 also belongs to the first sequence group (First locate RTCs, then locate RBCs, and then develop vehicle routes). Three subproblems (in sequence) and interactions between them are described below:

The only difference of DH2 from the DH1 is the formulation of Subproblem 1. In DH1SP1, neither DCs nor RBCs are considered while locating RTCs. In other words, only outbound transportations from RTCs are taken into account. In DH2SP1, we deal with a location-allocation problem considering a supply chain structure including DCs, RTCs, and TCs. In this structure, it is assumed that DCs are directly connected to RTCs, but not to RBCs. Although RBCs are not modelled in DH2SP1, while preparing data sets, the parameter corresponding to the weighted transportation cost between a DC and an RTC is calculated by taking the average cost of all possible transportation alternatives from this DC to the target RTC over candidate RBCs.

In summary, in DH2SP1 we also consider the inbound transportation costs of RTC, by assuming that RTCs are directly supplied by DCs with no RBCs in between.

Subproblem 1 (DH2SP1)

We consider a location-allocation problem which is stated as:

- Given a set of TCs with deterministic product demand, and DCs with known capacity levels;
- Determine: the number of RTCs to locate, their capacity levels, their location sites, assignment of both TCs and DCs to the opened RTCs, and amount of transfers between DCs and the opened RTCs,
- To minimize the total expected cost including the cost items listed below:
    - Fixed cost of opening RTCs,
    - Transportation cost directly from RTCs to TCs,
    - Transportation cost directly from DCs to RTCs.

Changes or additional assumptions, compared to the original supply chain, that are made before modelling Subproblem 1 are as follows:

- We do not consider RBCs in the chain.
- Shipments between RTCs and TCs are direct shipments.
- RTCs are not supplied by RBCs, but they are directly supplied by DCs and the shipments are direct shipments.
- Inventory costs at RTCs are ignored.

Subproblem 2 (DH2SP2) and Subproblem 3 (DH2SP3)

Subproblems are the same as the ones ("DH1SP2" and "DH1SP3") and described in DH1, except that they use the inputs from the solution of the problem "DH2SP1" instead of "DH1SP1".

Merging The Solutions of Subproblems to Obtain a Feasible solution to the Original Problem

The approach used to obtain a feasible solution is exactly the same as the approach applied in DH1.

The decomposition scheme is given in Figure 7.

5.2.1.2.2. Mathematical Representations of the Subproblems

5.2.1.2.2.1. Model Formulation of DH2 Subproblem 1 (DH2SP1 - RTC Location Problem)

Index Sets

K Set of Transfusion Centers (TCs)

J Set of potential Regional Transfusion Centers (RTCs)

T Set of Donation Centers (DCs)

M_j Set of capacity levels for RTC j ($j \in J$)

Parameters and Notation

μ_k Mean annual demand at TC k ($\forall k \in K$)

f_j^n fixed annual cost of opening and operating RTC j at capacity level n $(\forall j \in J, \forall n \in M_j)$

w_j^n capacity of RTC j at capacity level n $(\forall j \in J, \forall n \in M_j)$

CAP_t capacity for DC t ($\forall t \in T$)

r_{jk} weighted distance between RTC j and TC k ($\forall j \in J, \forall k \in K$)

a_{tj} distance between DC t and RTC j ($\forall j \in J, \forall t \in T$)

q annual number of visits of each vehicle

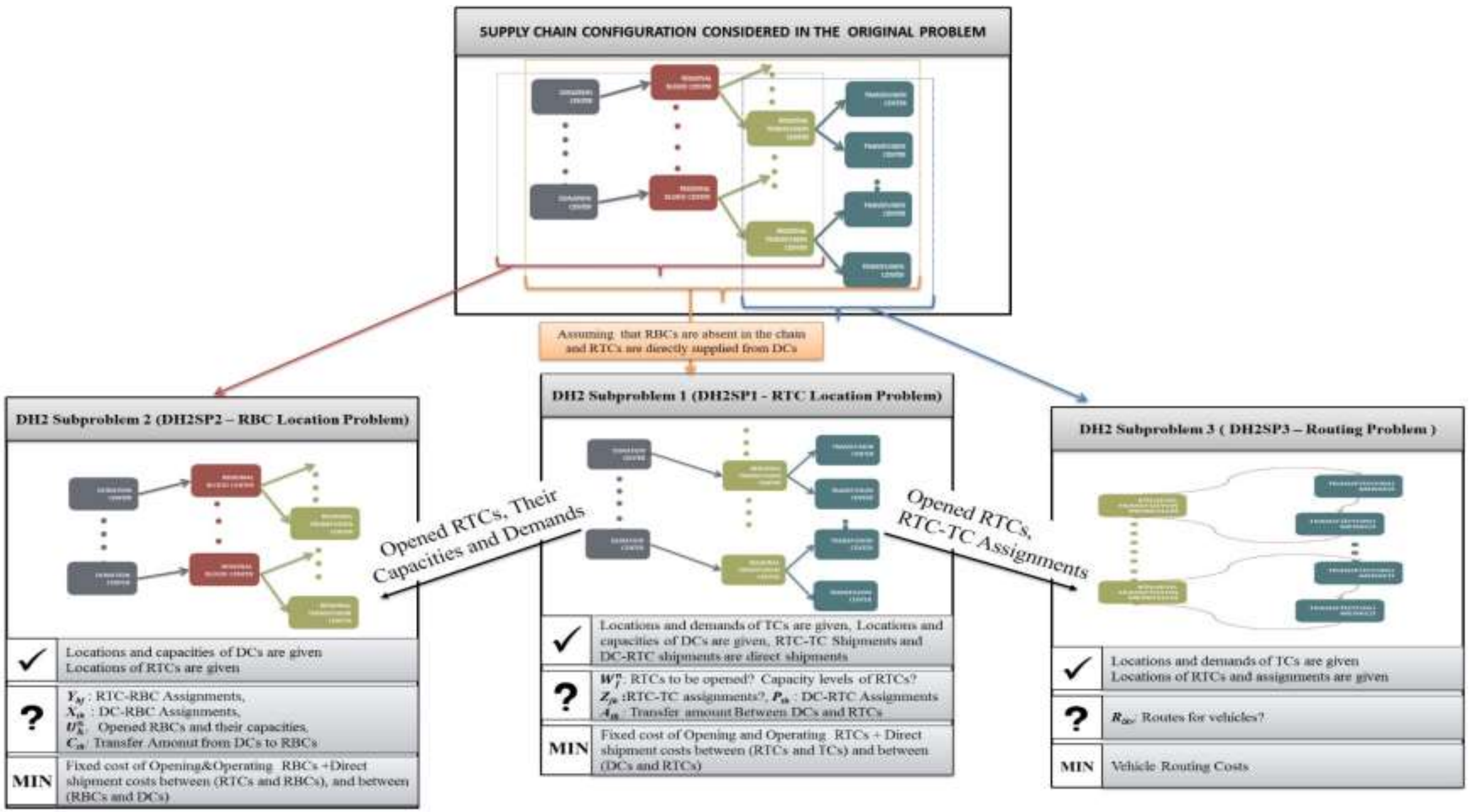


Figure 7. Decomposition Scheme of DH2

Decision Variables

$$Z_{jk} = \begin{cases} 1 \text{ if TC } k \text{ is assigned to RTC } j \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall k \in K)$$

$$W_j^n = \begin{cases} 1 \text{ if RTC } j \text{ is opened with capacity level } n \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall n \in M_j)$$

$$P_{tj} = \begin{cases} 1 \text{ if DC } t \text{ is assigned to RTC } j \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall\, t \in T)$$

A_{tj} = amount sent from DC t to RTC j $\qquad (\forall j \in J, \forall\, t \in T)$

DH2SP1 - RTC Location Problem

Minimize

$$\sum_{j \in J} \sum_{n \in M_j} f_j^n W_j^n + q \sum_{j \in J} \sum_{k \in K} Z_{jk}\, r_{jk} + \sum_{t \in T} \sum_{j \in J} a_{tj} A_{tj}$$

Subject to;

$$\sum_{k \in K} \mu_k Z_{jk} \leq \sum_{n \in M_j} w_j^n W_j^n \quad (\forall j \in J) \qquad \text{(DH2SP1-1)}$$

$$\sum_{n \in M_j} W_j^n \leq 1 \ (\forall j \in J) \qquad \text{(DH2SP1-2)}$$

$$\sum_{j \in J} Z_{jk} = 1 \ (\forall k \in K) \qquad \text{(DH2SP1-3)}$$

$$\sum_{j \in J} P_{tj} = 1 \ (\forall t \in T) \qquad \text{(DH2SP1-4)}$$

$$\sum_{j \in J} A_{tj} \leq CAP_{\mathrm{t}} \quad (\forall t \in T) \qquad \text{(DH2SP1-5)}$$

$$A_{tj} \leq BigM\; P_{tj} \ (\forall j \in J, \forall t \in T) \qquad \text{(DH2SP1-6)}$$

$$P_{tj} \leq \sum_{n \in \mathrm{M}_j} W_j^n \ (\forall j \in J, \forall t \in T) \qquad \text{(DH2SP1-7)}$$

$$\sum_{t \in T} A_{tj} \geq (1 + DRR) \sum_{k \in K} \mu_k Z_{jk} \quad (\forall j \in J) \qquad \text{(DH2SP1-8)}$$

$$Z_{jk} \in \{0,1\} \quad (\forall j \in J, \forall k \in K) \qquad \text{(DH2SP1-9)}$$

$W_j^n \in \{0,1\} \quad (\forall j \in J, \forall n \in M_j)$ (DH2SP1-10)

$P_{tj} \in \{0,1\} \quad (\forall j \in J, \forall t \in T)$ (DH2SP1-11)

$A_{tj} \geq 0 \quad (\forall t \in T, \forall j \in J)$ (DH2SP1-12)

Constraints

(DH2SP1-1)	Capacity of any RTC is not exceeded.
(DH2SP1-2)	Each RTC can be assigned to only one capacity level.
(DH2SP1-3)	Each TC can be assigned to only one opened RTC.
(DH2SP1-4)	Each DC can be assigned to only one RTC.
(DH2SP1-5)	Capacity of any DC is not exceeded.
(DH2SP1-6)	If DC *t* is not assigned to RTC *j*, no products can be sent from DC *t* to RTC *j*.
(DH2SP1-7)	If an RTC is not opened, no DCs can be assigned to that RTC.
(DH2SP1-8)	Amount sent from an RTC to TCs cannot exceed the amount received by that RTC from DCs (considering the disposal rate).
(DH2SP1-9) to (DH2SP1-11)	Integrality constraints on the binary variables.
(DH2SP1-12)	Non-negativity constraints on other decision variables.

5.2.1.2.2.2. Model Formulation of DH2 Subproblem 2 (DH2SP2 - RBC Location Problem)

It is the same model as the “DH1SP2- RBC Location problem” except that it uses the inputs from the solution of the problem “DH2SP1” instead of “DH1SP1”.

5.2.1.2.2.3. Model Formulation of DH2 Subproblem 3 (DH2SP3 - Routing Problem)

It is the same model as the "DH1SP3- Routing Problem" except that it uses the inputs from the solution of the problem "DH2SP1" instead of "DH1SP1".

5.2.1.3. Decomposition Heuristic 3 (DH3)

5.2.1.3.1. Decomposition Approach and Decomposition Scheme

Decomposition Heuristic 3 is a modified version of DH1, which applies an iterative solution approach. Instead of solving subproblems just sequentially, the heuristic starts with a sequential solution approach as we do in DH1. After solving the first three subproblems, the output of the third subproblem is used as an input for the second, and then the second and the third subproblems are solved iteratively. When the stopping criterion for the iterations is satisfied, the procedure again continues with a sequential solution approach and the fourth subproblem is solved.

The subproblems and the interactions between them are described below. Decomposition scheme and the flowchart of the procedure applied by DH3 are given in Figure 8, and Figure 9, respectively.

<u>Subproblem 1 (DH3SP1) and Subproblem 2 (DH3SP2)</u>

Subproblems are the same with the ones ("DH1SP1" and "DH1SP2") described in DH1, except that "DH3SP2" has capability to use inputs from both "DH3SP1" and "DH3SP3".

<u>Subproblem 3 (DH3SP3)</u>

We consider a location-allocation problem which is an extended version of DH3SP1. The subproblem is stated as:

- Given a set of TCs with deterministic product demand, and open RBCs;
- Determine: the number of RTCs to locate, their capacity levels, their location sites, assignment of TCs to the opened RTCs, assignment of the opened RTCs to RBCs, amount of transfers between the open RBCs and the already opened RTCs, and capacity levels of the RBCs,
- To minimize the total expected cost including the cost items listed below:
    - Fixed cost of opening RTCs
    - Fixed cost of the already opened RBCs
    - Transportation cost directly from RTCs to TCs
    - Transportation cost directly from RBCs to RTCs

Changes or additional assumptions, compared to the original supply chain, that are made before modelling the Subproblem 3 are as follows:

- Shipments between RTCs and TCs are direct shipments
- Inventory costs at RTCs are ignored

<u>Subproblem 4 (DH3SP4)</u>

Subproblem 4 is the same with the "DH1SP3" except that it uses the inputs from the solution of the problem "DH3SP3" instead of "DH1SP1".

<u>Merging The Solutions of Subproblems to Obtain a Feasible solution to the Original Problem</u>

While obtaining a feasible solution to the original problem, the listed decisions (with their corresponding decision variables) under each problem are consolidated, and then used as the input for the objective function of the original problem.

Subproblem 2 (DH3SP2)

- Opened RBCs and their capacities (U_h^n)
- RBC-RTC Assignments (Y_{hj})

- DC-RBC Assignments (X_{th})
- Amount of Transfers between DCs and opened RBCs (C_{th})
- Amount of Transfers between opened RBCs and RTCs (D_{hj})

Subproblem 3 (DH3SP3)

- Opened RTCs and their capacity levels (W_j^n)
- RTC-TC Assignments (Z_{jk})

Subproblem 4 (DH3SP4)

- Vehicle Routes (R_{lkv})

5.2.1.3.2. Mathematical Representations of the Subproblems

5.2.1.3.2.1. Model Formulation of DH3 Subproblem 1 (DH3SP1 - RTC Location Problem)

It is the same model as the “DH1SP1- RTC Location problem”.

5.2.1.3.2.2. Model Formulation of DH3 Subproblem 2 (DH3SP2 - RBC Location Problem)

It is the same model as the “DH1SP2-RBC Location problem” except that it has capability to use inputs from both “DH3SP1” and “DH3SP3”.

5.2.1.3.2.3. Model Formulation of DH3 Subproblem 3 (DH3SP3 - Iterative version of RTC Location-Allocation Model)

Index Sets

K Set of Transfusion Centers (TCs)

J Set of potential Regional Transfusion Centers (RTCs)

H Set of already opened Regional Blood Centers (RBCs)

M_j Set of capacity levels for RTC j ($j \in J$)

N_h Set of capacity levels for RBC h ($h \in H$)

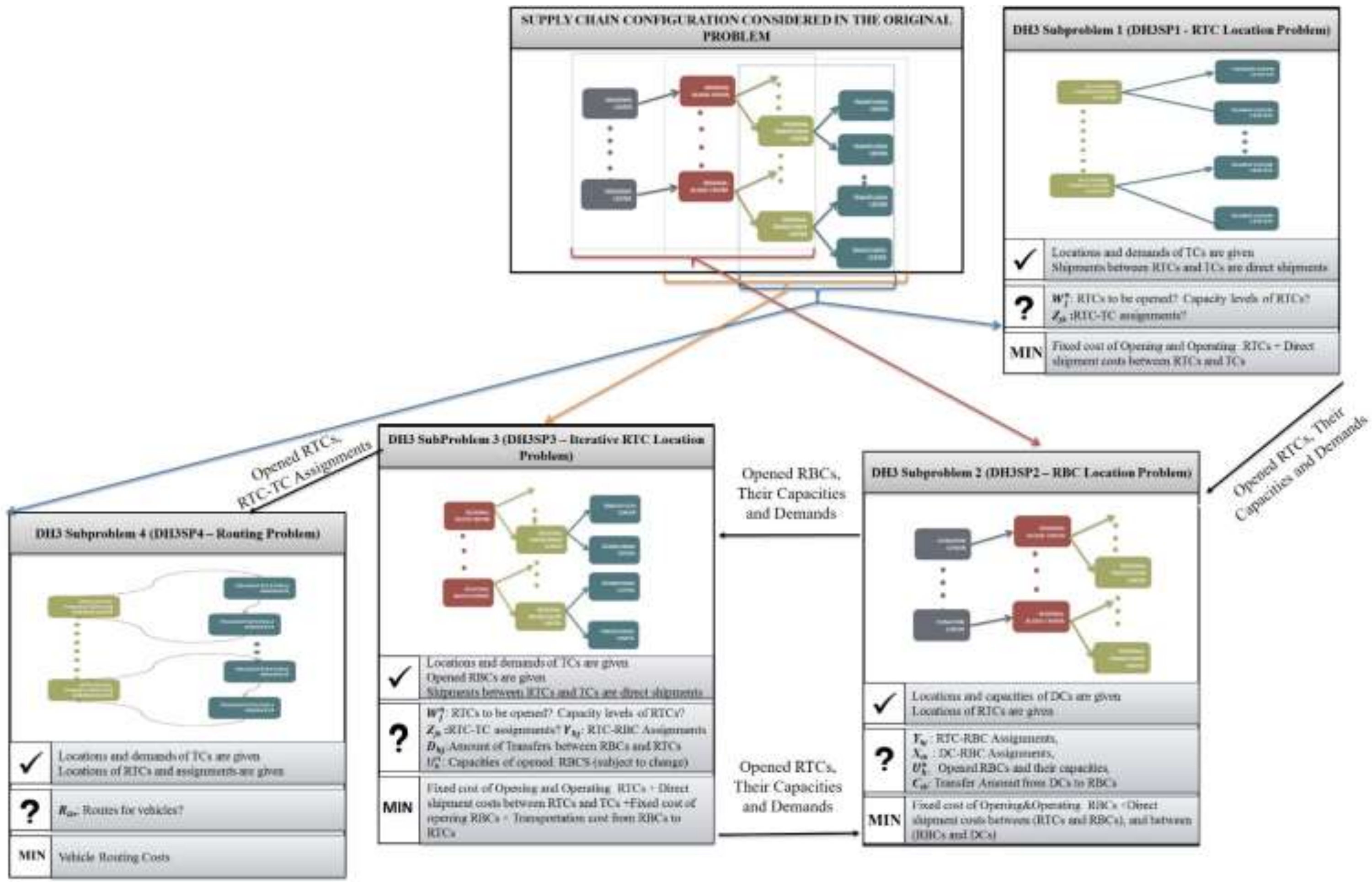


Figure 8. Decomposition Scheme of DH3

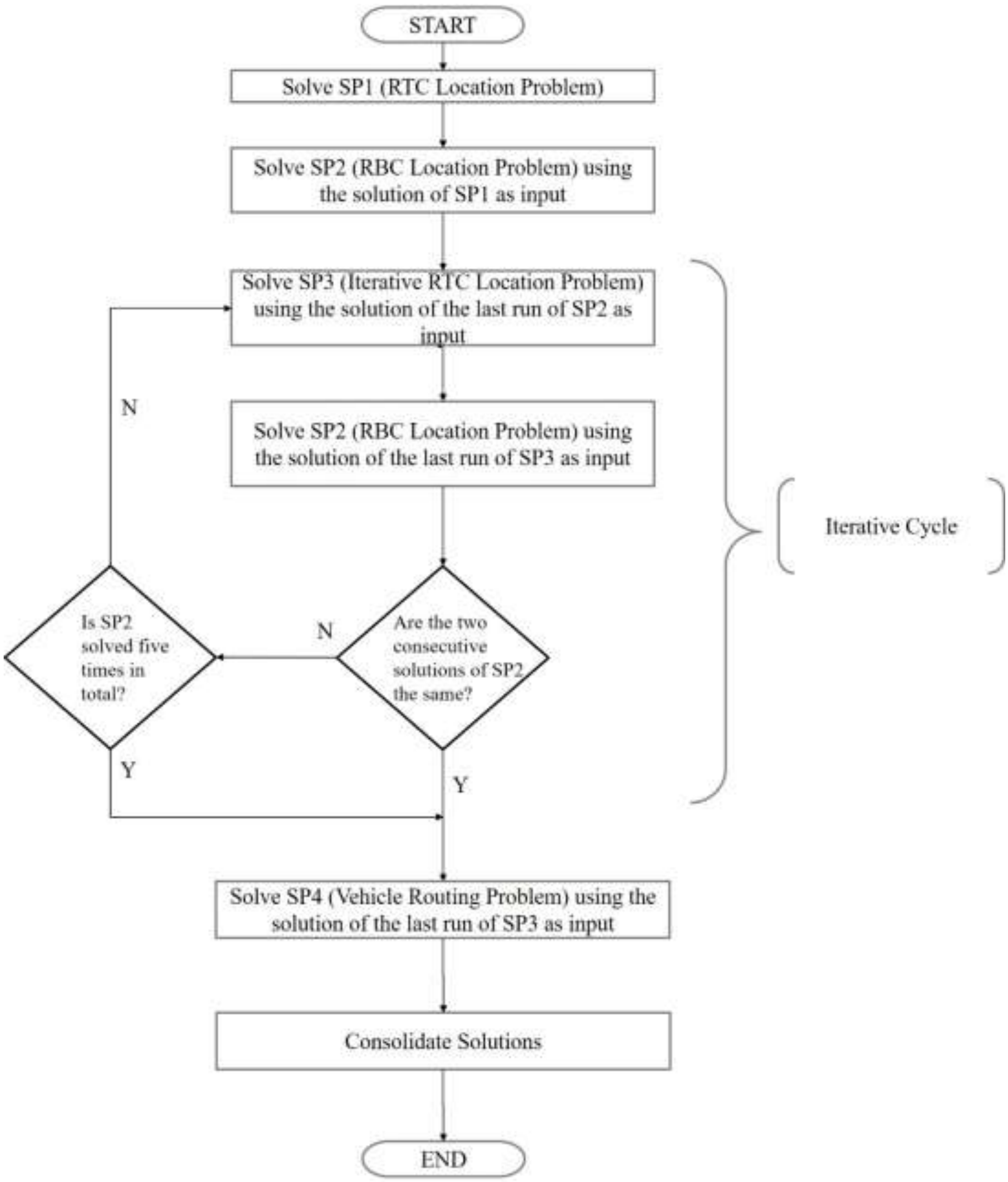


Figure 9. Flowchart of the procedure applied by DH3

Parameters and Notations

μ_k mean annual demand at TC k $(\forall k \in K)$

f_j^n fixed annual cost of opening and operating RTC j with capacity level n $\left(\forall j \in J, \forall n \in M_j\right)$

q annual number of visits of each vehicle

g_h^n fixed annual cost of opening and operating RBC h at capacity level n $(\forall h \in H, \forall n \in N_h)$

w_j^n capacity of RTC j at capacity level n $\left(\forall j \in J, \forall n \in M_j\right)$

u_h^n capacity of RBC h at capacity level n $(\forall h \in H, \forall n \in N_h)$

d_{jk} transportation cost between RTC j and TC k $(\forall j \in J, \forall k \in K)$

DRR blood disposal rate at any RBC

BigM big number

e_{hj} weighted distance between RTC j and RBC h $(\forall j \in J, \forall h \in H)$

Decision Variables

$$Z_{jk} = \begin{cases} 1 \text{ if TC } k \text{ is assigned to RTC } j \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall k \in K)$$

$$Y_{hj} = \begin{cases} 1 \text{ if RTC } j \text{ is assigned to RBC } h \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall h \in H)$$

$$W_j^n = \begin{cases} 1 \text{ if RTC } j \text{ is opened with capacity level } n \\ 0 \text{ otherwise} \end{cases} \qquad (\forall j \in J, \forall n \in M_j)$$

$$U_h^n = \begin{cases} 1 \text{ if RBC } h \text{ is opened with capacity level } n \\ 0 \text{ otherwise} \end{cases} \qquad (\forall h \in H, \forall n \in N_h)$$

D_{hj} : Amount sent from RBC h to RTC j $(\forall h \in H, \forall j \in J)$

DH3SP3 - Iterative version of RTC Location-Allocation Model

Minimize

$$\sum_{j \in J} \sum_{n \in M_j} f_j^n W_j^n + \sum_{h \in H} \sum_{n \in N_h} g_h^n U_h^n + \sum_{h \in H} \sum_{j \in J} e_{hj} D_{hj} + q \sum_{j \in J} \sum_{k \in K} d_{jk} Z_{jk}$$

Subject to;

$$\sum_{j \in J} Z_{jk} = 1 \ (\forall k \in K) \tag{DH3SP3-1}$$

$$\sum_{n \in M_j} W_j^n \leq 1 \ (\forall j \in J) \tag{DH3SP3-2}$$

$$\sum_{n \in N_h} U_h^n = 1 \ (\forall h \in H) \tag{DH3SP3-3}$$

$$\sum_{k \in K} \mu_k Z_{jk} \leq \sum_{n \in M_j} w_j^n W_j^n \ (\forall j \in J) \tag{DH3SP3-4}$$

$$\sum_{k \in K} \mu_k Z_{jk} \leq \sum_{h \in H} D_{hj} \ (\forall j \in J) \tag{DH3SP3-5}$$

$$\sum_{h \in H} Y_{hj} = \sum_{n \in M_j} W_j^n \ (\forall j \in J) \tag{DH3SP3-6}$$

$$\sum_{h \in H} D_{hj} \leq \sum_{n \in M_j} w_j^n W_j^n \ (\forall j \in J) \tag{DH3SP3-7}$$

$$(1 + DRR) \sum_{j \in J} D_{hj} \leq \sum_{n \in N_h} u_h^n U_h^n \ (\forall h \in H) \tag{DH3SP3-8}$$

$$D_{hj} \leq BigM\, Y_{hj} \ (\forall h \in H, \forall j \in J) \tag{DH3SP3-9}$$

$$Y_{hj} \leq \sum_{n \in M_j} W_j^n \ (\forall h \in H, \forall j \in J) \tag{DH3SP3-10}$$

$$Z_{jk} \in \{0,1\} \quad (\forall j \in J, \forall k \in K) \tag{DH3SP3-11}$$

$$Y_{hj} \in \{0,1\} \quad (\forall j \in J, \forall h \in H) \tag{DH3SP3-12}$$

$$W_j^n \in \{0,1\} \quad (\forall j \in J, \forall n \in M_j) \tag{DH3SP3-13}$$

$$U_h^n \in \{0,1\} \quad (\forall h \in H, \forall n \in N_h) \tag{DH3SP3-14}$$

$$D_{hj} \geq 0 \ (\forall h \in H, \forall j \in J) \tag{DH3SP3-15}$$

Constraints

(DH3SP3-1)	Each TC should be assigned to only one opened RTC
(DH3SP3-2)	Each RTC can be assigned to only one capacity level

(DH3SP3-3)	Each RBC should be assigned to only one capacity level
(DH3SP3-4)	Capacity of any RTC is not exceeded
(DH3SP3-5)	Demand of any RTC is satisfied
(DH3SP3-6)	Each RTC can be assigned to only one opened RBC
(DH3SP3-7)	If an RTC is not opened, no products can be sent to that RTC
(DH3SP3-8)	Amount sent from an RBC to RTCs cannot exceed opened capacity level of that RBC (considering the disposal rate)
(DH3SP3-9)	If RTC *j* is not assigned to RBC *h*, no products can be sent from RBC *h* to RTC *j*
(DH3SP3-10)	If an RTC is not opened, it cannot be assigned to any RBC
(DH3SP3-11) to (DH3SP3-14)	Integrality constraints on the binary variables
(DH3SP3-15)	Non-negativity constraints on other decision variables

5.2.1.3.2.4. Model Formulation of DH3 Subproblem 4 (DH3SP4 - Routing Problem)

It is the same model as the “DH1SP3- Routing Problem” except that it uses the inputs from the solution of the problem “DH3SP3” instead of “DH1SP1”.

5.2.1.4. Decomposition Heuristic 4 (DH4)

5.2.1.4.1. Decomposition Approach and Decomposition Scheme

DH4 is a modified version of DH3, which applies an iterative solution approach. Therefore, subproblems used in DH4, their interactions, and the flowchart of DH4 are the same as DH3, except the first subproblem. DH4 uses “DH2SP1” as the first subproblem instead of “DH1SP1” which is used in DH3. In “DH1SP1”, neither DCs nor RBCs are considered while locating RTCs. In other words, only outbound transportations from RTCs are taken into account. In "DH2SP1", we deal with a location-allocation problem considering a supply chain structure including DCs, RTCs, and TCs.

Decomposition scheme of the DH4 is given in Figure 10.

5.2.2. Hybrid Heuristics

Heuristics presented in this section incorporate the decomposition approaches presented in DH1-DH4 and a new simulated annealing approach. We present 4 hybrid heuristics (HH) called HH1, HH2, HH3, and HH4 which are the modified versions of the previously presented decomposition heuristics called DH1, DH2, DH3, and DH4, respectively. For each of the Hybrid Heuristics, instead of solving vehicle routing subproblem optimally by using an optimization software package, we solve vehicle routing problem by using a new simulated annealing procedure presented below. Decomposition approaches and the other subproblems are the same as in the decomposition heuristics. After RTC Location-Allocation and RBC Location-Allocation subproblems are solved using the optimization software package, locations of RTCs and TC-RTC assignments obtained from the solutions of these subproblems are used as input for the simulated annealing procedure developed for solving the vehicle routing subproblem. Before starting the simulated annealing procedure, vehicle routes are constructed for each opened RTC by using a modified version of the nearest neighbor algorithm and used as an initial feasible solution. The parameters, main steps of the simulated annealing procedure, and routing moves to generate neighboring solutions are defined in the following sections.

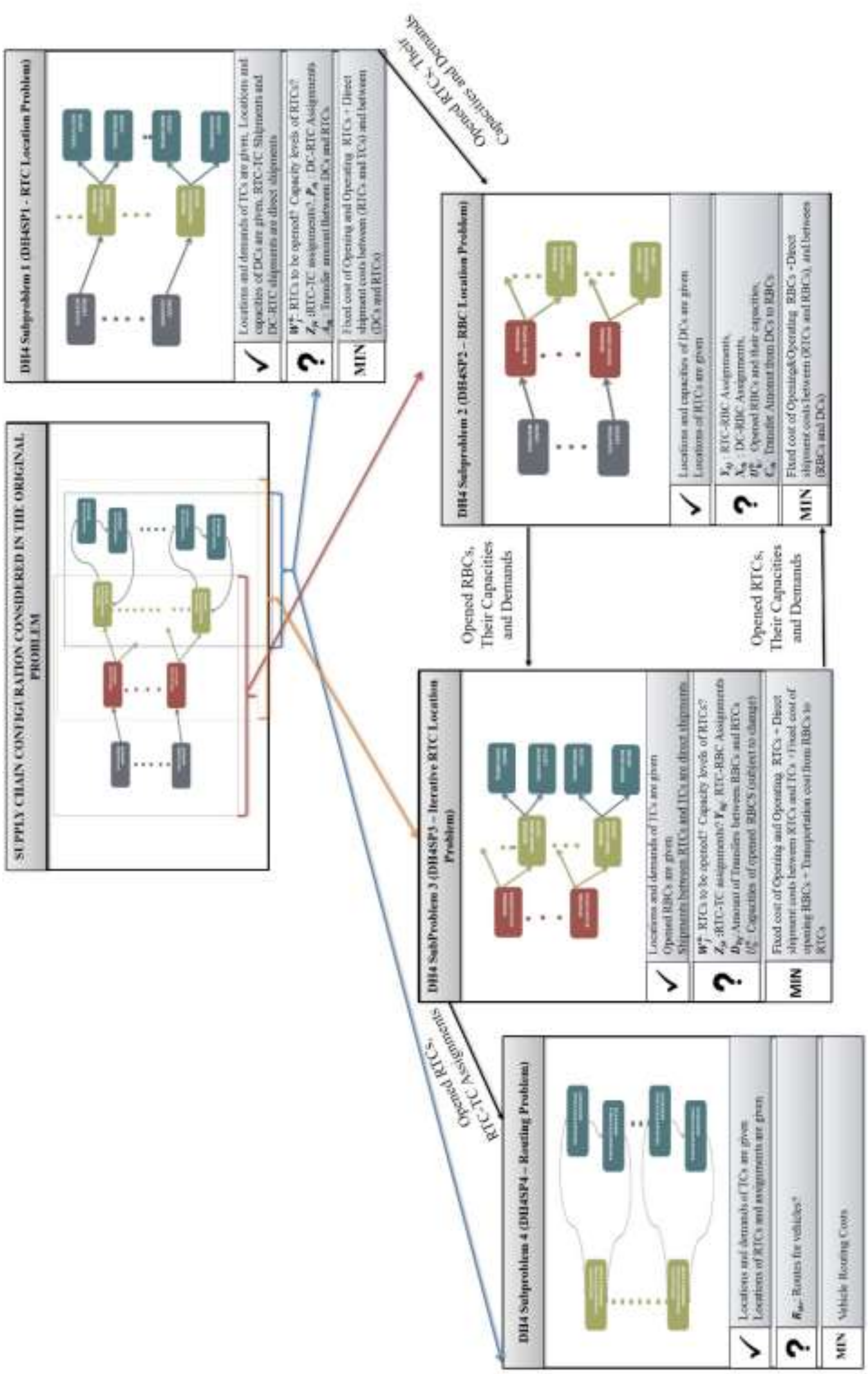


Figure 10. Decomposition Scheme of DH4

5.2.2.1. Constructing the Initial Feasible Solution

Using the locations of RTCs and TC-RTC assignments obtained from the solutions of the previously solved subproblems, the following main steps are applied for each opened RTC. In the following procedure, only TCs that are assigned to the RTC under consideration are used as candidates.

Step 1. Construct an empty Visited list

Step 2. Start with the RTC and find its nearest neighbor TC (tcnext) excluding TCs in the Visited list

Step 3. Add tcnext to Visited list

Step 4. From tcnext, find its nearest neighbor TC (tcnext1) excluding TCs in Visited list. If not found, go to Step 8

Step 5. From tcnext1, find its nearest neighbor TC (tcnext2). If not found, go to Step 7

Step 6. If RoutingCost(tcnext,tcnext1,tcnext2) <= Routing Cost(tcnext,RTC,tcnext2) and total demand of TCs in the route does not exceed the vehicle capacity, then, add tcnext1 to Visited list, set tcnext = tcnext1, and go to Step 3; otherwise add RTC to Visited list, and go to Step 2

Step 7. Add tcnext1 to Visited list

Step 8. Add RTC to Visited list and use Visited list as the vehicle route

5.2.2.2. Improvement Stage

At this stage, initial solution obtained by using the nearest neighbor algorithm is iteratively improved by modifying the vehicle routes. At each step, the heuristic considers a neighboring solution of the current solution, and probabilistically decides between moving to the neighboring solution and staying in the current solution. Procedure is repeated until either the target energy level or a given CPU time is reached.

Parameters of the simulated annealing procedure

T_0	: Starting temperature
T	: Current temperature
CR	: Cooling Rate
T_t	: Target Temperature
MI	: Maximum number of iterations at each temperature
NI	: Current iteration index $[1, MI]$.
X_0	: Initial solution obtained by the nearest neighbor algorithm
X	: Current solution
X_{nh}	: Neighboring solution of X in each iteration
X_b	: Best solution
$Cost(X)$	: Total Routing Costs (Objective function value of Vehicle Routing Subproblem) for solution X
$Dcost$	: Difference between objective function values of the neighboring solution and the current solution ($Dcost = Cost(X_{nh}) - Cost(X)$)
p	: Uniform random number between 0 and 1

Main steps of the simulated annealing procedure

Step 1. X_0 = initial solution obtained by the nearest neighbor algorithm, $X = X_0, X_b = X_0, T = T_0$

Step 2. $NI = 0$

Step 3. Randomly select one of the routing moves (probability of making reverse move, split or merge move is set to 0.50, 0.25 and 0.25, respectively), and apply it to X to generate X_{nh}. If X_{nh} is infeasible or move is not successful, repeat Step 3

Step 4. If $Dcost \leq 0$, then $X = X_{nh}$; otherwise go to Step 6

Step 5. If $Cost(X_{nh}) \leq Cost(X_b)$, then $X_b = X_{nh}$, otherwise go to Step 7

Step 6. Generate a p value, and calculate f value using the following formula: $f = e^{-(\frac{Dcost}{T})}$. If $p < f$, then $X = X_{nh}$

Step 7. $NI = NI + 1$

Step 8. If $NI > MI$, then go to Step 10; otherwise go to Step 3

Step 9. $T = CR\,T$

Step 10. If $T < T_t$, then stop, otherwise go to Step 2

Routing Moves used to generate neighboring solutions

- Split: Pick a random route and split it into two sub-routes from a randomly selected node (TC).
- Merge: Pick two routes at random and append the second to the first selected to form a single sub-route.
- Reverse: Pick a random route. Pick a random segment from the selected route (by random starting node and random route length). Reverse the order of nodes in the selected segment.

5.2.2.3. Obtaining a Feasible Solution to the Original Problem

In order to obtain a feasible solution to the original problem, the solutions obtained from the RTC Location-Allocation and RBC Location-Allocation subproblems and the solution obtained from the simulated annealing procedure are consolidated.

5.2.3. Simulated Annealing Heuristic for the Joint Location-Inventory-Routing Problem with Multiple Location Layers (SA)

The heuristic method consists of three stages:

1- Constructive stage: In this stage an initial solution is obtained randomly.
2- General improvement stage: The solution obtained at Stage 1 is iteratively improved by modifying the location, assignment, and routing decisions.
3- Best Solution Improvement Stage: The routing decisions of the best solution obtained at Stage 2 are improved iteratively.

In order to improve the current solution, we use a Simulated Annealing Heuristic combined with a Tabu list in order to prevent moves that generate the solutions previously visited. Main stages of the SA are demonstrated in Figure 11.

5.2.3.1. Constructive Stage

In the constructive stage, we first select capacity levels for each RTC at random, and then assign TCs to RTCs randomly. Based on TC-RTC assignments, we build vehicle routes using the nearest neighbor algorithm. Secondly, we randomly select capacity levels for RBCs, and assign the opened RTCs to RBCs. Finally DC-RBC assignments are decided randomly, and transfer amounts between DCs and RBCs are determined accordingly. After all assignments are determined, the solution is consolidated and cost of the initial feasible solution is calculated. Main steps followed to obtain the initial feasible solution are defined below:

TC-RTC Assignment

Step 1. Construct an empty set J'

Step 2. Put all the TCs into set K

Step 3. Randomly select a capacity level for each potential RTC, and set the selected capacity level of each RTC as its remaining capacity level

Step 4. Select a TC randomly

Step 5. Put all RTCs with their remaining capacity levels into set J

Step 6. Is J empty? If yes, select an RTC randomly from set J', increase its capacity level, re-compute its remaining capacity level, and put in into set J and go to step 7, if not, go to step 7

Step 7. Select an RTC randomly from set J and delete it from set J, put it into set J'

Step 8. If the demand of TC selected at step 4 is less than or equal to the remaining capacity level of RTC selected at Step 7, then assign the TC to the RTC, delete the TC from set K, update remaining capacity level of the RTC, and go to Step 9; otherwise go to Step 6

Step 9. Is K Empty? If yes, go to Step 10, if not go to Step 4

Step 10. Set the demand of each RTC to the total demand of TCs supplied by that RTC

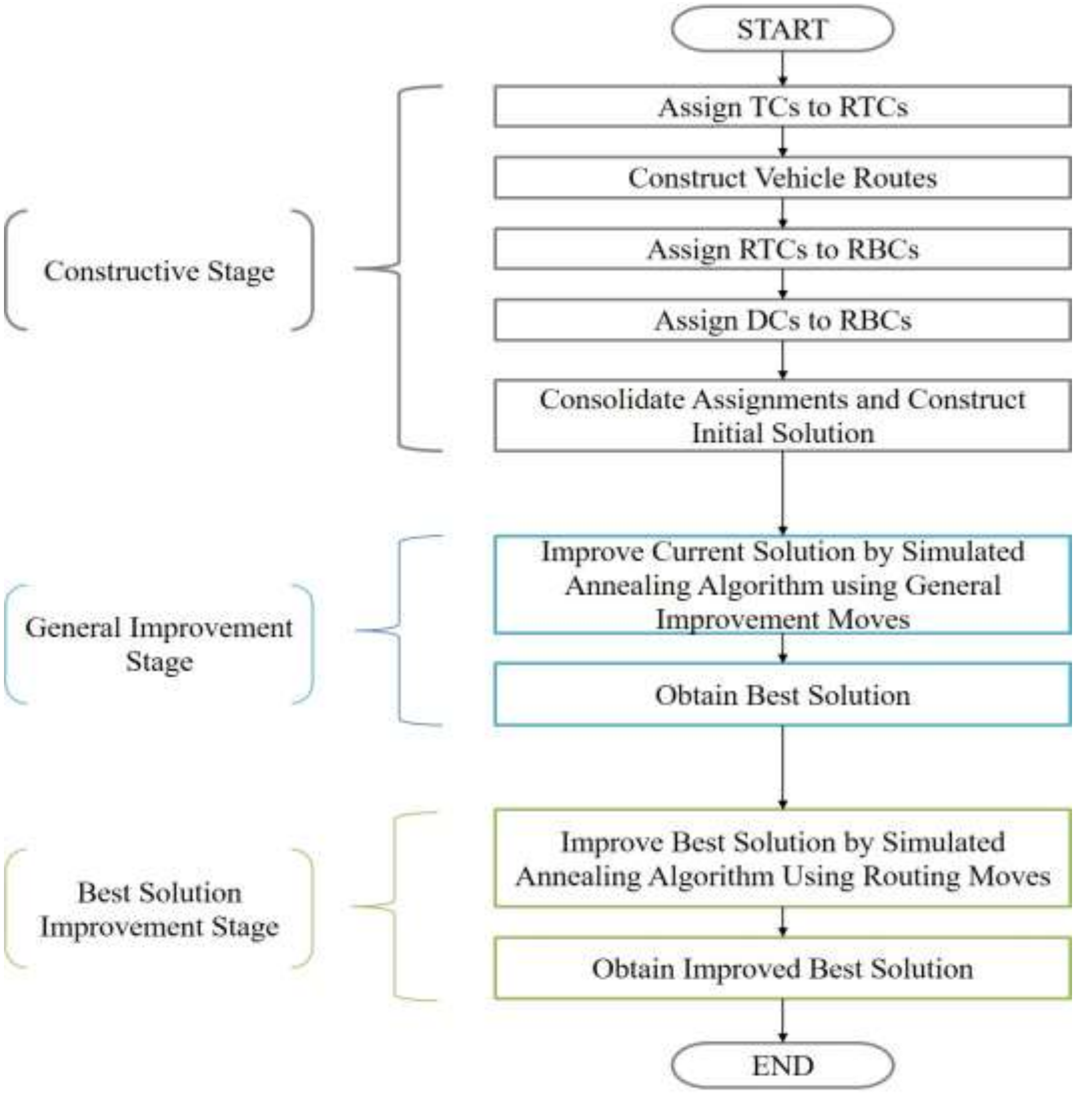


Figure 11. Stages of SA

Vehicle Routes

Step 11. Construct vehicle routes of the TCs for each opened TRC by using a modified version of the nearest neighbor algorithm (detailed steps are given in Section 5.2.2.1)

RTC-RBC Assignments

Step 12. Construct an empty set H'

Step 13. Empty set J

Step 14. Put all the opened RTCs (Result obtained from Step 1-10) into set J

Step 15. Randomly select a capacity level for each potential RBC, and set selected capacity level/blood disposal rate value of each RBC as its remaining capacity level

Step 16. Select an opened RTC randomly

Step 17. Put all RBCs with the remaining capacity levels into set H

Step 18. Is H empty? If yes, select an RBC randomly from set H', increase its capacity level, re-compute its remaining capacity level, and put in into set H, and go to step 19; if not, go to step 19

Step 19. Select an RBC randomly from set H, and delete it from set H, put it into set H'

Step 20. If the demand of RTC selected at step 16 is less than or equal to the remaining capacity level of RBC selected at Step 19, then assign the RTC to the RBC, delete the RTC from set J, update remaining capacity level of the RBC, and go to Step 21; otherwise go to Step 18

Step 21. Is J Empty? If yes, go to Step 22; if not, go to Step 16

Step 22. Demand of each RBC = Blood disposal rate * total demand of RTCs supplied by that RBC

DC-RBC Assignments

Step 23. Empty set H'

Step 24. Empty set H

Step 25. Put all the opened RBCs (Result obtained from Step 12-22) into set H

Step 26. Put all DCs into set T

Step 27. Select an RBC randomly from set H

Step 28. Randomly select a DC from set T

Step 29. Assign DC selected at step 28 to RBC selected at Step 27, and delete the DC from set T

Step 30. Transfer amount between DC and RBC = min {capacity level of DC, (remaining demand of RBC – capacity level of DC)}

Step 31. Update the remaining demand of RBC using transfer amount between DC and RBC

Step 32. If the remaining demand of RBC is equal to zero, then put RBC into set H' and go to 33, otherwise go to step 28

Step 33. Is H Empty? If yes, go to Step 34; if not, go to Step 27

Step 34. Is T Empty? If yes, go to 35; if not, select an RBC from H', and assign remaining DCs to that RBC, and transfer amount of remaining DCs to zero

Step 35. Calculate the total cost of the initial solution

5.2.3.2. General Improvement Stage

At this stage, initial solution obtained at the constructive stage is iteratively improved by modifying TC-RTC, RTC-RBC, DC-RBC assignments, vehicle routes, locations and capacity levels of RBCs and RTCs, transfer amounts between DCs and RBCs. At each step, the heuristic considers some neighboring solution of the current solution, and probabilistically decides between moving to the neighboring solution and staying in the current solution. These probabilities ultimately lead the heuristic to move to solutions of lower energy. This step is repeated until either the target energy level or a given CPU time is reached. After stopping condition is met, best solution obtained at the general improvement stage is used as an input for the best solution improvement stage. The parameters and the main steps of the simulated annealing procedure, and moves used at the general improvement stage to generate neighboring solutions are as follows:

<u>Parameters of the simulated annealing procedure</u>

T_0 : Starting temperature

T : Current temperature

CR : Cooling Rate

T_t : Target Temperature

MI : Maximum number of iterations at each temperature

NI : Current iteration index [1, *MI*]

X_0 : Initial solution

X : Current solution

X_{nh} : Neighboring solution of X at each iteration

X_b : Best solution

$Cost(X)$: Total Cost (Objective function value) for solution X

$Dcost$: Difference between objective function values of the neighboring solution and the current solution ($Dcost = Cost(X_{nh}) - Cost(X)$)

p : Uniform random number between 0 and 1

<u>Main steps of the simulated annealing procedure</u>

Step 1. X_0 = initial solution found at the construction stage, $X = X_0, X_b = X_0, T = T_0$

Step 2. $NI = 0$

Step 3. Randomly select one of the general improvement moves, and apply it to X to generate X_{nh}. If X_{nh} is infeasible or move is not successful, repeat Step 3

Step 4. Is the obtained neighboring solution (X_{nh}) in the tabu list? If yes, go to Step 5; otherwise, go to Step 6

Step 5. If $Cost(X_{nh}) \leq Cost(X_b)$, then $X = X_{nh}$, $X_b = X_{nh}$, and go to Step 10; otherwise, go to Step 3

Step 6. Add X_{nh} to tabu list

Step 7. If $Dcost \leq 0$, then $X = X_{nh}$; otherwise go to Step 9

Step 8. If $Cost(X_{nh}) \leq Cost(X)$, then $X_b = X_{nh}$, otherwise go to Step 10

Step 9. Generate a p value, and calculate f value using the following formula: $f = e^{-(\frac{Dcost}{T})}$. If $p < f$, then $X = X_{nh}$

Step 10. $NI = NI + 1$

Step 11. If $NI > MI$, then go to Step 12; otherwise go to Step 3

Step 12. $T = CR$ T

Step 13. If $T < T_t$, then stop, otherwise go to Step 2

Moves used at the general improvement stage

- OpenRTC: Pick an unopened RTC, open it, and assign a random capacity level to the RTC. Randomly pick TCs that are previously assigned to other RTCs, and reassign them to the new RTC until it can supply the demand. Re-compute capacities of the old RTCs, if there are no TCs assigned to any of the previously opened RTCs, then close it. Re-compute vehicle routes according to the new TC-RTC assignments. Re-compute RTC-RBC and RBC-DC assignments.
- CloseRTC: Pick an opened RTC and close it. Distribute its TCs to other opened RTCs, and increase capacity levels as needed. Re-compute vehicle routes according to the new TC-RTC assignments. Re-compute RTC-RBC and RBC-DC assignments.
- ExchangeRTC: Pick two random opened RBCs, and swap their RTCs and DCs. Re-compute RBC Capacity Levels.
- CloseOpenRTC: Close one RTC at random. Open one RTC randomly, and transfer TCs and RBC from closed RTC to the new RTC. Re-compute vehicle routes according to the new TC-RTC assignments. Re-compute RTC-RBC and RBC-DC assignments.
- CloseOpenRBC: Close one RBC at random. Open one RBC randomly, and transfer RTCs and DCs from the closed RBC to the new RBC.
- ExchangeTCs: Pick two opened RTCs randomly and exchange their TCs. Re-compute vehicle routes according to the new TC-RTC assignments. Re-compute RTC-RBC and RBC-DC assignments.
- ExchangeTCsPartially: Pick two opened RTCs randomly. Randomly pick one TC for each and exchange. Re-compute vehicle routes according to the new TC-RTC assignments. Re-compute RTC-RBC and RBC-DC assignments.

- OptimizeByDistanceDCs: Given RBCs and their demands, assign each DC to the RBC with the lowest travel cost. If the DC cannot be assigned to the lowest travel cost, try the next lowest.

5.2.3.3. Best Solution Improvement Stage

Best solution obtained at the general improvement stage is used as an input for this stage, and it is improved by modifying the vehicle routing decisions using different moves. The parameters, the main steps of the simulated annealing procedure, and moves used at the best improvement stage to generate the neighboring solutions are the same as the ones presented in Section 5.2.2.2. The only difference is that the procedure in SA uses the solution obtained at the general improvement stage instead of the solution obtained throughout the nearest neighbor procedure presented in the hybrid heuristics for constructing the initial feasible solution.

CHAPTER 6

IMPLEMENTATION OF THE SOLUTION APPROACHES

In this chapter, we present the computer implementation of the solution approaches proposed in our study, and discuss the verification and validation of the models and computer codes of the solution approaches.

6.1. Implementation of the Optimal Solution Method

We implemented optimal solution methods using GAMS (The General Algebraic Modeling System) software and prepared GAMS code of the original model. We are dealing with a relatively large model, and in our computational studies, we work with various problem instances of several sizes. Therefore, it makes sense to split the GAMS code into different files in order not to have difficulties while defining the input parameters and reporting the results. In our modelling approach, we have separate files for model algebra, input and output data. In other words, we use MS Excel for data import and export. GAMS model reads model inputs from Excel sheets and again exports the results to another excel file. Figure 12 shows all these processes of the modelling approach.

6.1.1. Input Files

GAMS model reads both the sets and the parameters used in the model from different Excel files. The file called “Gsets.xlsx” includes the sets definition. The sets defined in this file are as follows:

- Set of Transfusion Centers (TCs)

- Set of potential Regional Transfusion Centers (RTCs)
- Superset of TCs and RTCs
- Set of potential Regional Blood Centers (RBCs)
- Set of Donation Centers (DCs)
- Set of capacity levels for RTCs
- Set of capacity levels for RBCs
- Set of vehicles

A sample Gsets.xlsx file is shown in Figure 13.

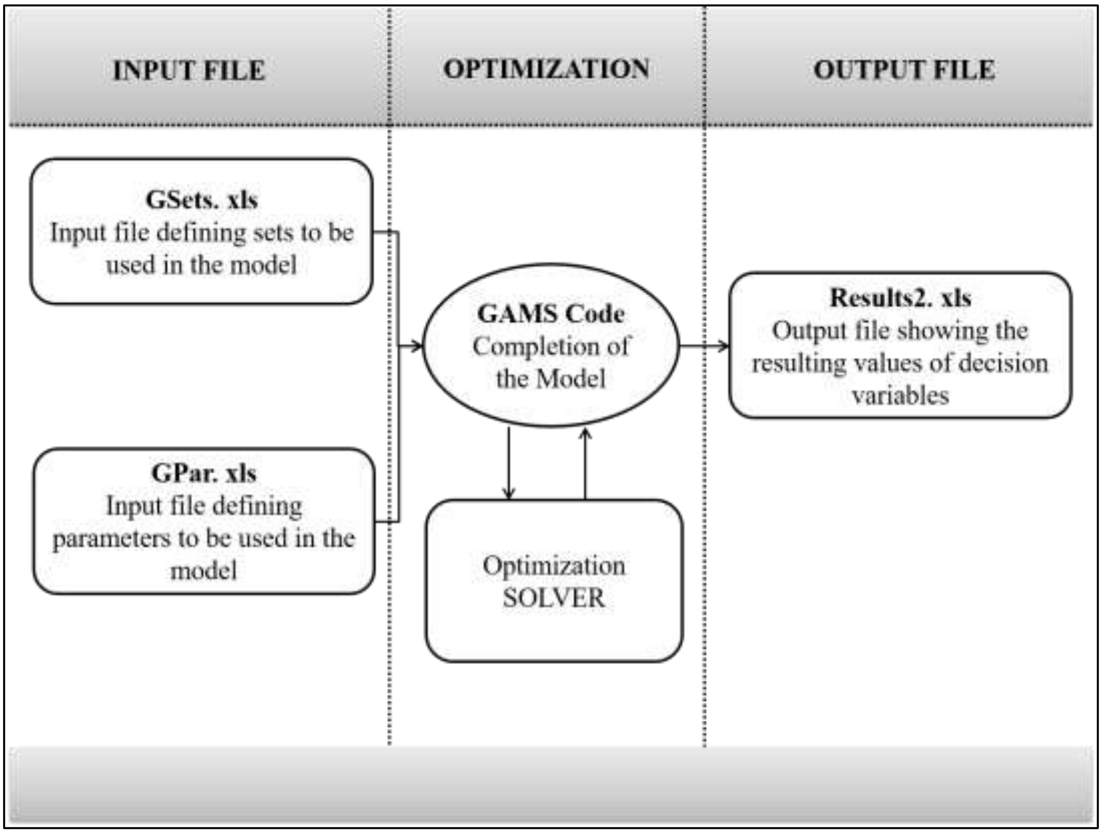


Figure 12. Structure of the GAMS Model

As similar to the set definitions, GAMS model reads parameters used in the model from the file called “Gpar.xlsx”. Parameters defined in this file are as follows:

- Mean annual demand at TCs
- Variance of annual demand at TCs
- Capacities for DCs
- Annual inventory holding cost per unit of blood at RTC*s*
- Fixed cost of placing an order to RBCs by RTCs
- Fixed annual costs of opening and operating RTCs for different capacity levels
- Fixed annual costs of opening and operating RBCs for different capacity levels
- Maximum capacities for different capacity levels for RTCs
- Maximum capacities for different capacity levels for RBCs
- Transportation costs between TCs and RTCs, and among TCs
- Weighted distances between DCs and RBCs
- Weighted distances between RBCs and RTCs

Samples of GPar.xlsx file are shown in Figures 14 and 15.

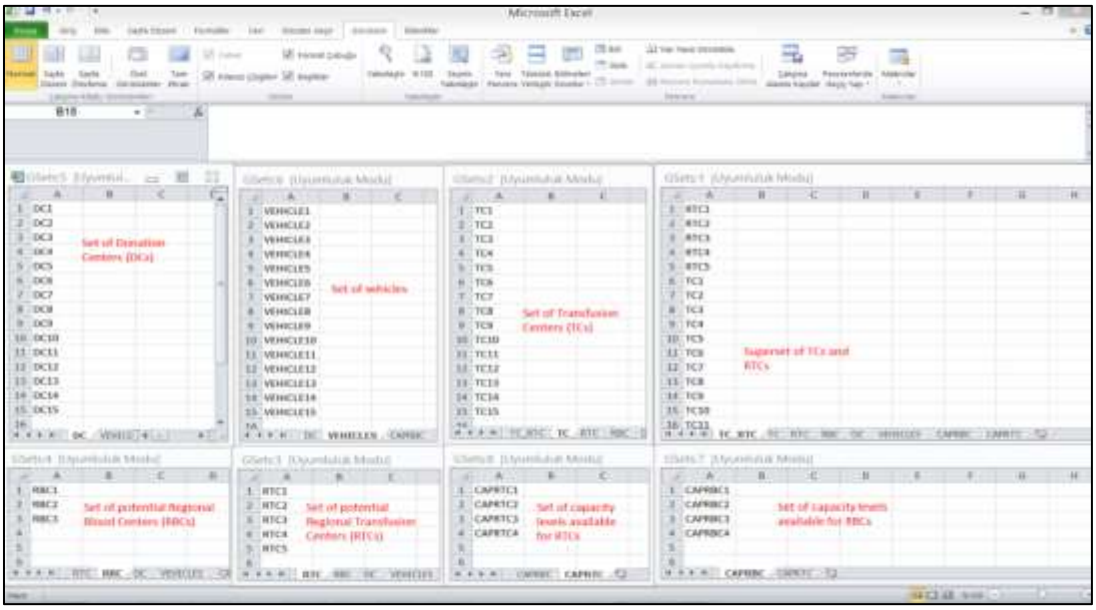


Figure 13. Excel sheets of a sample GSets.xlsx file

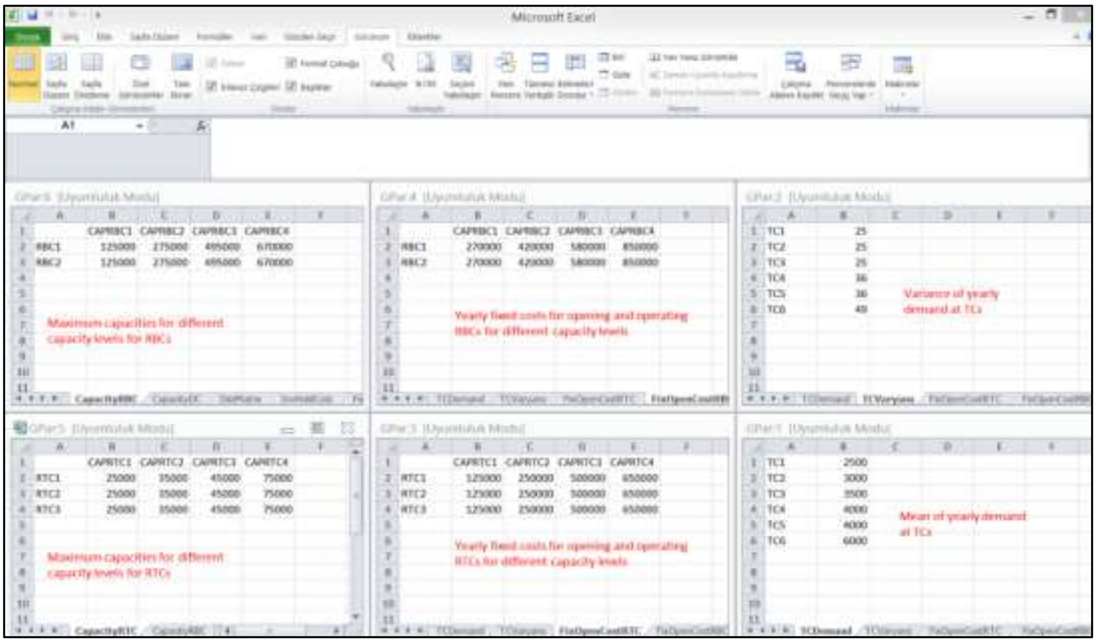


Figure 14. Excel sheets of a sample GPar.xlsx file – Part I

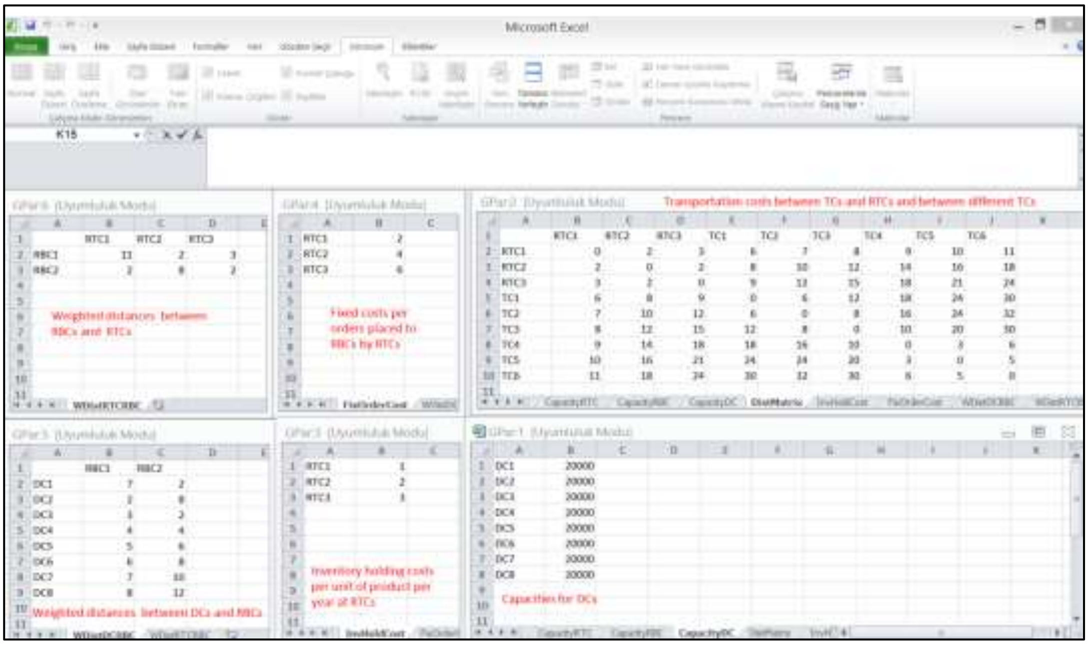


Figure 15. Excel sheets of a sample GPar.xlsx file – Part II

6.1.2. GAMS Code

The model is coded using GAMS V23.5.1. The scalars in the model are not to be changed frequently for different problem instances. Therefore, instead of reading from a separate Excel file, the scalars are included in the code, and defined in the GAMS code as follows:

- Blood disposal rate at RBCs
- Big number (or highest capacity level associated with the facility type)
- Lead time (in years) of RTCs
- Annual number of visits of each vehicle
- α-percentile of standard normal distribution
- Annual delivery capacity of a vehicle

6.1.3. Output File

Results of the model are exported to an Excel file. The file called “Results2.xlsx” includes the following information:

- Total cost
- Vehicle routes
- TC-RTC Assignments
- RTC-RBC Assignments
- DC- RBC Assignments
- Opened RBCs and their capacity levels
- Opened RTCs and their capacity levels
- Amounts sent from DCs to RBCs
- Amount sent from RBCs to RTCs
- CPU Time and Summary Tables

A sample Results2.xlsx file is shown in Figure 16.

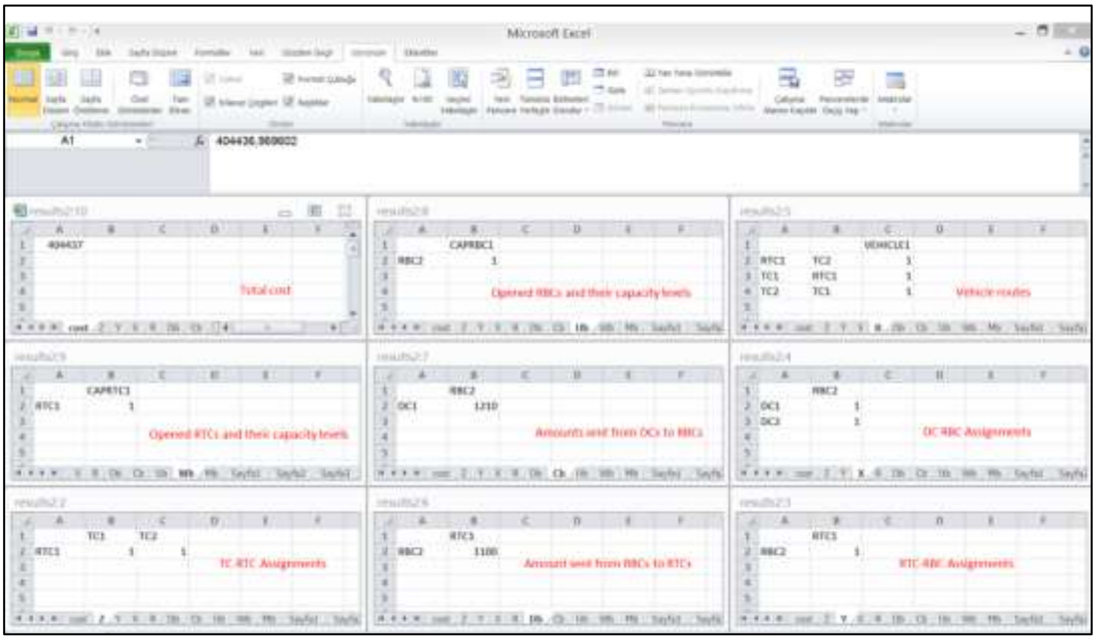


Figure 16. Excel sheets of a sample Results2.xlsx file

6.2. Implementation of the Decomposition Heuristics

6.2.1. Preparation of the GAMS Codes for DH1 and DH2

For DH1 and DH2, we deal with 3 subproblems which should be solved sequentially in one run. After solutions are completed, the results of the subproblems should be consolidated to obtain a feasible solution to the original problem. Hence, we prepare a separate GAMS model for each subproblem and prepare another GAMS file (called "Start Solution"), allowing us to call different GAMS models (corresponding to each subproblem) sequentially to consolidate the results obtained from different GAMS models. Once the "Start Solution" file is run, it calls the GAMS models prepared for each subproblem with the defined sequence in the file, and then it calls the GAMS Model of the Original Problem (A modified version of the model described in Section 6.1 to allow for importing the values of the decision variables in a consolidated manner from the output files of the subproblems). The modified version of the GAMS Model representing the original problem imports the consolidated solution of the Decomposition Heuristic, checks the feasibility, and then calculates the values of the objective function terms and the total cost. The model can also accept this solution as an initial feasible solution and continue to solve the problem according to the determined solver parameters, if its configuration is set to do so. Thus, all subproblems and main problems are solved in only a single run.

In the intermediate steps of the solution approach, outputs of the previously solved models should be imported as an input to the following one, and also the detailed results and CPU times of the subproblems should be recorded for reporting and verification purposes. Therefore, some supporting files are used to manage these processes. The files are listed below:

- GDX Files: gdx is a common file format of GAMS program to import and export data. Gdx files listed below are used to import the results of subproblems to the modified version of the GAMS model representing the original problem. Imported data are used to consolidate the results of the subproblems, and to check the feasibility of the solution.
    - ResultsRTC.gdx: Records the results of Subproblem 1
    - ResultRBC.gdx: Records the results of Subproblem 2
    - ResultsRouting.gdx: Records the results of Subproblem 3
- Excel Files: Input files (GSets.xlsx and GPar.xlsx) are the prepared ones; the same files are used by all GAMS models and the heuristics presented in this report. ResultsIN.xlsx and Results2.xlsx files are also common, and they are updated by GAMS models throughout the procedures when necessary.
    - GSets.xlsx: Includes sets definitions described in Section 6.1.1.
    - GPar.xlsx: Includes the parameters used in the model. This is a modified version of the Gsets.xlsx file described in Section 6.1.1. The modified version also allows to import and export data between the subproblems. The detailed information about the results of subproblems is also stored in this file for reporting and verification purposes.

- Results2.xlsx: Includes the results of the modified GAMS Model representing the original problem. This is a modified version of the output file described in Section 6.1.1. The modified version also includes the values of the objective function terms, the total cost calculated at the end of the solution procedure, and CPU time used in a single run of the model.
- ResultsIN.xlsx: Records the decisions obtained after solving the subproblems and CPU time information of each GAMS run. It allows to import and export data between subproblems. It also includes summary tables showing the values of the objective function terms and the total cost calculated at the end of the heuristic solution procedure. Samples of ResulsIN.xlsx files are shown in Figures 17, 18, 19, and 20.

Interaction between different GAMS models and supporting files in a single run is schematized in Figure 21**.** While preparing the templates of supporting files, special effort is given to develop appropriate common formats which allow for using the same file format during the execution of a DH1 and DH2. Therefore, the main process defined in Figure 21 and the descriptions given in this subsection are valid for both DH1 and DH2. However, GAMS codes of the subproblems differ from DH1 to DH2, especially for subproblem 1 (other subproblems only have minor differences in terms of the imported data).

6.2.1. Preparation of the GAMS Code for the DH3 and DH4

For DH3 and DH4, we are dealing with 4 subproblems which should be solved according to a pre-determined sequence in one run, and within this sequence, two of them should be solved iteratively until a stopping criterion is satisfied. While preparing GAMS codes for DH3 and DH4, we use a similar logic with the one applied for DH1 and DH2. In this respect, we prepare a separate GAMS code for the additional subproblem which we call Iterative RTC Location Problem. In addition to that, we modify the “Start Solution” file which determines the solution sequence of the subproblems.

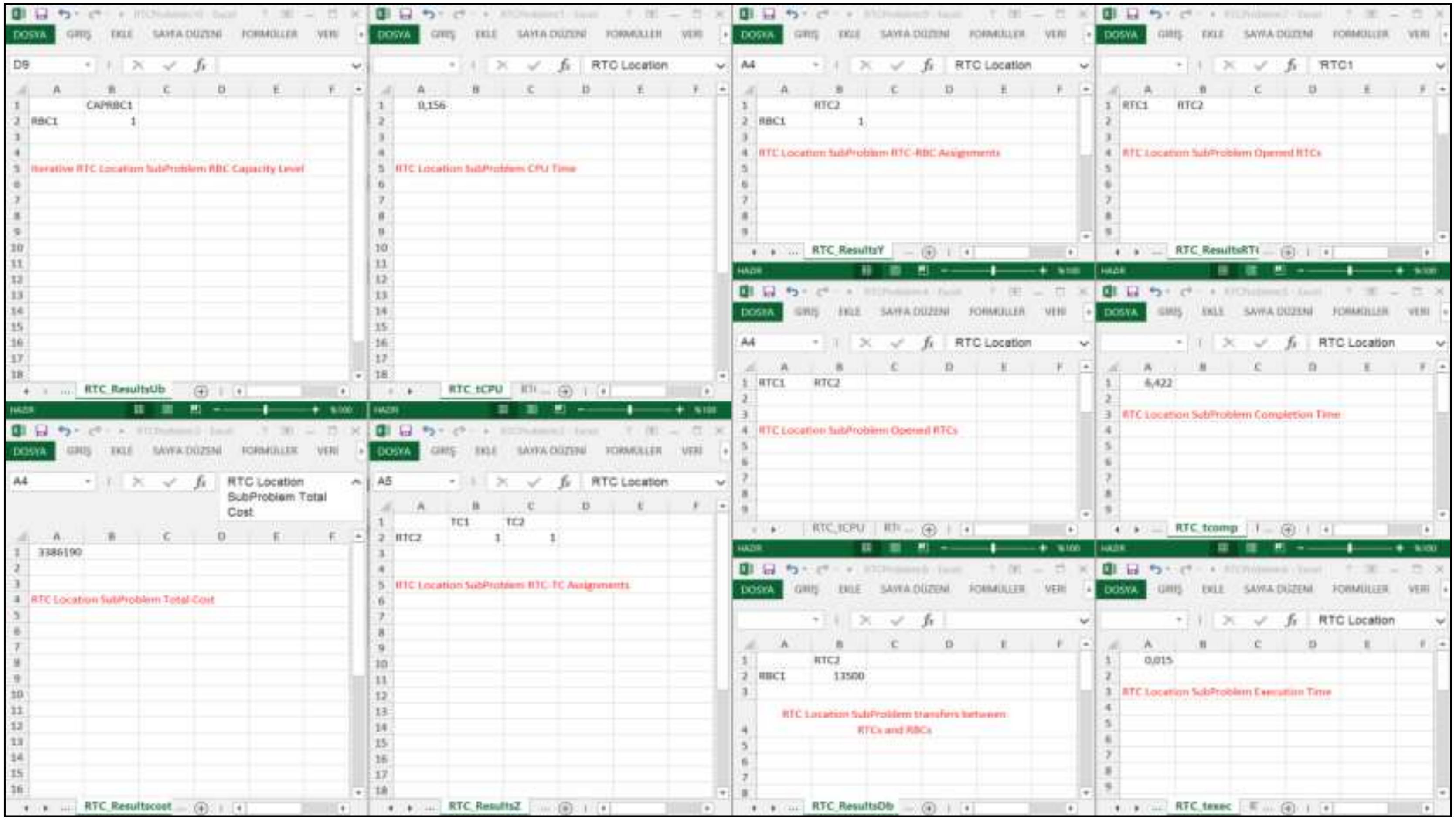


Figure 17. Excel sheets of a sample ResultsIN.xlsx file (RTC Location Subproblem)

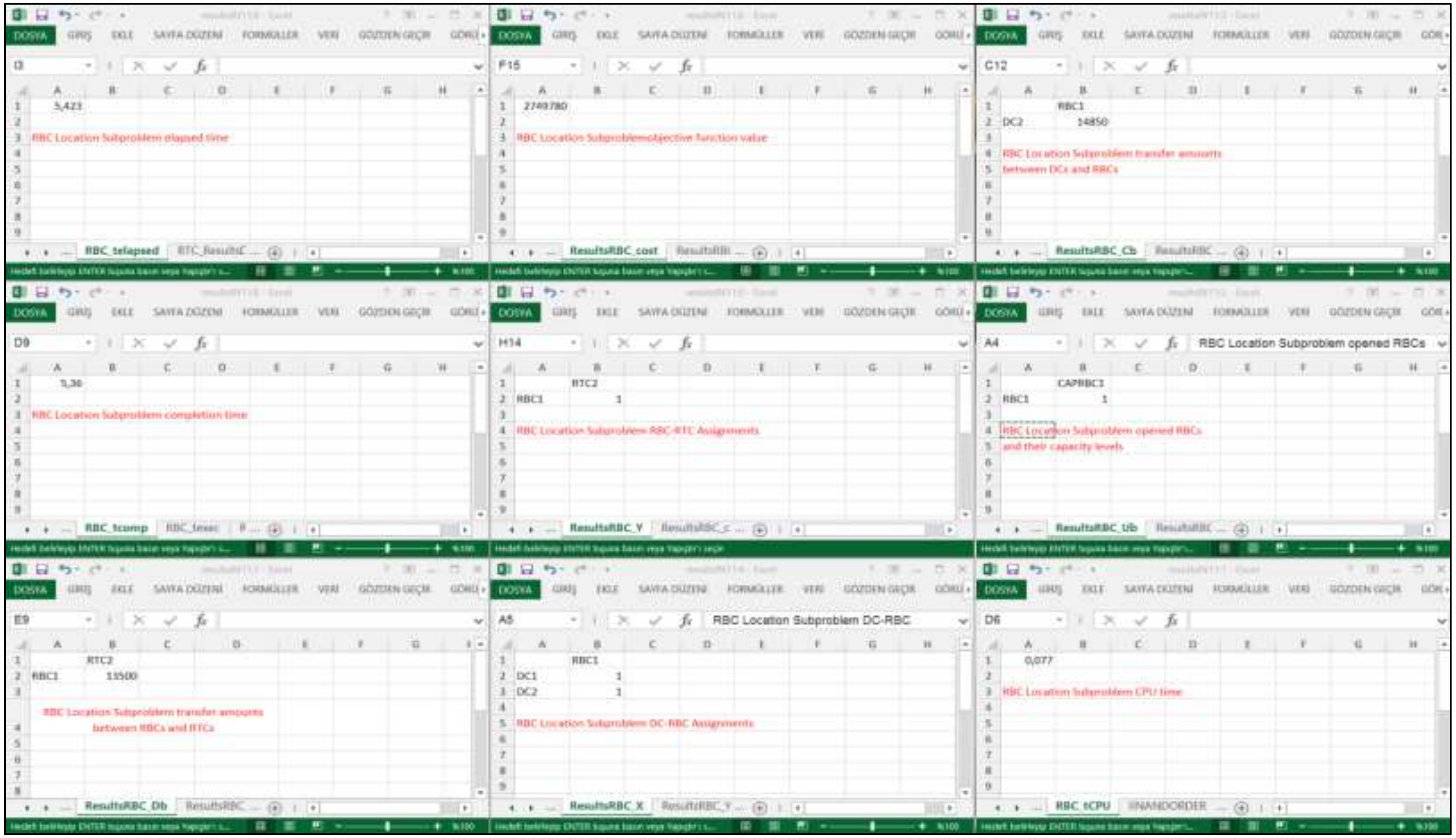


Figure 18. Excel sheets of a sample ResultsIN.xlsx file (RBC Location Subproblem)

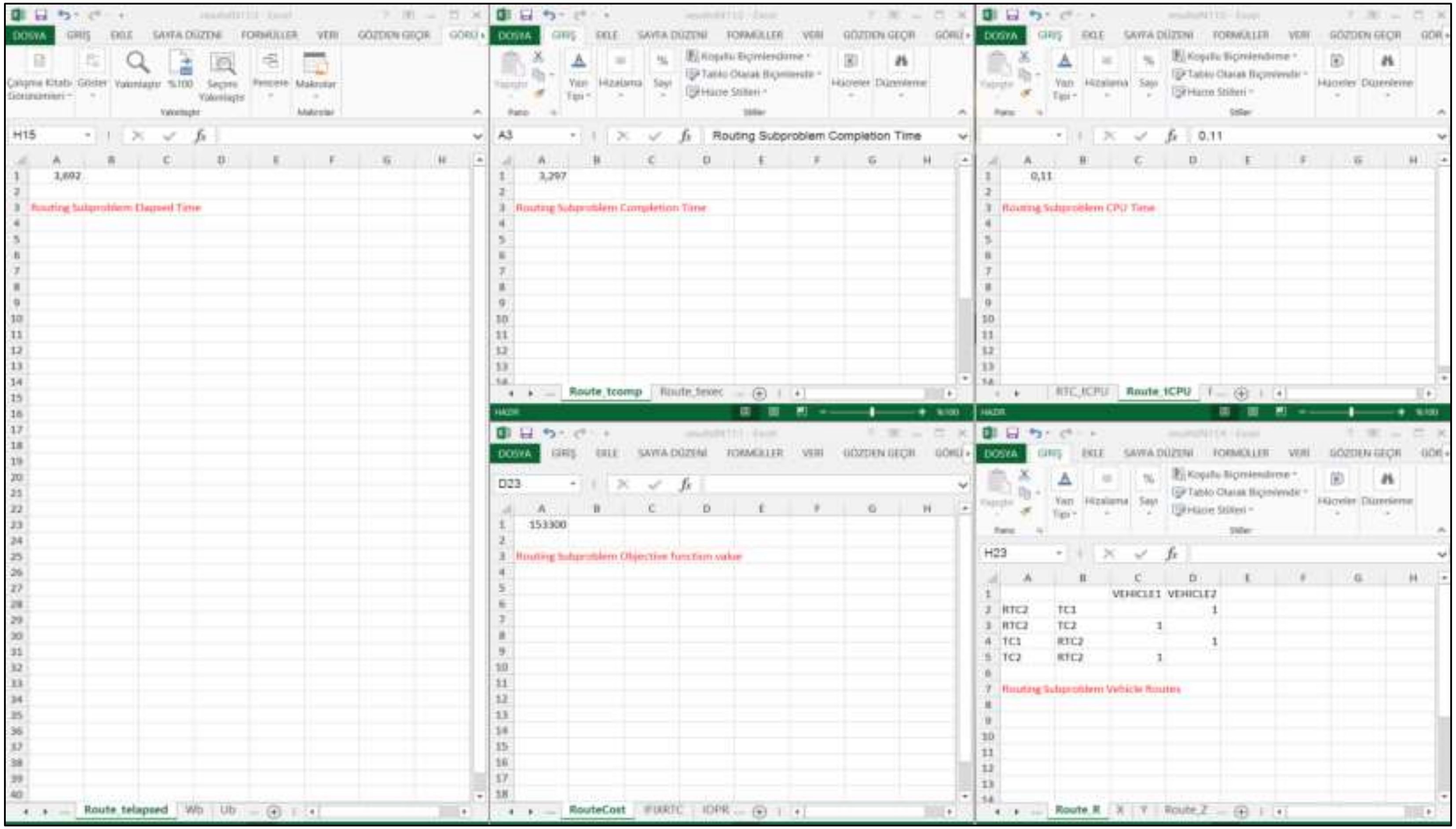


Figure 19. Excel sheets of a sample ResultsIN.xlsx file (Routing Subproblem)

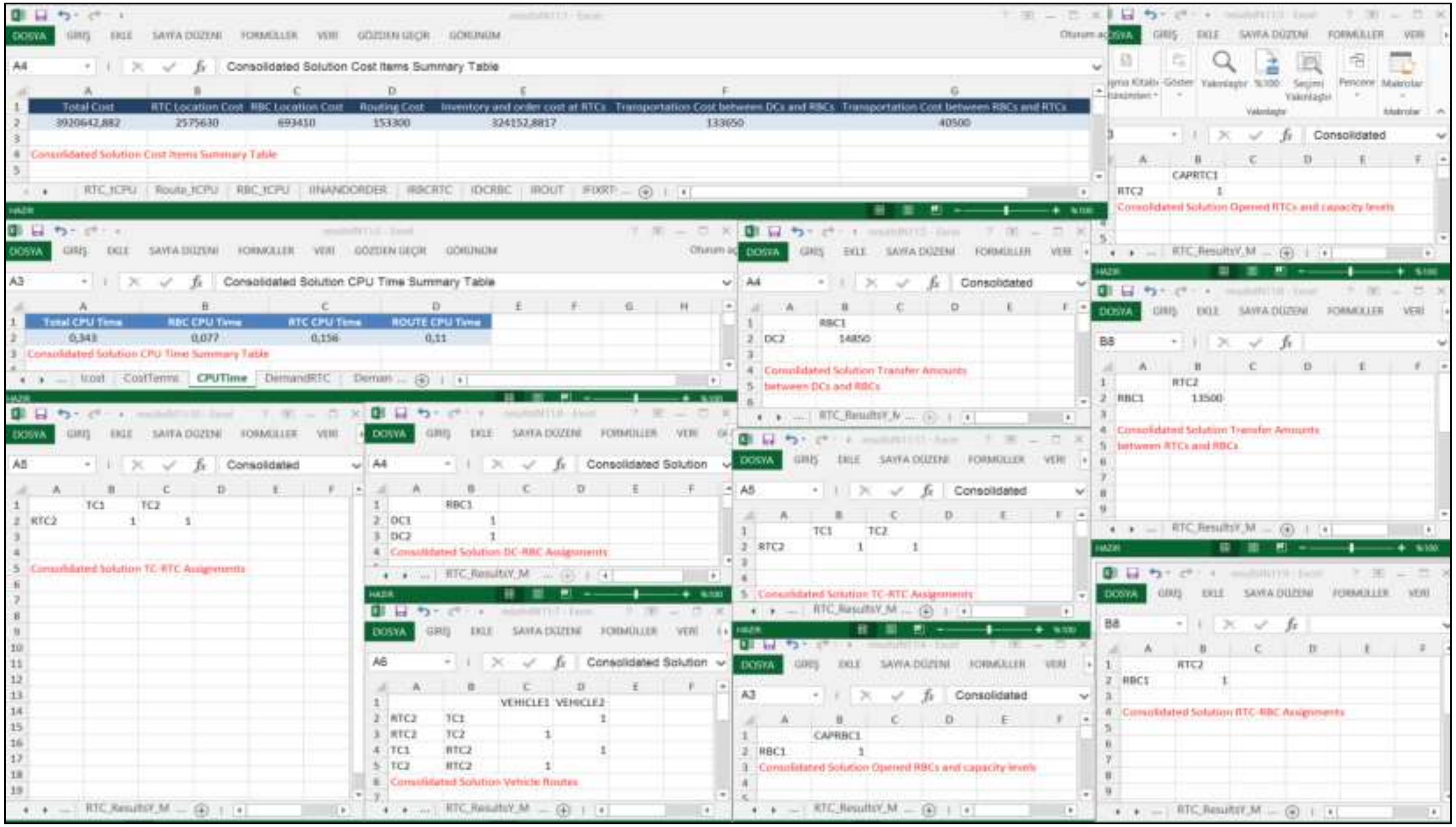


Figure 20. Excel sheets of a sample ResultsIN.xlsx file (Consolidated Solution)

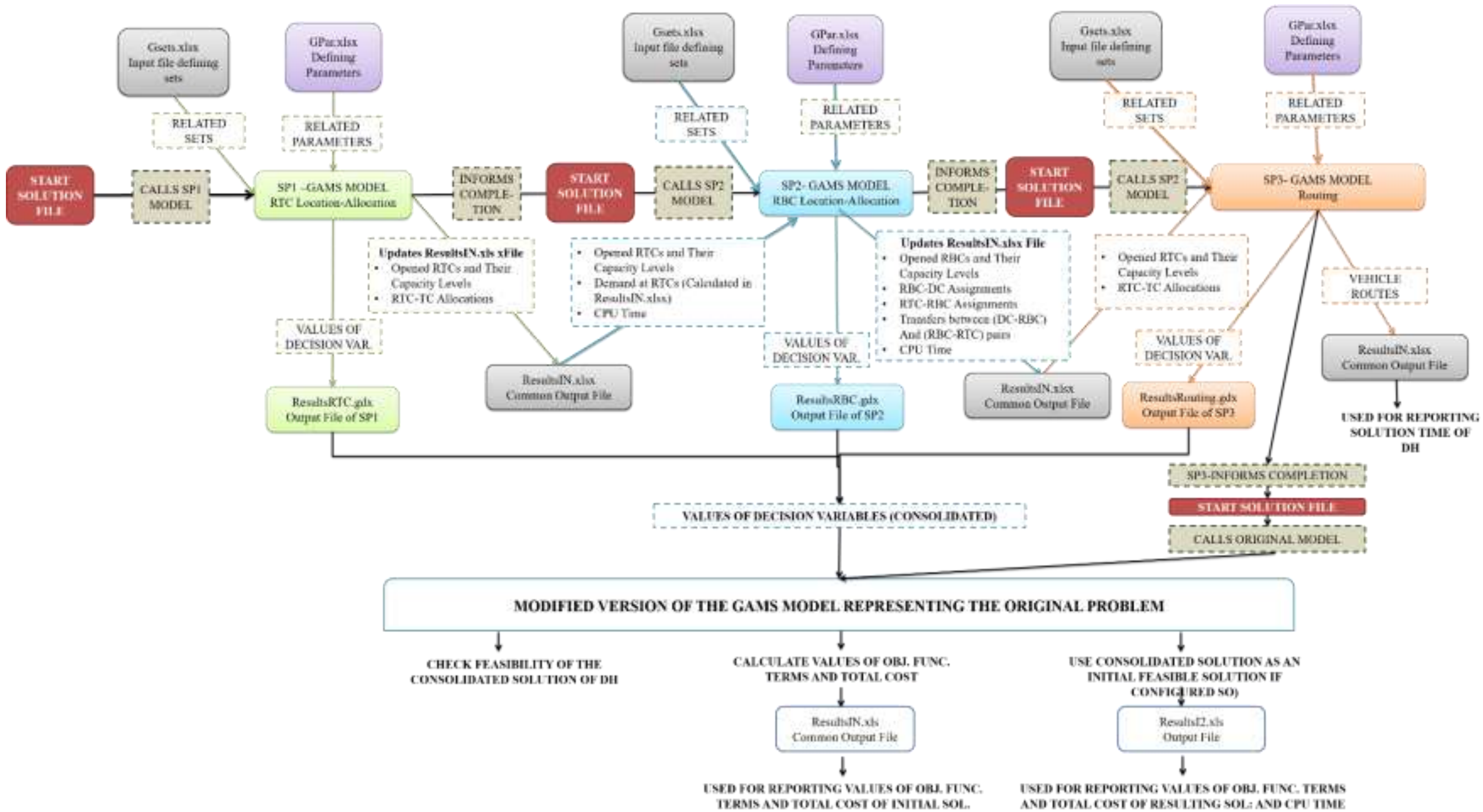


Figure 21. Interaction between Different GAMS Models and Supporting Files (DH1 and DH2)

“Start Solution” file used for DH3 and DH4 first calls SP1, SP2 (using the solution of SP1 as input), SP3 (using the solution of SP2 as input), respectively. After SP3 is solved, it calls again SP2, but this time using the solution of SP3 as input. Then it checks whether two consecutive solutions of SP2 are the same. If the values obtained from those solutions are different, then it calls SP3 (using the solution obtained from the last run of SP3 as input) and SP2 (using the solution obtained from the last run of SP3 as input) again, until the same solution is obtained or SP2 is solved 5 times in a single run. When one of the stopping criteria is satisfied, “Start Solution” file calls SP4 and the modified version of the GAMS Model representing the original problem. The rest of the procedure is the same as the ones applied in DH1 and DH2.

Interaction between different GAMS models and supporting files in a single run is schematized in Figure 22.

6.3. Implementation of the Hybrid Heuristics

GAMS codes used in implementation of the hybrid heuristics for solving RTC Location-Allocation and RBC Location-Allocation subproblems are the same as the corresponding decomposition heuristic. However, the method used to solve vehicle routing subproblem differs. Therefore “Start Solution” file is modified so as to stop the GAMS run before solving the vehicle routing subproblem and producing the consolidated solution. Instead of solving vehicle routing subproblem using GAMS model, the ResultsIN.xlsx file generated from the solutions of RBC and RTC Location-Allocation models are used as an input for the Simulated Annealing Application Tool which applies the simulated annealing procedure presented in Section 5.2.2. This tool also uses Gpar.xlsx and GSets.xlsx files as input files. After solving the vehicle routing subproblem, the solutions of all subproblems are consolidated, and the values of decision variables, objective function cost terms and CPU time information are reported by the Simulated Annealing Application Tool developed for the implementation of the hybrid heuristics, instead of the using the modified GAMS code representing the original problem. Simulated Annealing Application Tool has the capability to solve more than one problem instance in a single run. Therefore it includes two different output file format:

- Summary.xlsx: Gives a summary of all problem instances solved in a single run. It includes problem identification information (problem number, number of potential RTCs, number of potential RBCs, number of available vehicles, etc.), the resulting values of the objective function terms, and CPU time. A sample of Summary.xlsx file is shown in Figure 23.
- Details.txt: Gives the resulting values of decision variables and basic statistics about the solution process of a single problem instance. This file is generated for all problem instances solved in a single run separately. A sample of Details.txt file is shown in Figure 24.

Interaction between different GAMS models, Simulated Annealing Application Tool and supporting files in a single run is schematized in Figure 25**.** The principles used during the design and coding of the Simulated Annealing Application Tool are explained in Section 6.4**,** as the functions of the Simulated Annealing Application Tool used in the implementation of the hybrid heuristics demonstrate only a small part of its capabilities.

6.4. Implementation of the Simulated Annealing Heuristic

Simulated Annealing Application Tool is written using Visual Studio 2015 with C# (C Sharp) programming language. Graphical User Interface is developed using Microsoft WinForms framework. Open source Excel add-in is used for reading parameter files. The Simulated Annealing Application Tool reads problem parameters and sets from GPar.xlsx and GSets.xlsx files. After the solution procedure is applied, results are written in output files called Summary.xlsx and Details.txt. The main information flow is schematized in Figure 26.

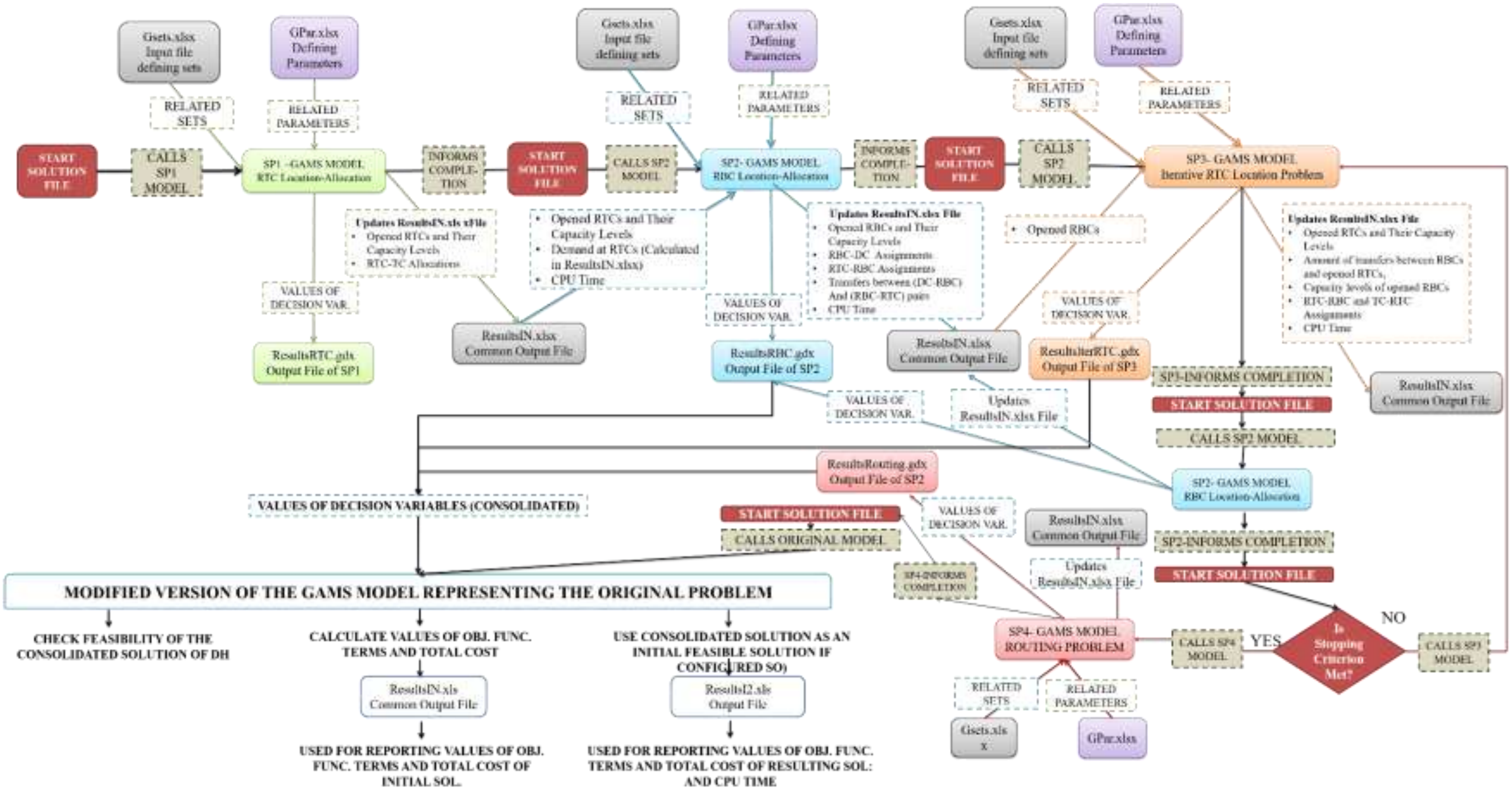
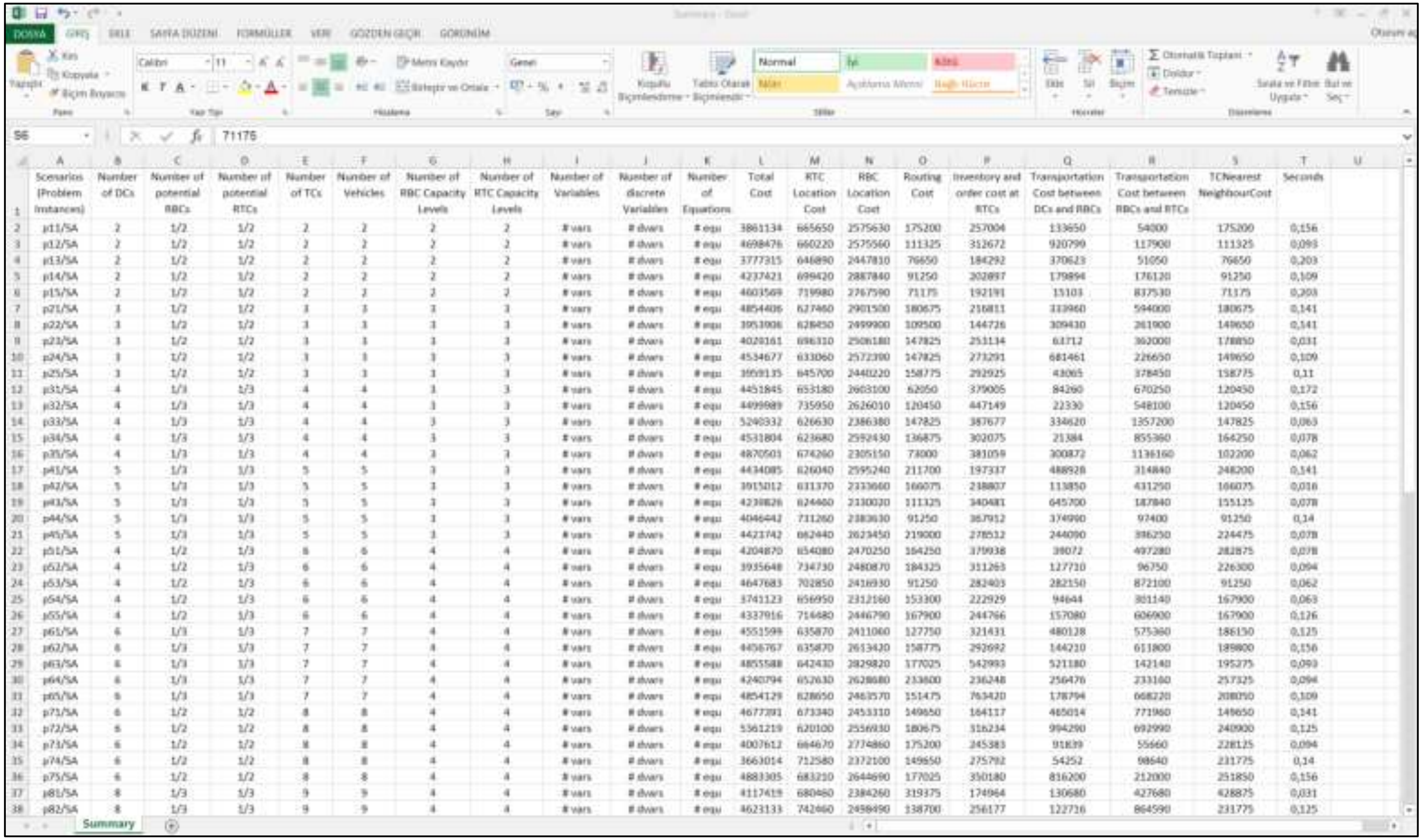


Figure 22. Interaction between Different GAMS Models and Supporting Files (DH3 and DH4)



Scenarios (Problem Instances)	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels	Number of Variables	Number of discrete Variables	Number of Equations	Total Cost	RTC Location Cost	RBC Location Cost	Routing Cost	Inventory and order cost at RTCs	Transportation Cost between DCs and RBCs	Transportation Cost between RBCs and RTCs	TCNearest NeighbourCost	Seconds
p11/SA	2	1/2	1/2	2	2	2	2	# vars	# dvars	# equ	3861134	665650	2575630	175200	257004	133650	54000	175200	0,156
p12/SA	2	1/2	1/2	2	2	2	2	# vars	# dvars	# equ	4698476	660220	2575560	111325	312672	920799	117900	111325	0,093
p13/SA	2	1/2	1/2	2	2	2	2	# vars	# dvars	# equ	3777315	646890	2447810	76650	184292	370623	51050	76650	0,203
p14/SA	2	1/2	1/2	2	2	2	2	# vars	# dvars	# equ	4237421	699420	2887840	91250	202897	179894	176120	91250	0,109
p15/SA	2	1/2	1/2	2	2	2	2	# vars	# dvars	# equ	4603569	719980	2767590	71175	192191	15103	837530	71175	0,203
p21/SA	3	1/2	1/2	3	3	3	3	# vars	# dvars	# equ	4854406	627460	2901500	180675	216811	333960	594000	180675	0,141
p22/SA	3	1/2	1/2	3	3	3	3	# vars	# dvars	# equ	3953906	628450	2499900	109500	144726	309430	261900	149650	0,141
p23/SA	3	1/2	1/2	3	3	3	3	# vars	# dvars	# equ	4020161	696310	2506180	147825	253134	63712	362000	178850	0,031
p24/SA	3	1/2	1/2	3	3	3	3	# vars	# dvars	# equ	4534677	633060	2572390	147825	273291	681461	226650	149650	0,109
p25/SA	3	1/2	1/2	3	3	3	3	# vars	# dvars	# equ	3959135	645700	2440220	158775	292925	43065	378450	158775	0,11
p31/SA	4	1/3	1/3	4	4	3	3	# vars	# dvars	# equ	4451845	653180	2603100	62050	379005	84260	670250	120450	0,172
p32/SA	4	1/3	1/3	4	4	3	3	# vars	# dvars	# equ	4499989	735950	2626010	120450	447149	22330	548100	120450	0,156
p33/SA	4	1/3	1/3	4	4	3	3	# vars	# dvars	# equ	5240332	626630	2386380	147825	387677	334620	1357200	147825	0,063
p34/SA	4	1/3	1/3	4	4	3	3	# vars	# dvars	# equ	4531804	623680	2592430	136875	302075	21384	855360	164250	0,078
p35/SA	4	1/3	1/3	4	4	3	3	# vars	# dvars	# equ	4870501	674260	2305150	73000	381059	300872	1136160	102200	0,062
p41/SA	5	1/3	1/3	5	5	3	3	# vars	# dvars	# equ	4434085	626040	2595240	211700	197337	488928	314840	248200	0,141
p42/SA	5	1/3	1/3	5	5	3	3	# vars	# dvars	# equ	3915012	631370	2333660	166075	238807	113850	431250	166075	0,016
p43/SA	5	1/3	1/3	5	5	3	3	# vars	# dvars	# equ	4239826	624460	2330030	111325	340481	645700	187840	155125	0,078
p44/SA	5	1/3	1/3	5	5	3	3	# vars	# dvars	# equ	4046442	731260	2383630	91250	367912	374990	97400	91250	0,14
p45/SA	5	1/3	1/3	5	5	3	3	# vars	# dvars	# equ	4421742	662440	2623450	219000	278512	244090	386250	224475	0,078
p51/SA	4	1/2	1/3	6	6	4	4	# vars	# dvars	# equ	4204870	654080	2470250	164250	379938	39072	497280	282875	0,078
p52/SA	4	1/2	1/3	6	6	4	4	# vars	# dvars	# equ	3935648	734730	2480870	184325	311263	127710	96750	226300	0,094
p53/SA	4	1/2	1/3	6	6	4	4	# vars	# dvars	# equ	4647683	702850	2416930	91250	282403	282150	872100	91250	0,062
p54/SA	4	1/2	1/3	6	6	4	4	# vars	# dvars	# equ	3741123	656950	2312160	153300	222929	94644	301140	167900	0,063
p55/SA	4	1/2	1/3	6	6	4	4	# vars	# dvars	# equ	4337916	714680	2446790	167900	244766	157080	606900	167900	0,126
p61/SA	6	1/3	1/3	7	7	4	4	# vars	# dvars	# equ	4551599	635870	2411060	127750	321431	480128	575360	186150	0,125
p62/SA	6	1/3	1/3	7	7	4	4	# vars	# dvars	# equ	4456767	635870	2613420	158775	292692	144210	611800	189800	0,156
p63/SA	6	1/3	1/3	7	7	4	4	# vars	# dvars	# equ	4855588	642430	2829820	177025	542993	521180	142140	195275	0,093
p64/SA	6	1/3	1/3	7	7	4	4	# vars	# dvars	# equ	4240794	652630	2628680	233600	236248	256476	233160	257325	0,094
p65/SA	6	1/3	1/3	7	7	4	4	# vars	# dvars	# equ	4854129	628650	2463570	151475	763420	178794	668220	208050	0,109
p71/SA	6	1/2	1/2	8	8	4	4	# vars	# dvars	# equ	4677391	673340	2453310	149650	164117	465014	771960	149650	0,141
p72/SA	6	1/2	1/2	8	8	4	4	# vars	# dvars	# equ	5361219	620100	2556930	180675	316234	994290	692990	240900	0,125
p73/SA	6	1/2	1/2	8	8	4	4	# vars	# dvars	# equ	4007612	664670	2774860	175200	245383	91839	55660	228125	0,094
p74/SA	6	1/2	1/2	8	8	4	4	# vars	# dvars	# equ	3663014	712580	2372100	149650	275792	54252	98640	231775	0,14
p75/SA	6	1/2	1/2	8	8	4	4	# vars	# dvars	# equ	4883305	683210	2644690	177025	350180	816200	212000	251850	0,156
p81/SA	8	1/3	1/3	9	9	4	4	# vars	# dvars	# equ	4117419	680460	2384260	319375	174964	130680	427680	428875	0,031
p82/SA	8	1/3	1/3	9	9	4	4	# vars	# dvars	# equ	4623133	742460	2498490	138700	256177	122716	864590	231775	0,125

Figure 23. A sample Summary.xlsx file

```
Method SA
------
RBC1 C153,658 R61,686 D14,85
 RTC2 C41,669 D13,5
  D13500=TC2(12)><|RTC2(12)|>TC1(30)><|RTC2(30)|>=84=21000
 DC1
- Unassigned RBCs: RBC2 | RTCs: RTC1 | DCs: DC2
- Remaining RTC Capacity : 28169 | RBC Capacity : 138808
- RBC Demand - Receivable = -46836
Cost=RBCOpen:2575630 + RTCOpen:693410 + DC->RBC:1366200 + RBC->RTC:40500 + RTC->TC:21000(21000) + InvHold:324153
-5.020.893,00 ₺
Generations: Total=337595 Feasible=150065 in 1586 msecs. CacheHit: 0.
Best
---- :  0:ReallocateTCs 1:ExchangeTCs 2:CloseOpenRTC 3:ReallocateRTCs 4:ExchangeRTCs 5:CloseOpenRBC
6:OptimizeByDistanceDCs 7:OpenRTC 8:ExchangeTCPartial
Moves: MI1:0(0-NaNusec), MI2:0(0-NaNusec), M0:37749(37749-NaNusec), M1:37477(37477-NaNusec), M2:37638(0-2,52usec),
M3:37427(37427-NaNusec), M4:37560(37560-NaNusec), M5:37342(0-1,18usec), M6:37698(0-1,17usec), M7:37387(0-9,15usec),
M8:37317(37317-NaNusec), GEN:0(0-NaNusec)
BestMoves: MI1:0, MI2:0, M0:0, M1:0, M2:0, M3:0, M4:0, M5:0, M6:0, M7:1, M8:0, GEN:0
RBC1 C153,658 R85,312 D14,85
 RTC1 C47,31 D13,5
  D13500=TC1(23)>TC2(46)><|RTC1(27)|>=96=24000
 DC2
- Unassigned RBCs: RBC2 | RTCs: RTC2 | DCs: DC1
- Remaining RTC Capacity : 33810 | RBC Capacity : 138808
- RBC Demand - Receivable = -70462
Cost=RBCOpen:2575630 + RTCOpen:665650 + DC->RBC:133650 + RBC->RTC:54000 + RTC->TC:24000(24000) + InvHold:257004
-3.709.934,00 ₺
```

Figure 24. A sample Details.txt file

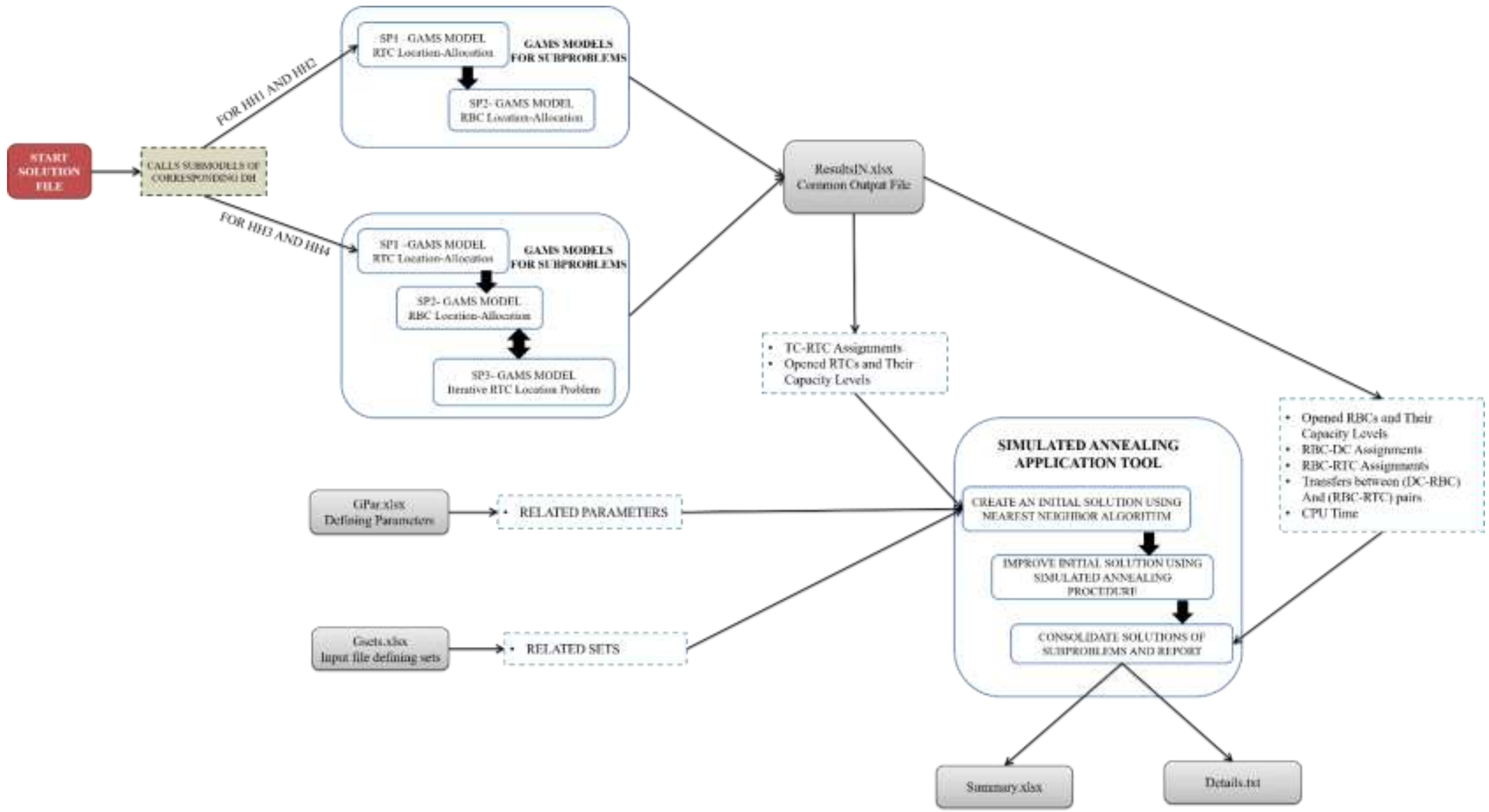


Figure 25. Interaction between Different GAMS Models, Simulated Annealing Application Tool and supporting files (HHs)

After reading the problem parameters and sets from input files, the tool starts an internal procedure. First the main function "Solve" is called, then this function calls "GenerateSolution" sub-function which finds an initial feasible solution to the original problem using TC-RTC, RTC-RBC, and DC-RBC assignment procedures defined in Section 5.2.3.1, and also using nearest neighbor algorithm defined in Section 5.2.2.1. After an initial solution is obtained, "MakeMove" function is called by "GenerateSolution" function. "MakeMove" function is repeated until the solution loop is terminated by reaching one of the stopping criteria. Within the loop of this function, the tool randomly calls one of the sub-functions each of which corresponds to a different kind of move developed to improve the current solution. After one of the stopping criteria is reached, this time, the tool calls "EnhanceRoutes" function which starts the best solution improvement stage in which the routing decisions are improved. The code map of the Simulated Annealing Application Tool which demonstrates the procedure explained above is presented in Figure 27.

A graphical user interface (GUI) is also developed and a screenshot of the interface is presented in Figure 28. This interface allows the user to define the basic parameters of the problem such as visits per year, lead time, fill rate and wastage rate. It also includes data fields to define the target folder for input files and for selecting the problem instance(s) to be solved in a single run. The user can also select the moves to be used in the simulated annealing heuristic and change the parameters of the solution procedures such as Target Temperature, initial temperature, decreasing rate, tabu list size, maximum allowable CPU time, and maximum number of iterations at each temperature. After defining the parameters and selecting problem instances to be solved, the user selects one of two commands below to start the solution procedure;

- "ReadComputeShortest": Used for implementation of the hybrid heuristics,
- "Run": Used for implementation of the simulated annealing heuristic.

After the problem is solved, a summary of the procedure and the solution obtained are shown at the right part of the screen, and the output files are generated in the target folder. After the output files are created, the objective function value obtained after each iteration is also represented graphically (A sample screenshot is given in Figure 29).

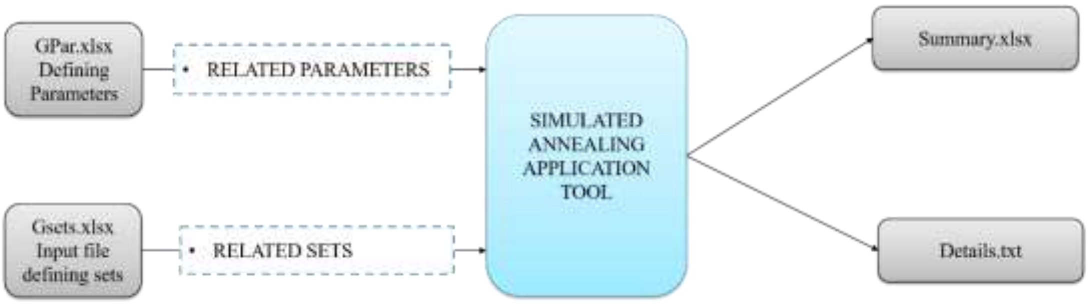


Figure 26. The main information flow of the Simulated Annealing Application Tool

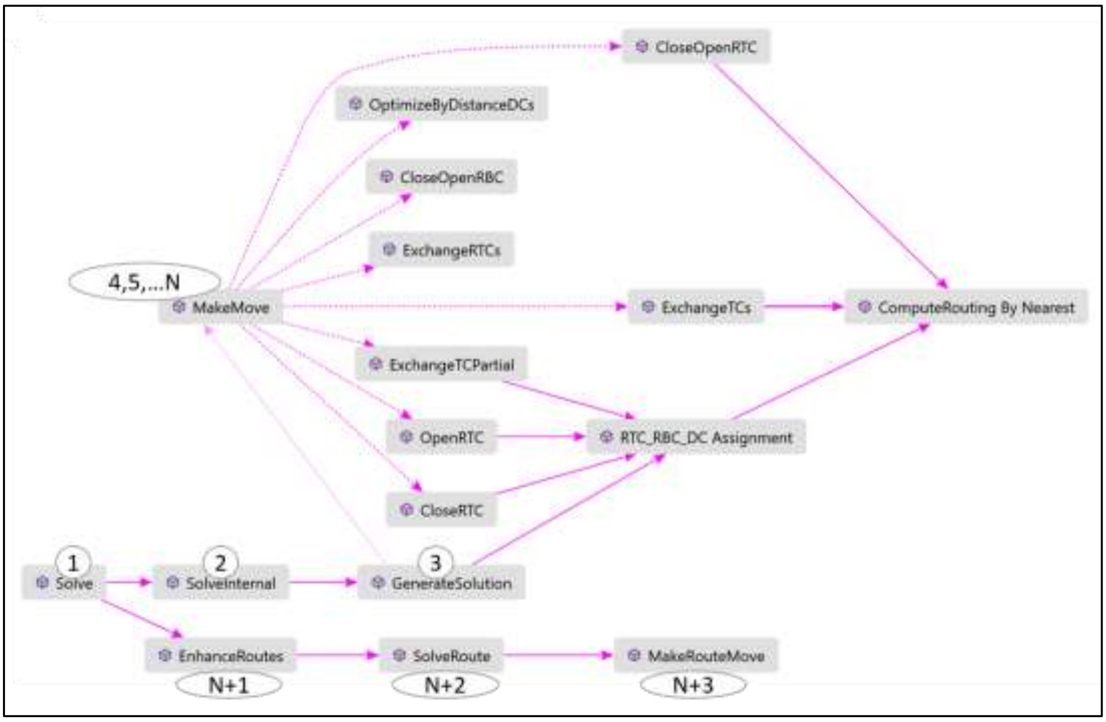


Figure 27. Code Map of the Simulated Annealing Application Tool

Figure 28. Sample Screenshots of the Simulated Annealing Tool- Part I (HHs)

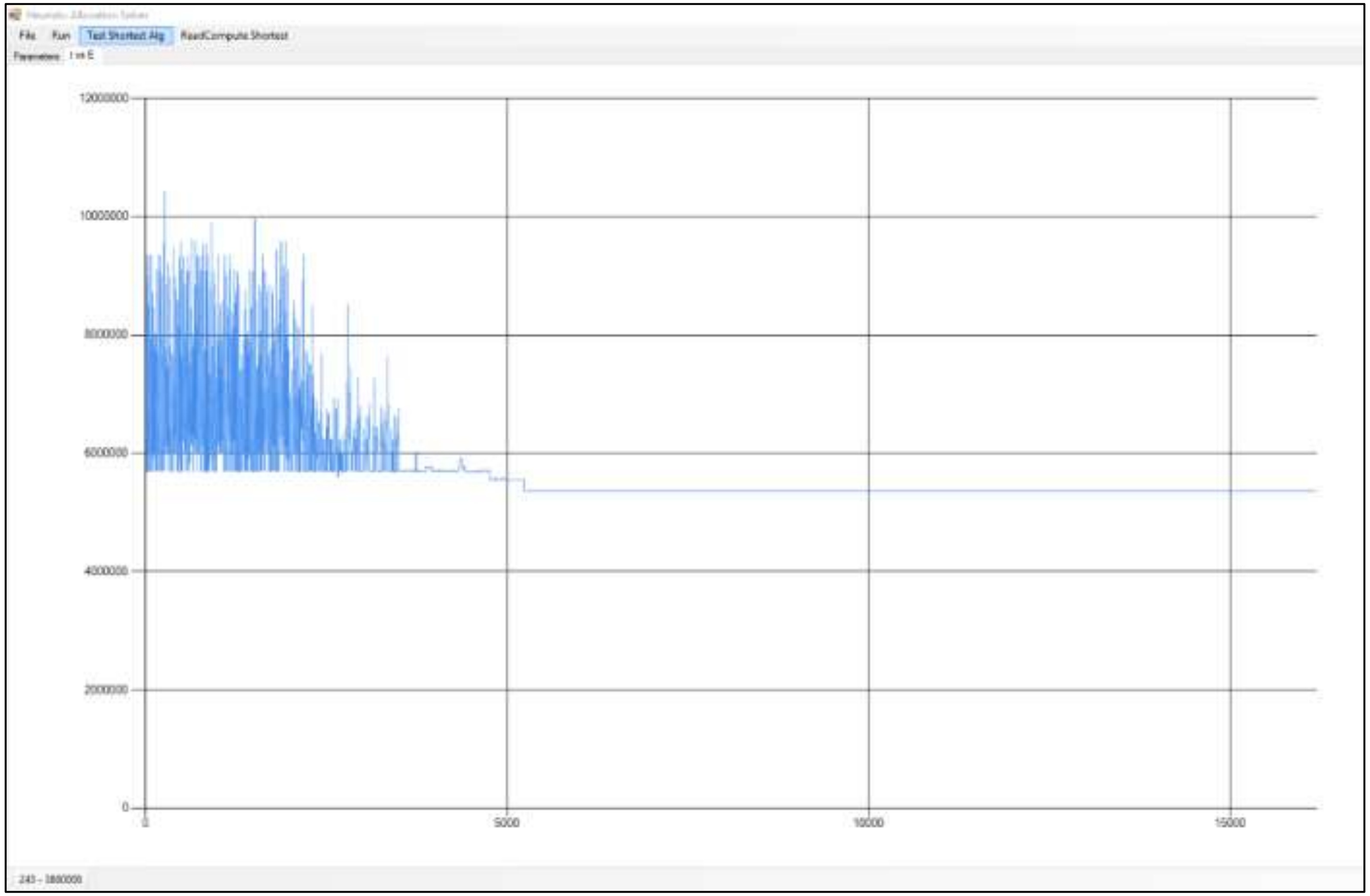


Figure 29. Sample Screenshots of the Simulated Annealing Tool- Part II

6.5. Verification and Validation of the Models and Computer Codes of the Heuristics

Verification and validation steps applied during our study can be categorized in two groups:

- Conceptual validity: Examining the reasonability of the theories and assumptions used in the modelling process.
- Model verification and operational validity: Examining the correctness of the computer implementation, the accuracy of the model outputs and applicability of the outputs to the problem domain.

6.5.1. Conceptual Model Validation

We applied face validation, one of the well-known techniques, for conceptual model validation. In this technique, field experts evaluate the correctness of the conceptual model and reasonability of the assumptions. In order to get the evaluation of experts and reflect their recommendations and feedbacks to the modelling approach, we made interviews with blood bank staff, administrators of blood establishments, and IT experts during the modelling process. We finalized the conceptual design and validity of the models with the help of their contributions.

6.5.2. Model Verification and Operational Validity

The main aim of model verification is to eliminate the errors resulting due to the faults in model formulation and/or computer implementation. In order to eliminate errors and verify the model implementation, we removed the bugs in codes using the editors of the software development platforms. The main aim of operational validity is to ensure that the model has the required accuracy to be applicable to the problem domain or to be able to produce meaningful results for its intended purpose. There are several methods used for operational validity such as extreme condition tests (checking plausibility of the model's output against any extreme and unlikely combination of input and internal parameters), face validity, degenerate tests (testing the degeneracy of the model's behavior by selecting values of the input and internal parameters appropriately), historical data validation, and comparison to other models (Sargent, 1998). However, some of these methods cannot be applied in our study. The proposed supply chain structure in our study has no historical data as it has not been implemented yet. Comparison with other models is also inapplicable, as there are no other models developed and validated for the same problem. Consequently, we use degenerate tests, face validity, and extreme condition tests methods for testing the operational validity in our case. We also use different problem instances to check the consistency of the model outputs for both validation and verification purposes.

We first apply extreme condition and degenerate tests using a baseline scenario and its variants (generated by changing the input parameters of the baseline problem) to validate the model representing the original problem (the implementation of the optimal solution method). Afterwards we apply consistency checks on model outputs of all proposed solution methods obtained by solving different problem instances.

6.5.2.1 Degenerate and Extreme Condition Tests

In order to check model's behavior against changes in parameters and conditions, we need a reference point. Therefore, we first construct a baseline scenario, that is a basic instance of the problem generated using the input parameters given in Appendix A. In this instance of the problem, we consider a blood supply chain consisting of:

- 2 Donation Centers
- 2 Potential Regional Blood Centers (each with two different capacity levels)
- 2 Potential Regional Transfusion Centers (each with two different capacity levels)
- 2 Transfusion Centers
- 2 vehicles

The problem defined by the baseline scenario is solved using the GAMS code developed for implementation of the optimal solution method, and the results are presented in Appendix A. We obtain a reference point by solving the baseline problem and subsequently we develop degenerate and extreme conditions test scenarios by changing the input parameters of the baseline problem.

- Degenerate Test Scenarios: We construct six different degenerate test scenarios by making changes on the baseline problem input parameters as defined below.
    - DT Scenario 1: Decrease the annual demand at TCs to lower levels
    - DT Scenario 2: Decrease the variance of the annual demand at TCs to lower levels
    - DT Scenario 3: Increase the annual inventory holding costs per unit of product at RTCs to a higher level
    - DT Scenario 4: Increase the transportation costs of TC1 to other facilities, except RTC2 to a huge number (two times the fixed opening cost of RTC2)
    - DT Scenario 5: Increase the lead time between RBCs and RTCs to a higher level
    - DT Scenario 6: Increase the transportation cost between RBC2 and RTC1 to a very high level
- Extreme Condition Test Scenarios: We also construct eight different extreme condition test scenarios by making changes on the baseline problem input parameters as defined below.
    - ECT Scenario 1: Decrease the total capacity of the DCs to such a level that it is less than the total demand of the TCs
    - ECT Scenario 2: Set the weighted distances from DC2 to all RBCs to 0, and set the capacity of DC2 to a level higher than the total demand of all TCs x (1+ DDR)
    - ECT Scenario 3: Decrease the total highest capacity of RBCs to such a level that it is less than the total demand of the TCs
    - ECT Scenario 4: Set the fixed opening cost of RBC1 to 0
    - ECT Scenario 5: Decrease the total highest capacity of RTCs to such a level that it is less than the total demand of the TCs
    - ECT Scenario 6: Set the fixed opening cost of RTC2 to 0

- ECT Scenario 7: Decrease the total capacity of all vehicles to such a level that it is less than the total demand of the TCs
- ECT Scenario 8: Set the annual number of visits of each vehicle in a year to 0.

Fourteen problem instances defined by the above test scenarios are solved using the GAMS code developed for implementation of the optimal solution method. The expected results of the problem instances are checked according to Table 2 below for each scenario. These results indicate that the model is validated by the degenerate and extreme conditions techniques using the test problems.

6.5.2.2 Consistency Tests

We prepare test problems (consistency test scenarios) having different sizes to apply consistency controls. Consistency Test Problems (CTPs) are solved by using the computer codes developed to implement the proposed solution methods (optimal solution method, decomposition heuristics, hybrid heuristics, and simulated annealing heuristic) in our study. The size of CTPs and summary of the solutions obtained by the proposed solution methods are given in Appendix B**.** For each problem instance, including the baseline problem, consistency checks are applied on the solutions obtained by using the proposed methods to see whether the following conditions hold true or not:

- Each TC is included on exactly one vehicle route
- Vehicle, DC, RBC and RTC capacity constraints are not violated
- There are no subtours
- Demand at RTCs are satisfied
- Each RTC is assigned to only one opened RBC
- Each DC is assigned to only one opened RBC
- There are no blood transfers between any unassigned facility pairs
- There are no material flows over an unopened RBC or RTC

Consistency conditions are found to hold true for all of the test problems.

Table 2. Expected Results of the Degenerate and Extreme Test Scenarios

Scenario	**Expected Result in the Solution**
DT Scenario 1	Total cost will be decreased
DT Scenario 2	Total cost will be decreased
DT Scenario 3	Total cost will be increased
DT Scenario 4	RTC2 will be opened, and TC1 will be assigned to a route starting form RTC2
DT Scenario 5	Total cost will be increased
DT Scenario 6	RBC2-RTC1 assignment will not hold
ECT Scenario 1	Infeasibility
ECT Scenario 2	Blood needed to satisfy the demand of all TCs will only be obtained from DC2
ECT Scenario 3	Infeasibility
ECT Scenario 4	Instead of RBC2, RBC1 will be opened
ECT Scenario 5	Infeasibility
ECT Scenario 6	Instead of RTC1, RTC2 will be opened
ECT Scenario 7	Infeasibility
ECT Scenario 8	Infeasibility

CHAPTER 7

COMPUTATIONAL STUDY

In order to evaluate the performance of the solution methods proposed, we conduct numerical studies on several problem instances (final test scenarios) grouped into two categories. First category includes small and medium-sized problem instances, while the second includes the large-sized ones.

7.1. Preparation of the Problem Instances

Twenty instance groups having different sizes are defined for the first category (small and medium-sized problem instances) and for each instance group (IG) 5 different problem instances are generated, corresponding to 100 problem instances in total. For the second category (large-sized problem instances), 10 test IGs are defined, and again 5 different problem instances are generated for each group, corresponding to 50 problem instances in total. Sizes of the problem instances for each IG belonging to the first and the second categories are given in Tables 3 and 4, respectively.

In order to eliminate the effect of parameter dependency on the performance of the solution methods, we generate random values for the problem parameters as defined below:

- Mean annual demand at TCs
  - Mean annual demand at TCs, which are also candidates for an RTC, is drawn uniformly from [150, 1650] blood units

- Mean annual demand at the other TCs is drawn uniformly from [2100, 9900] blood units

- Standard deviation of annual demand at TCs is drawn uniformly from [0.05* demand at that TC, 0.1* demand at that TC]
- Capacities for DCs are drawn uniformly from [45,000, 95,000] blood units
- Annual inventory holding cost per unit of blood at RTCs is drawn uniformly from [365, 1,095] TL
- Fixed cost of placing an order to RBCs by RTCs is drawn uniformly from [600, 4,000] TL
- Fixed annual cost of opening and operating RTCs for different capacity levels:
  - For the first capacity level it is drawn uniformly from [62,000, 75,000] TL
  - For the second capacity level it is drawn uniformly from [76,000, 85,000] TL
  - For the third capacity level it is drawn uniformly from [86,000 , 92,000] TL
  - For the fourth capacity level it is drawn uniformly from [93,000, 103,000] TL
- Fixed annual cost of opening and operating RBCs for different capacity levels:
  - For the first capacity level it is drawn uniformly from [230,000, 300,000] TL
  - For the second capacity level it is drawn uniformly from [370,000, 420,000] TL
  - For the third capacity level it is drawn uniformly from [490,000, 570,000] TL
  - For the fourth capacity level it is drawn uniformly from [600,000, 700,000] TL
- Maximum capacity for different capacity levels for RTCs:
  - For the first capacity level it is drawn uniformly from [36,000, 50,000] blood units
  - For the second capacity level it is drawn uniformly from [55,000, 70,000] blood units

- For the third capacity level it is drawn uniformly from [75,000, 85,000] blood units
- For the fourth capacity level it is drawn uniformly from [90, 000, 125,000] blood units

Table 3. Size of Problem Instances for Each IG Belonging to the First Category (Small and Medium-Sized Problem Instances)

Instance Group	Size of instances						
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels
IG1	2	2	2	2	2	2	2
IG2	3	2	2	3	2	3	3
IG3	4	3	3	4	3	3	3
IG4	5	3	3	5	3	3	3
IG5	4	2	3	6	3	4	4
IG6	6	3	3	7	3	4	4
IG7	6	2	2	8	3	4	4
IG8	8	3	3	9	3	4	4
IG9	8	3	3	10	4	4	4
IG10	10	3	3	12	4	4	4
IG11	10	3	4	14	4	4	4
IG12	12	3	4	16	4	4	4
IG13	12	3	4	18	4	4	4
IG14	12	3	5	20	4	4	4
IG15	14	4	5	25	5	4	4
IG16	16	4	5	30	5	4	4
IG17	16	4	6	35	5	4	4
IG18	18	4	6	40	5	4	4
IG19	20	4	6	45	5	4	4
IG20	22	5	6	50	5	4	4

Table 4. Size of Problem Instances for Each IG Belonging to the Second Category (Large-Sized Problem Instances)

Instance Group	Size of instances						
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels
IG21	20	10	15	100	20	4	4
IG22	25	11	20	150	25	4	4
IG23	30	12	30	200	30	4	4
IG24	30	12	40	300	40	4	4
IG25	35	13	45	400	40	4	4
IG26	40	14	65	600	60	4	4
IG27	45	15	85	800	80	4	4
IG28	50	16	100	1000	100	4	4
IG29	55	17	130	1200	130	4	4
IG30	60	20	150	1400	150	4	4

- Maximum capacity for different capacity levels for RBCs:
  - For the first capacity level it is drawn uniformly from [130,000, 180,000] blood units
  - For the second capacity level it is drawn uniformly from [200,000, 230,000] blood units
  - For the third capacity level it is drawn uniformly from [250,000, 290,000] blood units
  - For the fourth capacity level it is drawn uniformly from [300,000, 370,000] blood units
- Transportation costs between TCs and RTCs and among TCs are drawn uniformly from [1, 49] TL
- Cost-weighted distances between DCs and RBCs are drawn uniformly from [1, 101] TL/blood unit
- Cost-weighted distances between RBCs and RTCs are drawn uniformly from [1, 61] TL/blood unit
- Blood disposal rate at RBCs is set as 0.1

- Lead time (in years) between RBCs and RTCs is set as 0.003
- Annual number of visits of each vehicle is set as 1825
- α-percentile of standard normal distribution is set as 0.95

7.2. Computational Results

Problem instances are run on a Windows PC with i7-4700MQ Processor and 16 GB DDRIII RAM. Mathematical models are solved using GAMS v23.5.1. We use iteration limitation (2,000,000,000) and relative termination tolerance limit (the solver stops the solution process when the proportional difference between the solution found and the best theoretical objective function is guaranteed to be smaller than the specified value, which is 0.001) while solving the problem instances. Other solution parameters used during computational studies are as follows:

- Optimal Solution Method
  - Solver: GAMS BARON
  - CPU Time Limitations:
    - For problem instances in IG1-IG6 : 3,600 seconds
    - For problem instances in IG7-IG14: 10,800 seconds
    - For problem instances in IG15: 14,400 seconds
    - For problem instances in IG16-IG17: 28,800 seconds
    - For problem instances in IG18: 36,000 seconds
    - For problem instances in IG19: 43,200 seconds
    - For problem instances in IG20: 86,400 seconds
    - One problem instance belonging to each IG between 7 and 20 is solved using the CPU time limitation of 432,000 seconds to analyze the effect of CPU time limitation on the performance of the optimal solution method.
- Decomposition Heuristics
  - Solver for Subproblems: GAMS CPLEX
  - CPU Time Limitation

- For RTC and RBC location Subproblems: 120 seconds
- For Routing Subproblems: 600 seconds

- Hybrid Heuristic
  - Solver for Subproblems (RTC and RBC Location Subproblems): GAMS CPLEX
  - CPU Time Limitation
    - For RTC and RBC location Subproblems: 120 seconds
    - For Routing Subproblems: 600 seconds
  - Simulated Annealing Parameters for Routing Subproblem
    - CPU Time Limitation: 600 seconds
    - Starting temperature: 10,000,000
    - Cooling Rate: 0.99
    - Target Temperature: 0.1
    - Maximum number of iterations at each temperature: 200
    - Maximum Tabu List Size: 10,000
- Simulated Annealing Heuristic
  - Simulated Annealing Parameters for Constructive and General Improvement Stages
    - CPU Time Limitation: 240 seconds
    - Starting temperature: 100,000,000, Target Temperature: 0.1
    - Cooling Rate: 0.99 (for large-sized problem instances 0.9)
    - Maximum number of iterations at each temperature: 100
    - Maximum Tabu List Size: 10,000
  - Simulated Annealing Parameters for Best Solution Improvement Stage
    - CPU Time Limitation: 600 seconds
    - Starting temperature: 10,000,000, Target Temperature: 0.1
    - Cooling Rate: 0.99
    - Maximum number of iterations at each temperature: 200
    - Maximum Tabu List Size: 10,000

7.2.1. Results of Small and Medium-Sized Problem Instances

In order to develop benchmarks for the performance comparison of the proposed solution methods, we first solve the small and medium-sized problem instances by using the optimal solution method. Results obtained by solving the problem instances with the optimal solution method and the indicators representing the performance of the method are given in Appendix C. The same problem instances are then solved by using the proposed heuristic solution methods. Summary of runs indicating performance comparisons of the heuristic solution methods with the optimal solution method for small and medium-sized problem instances are given in Table 5, and comparisons of the average values by instance groups are presented in Table 6.

As it can be depicted from Appendix C, and Table 5, the optimal solution method reaches the optimal solution (within termination tolerance limit) for small-sized instances (up to IG8). However, as the problem size increases, the quality of the solutions obtained by the optimal solution method deteriorates, even for the medium-sized problem instances (after IG7) solved with a solution time limit up to 120 hours.

SA finds the optimal solutions for the small-sized problem instances, except, only one instance for which it has a small percentage gap value of 0.25%. However, DH1 finds the optimal solution only for 50% of the problem instances, and percentage gap values are ranging from 1.45% to 22.20% for the remaining instances. DH2, DH3, and DH4 find the optimal solution for more than 75% of the small-sized problem instances, and provide relatively better solutions compared to DH1 for the remaining instances (percentage gap values are ranging from 0.88% to 10.04%, from 0.25% to 9.80%, and from 0.25% to 2.55%, respectively). For small-sized problem instances HH1, HH2, HH3, and HH4 present exactly the same performances as DH1, DH2, DH3 and DH4, respectively.

Table 5. Comparison of the Performances of the Heuristic Solution Methods with the Optimal Solution Method for Small and Medium-Sized Problem Instances

		Optimal Solution Method			DH1		DH2		DH3		DH4		HH1		HH2		HH3		HH4		SA	
Instance Group	Test Instance	CPU Time (Seconds)	Relative Gap (%) ***	Objective Function Value	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **
IG1	IG1-1	0.09	0.10	3,861,134	0.20	0.00	0.20	0.00	0.34	1.54	0.50	1.54	1.85	0.00	1.77	0.00	2.14	1.54	2.48	1.54	2.01	0.00
IG1	IG1-2	0.13	0.10	4,698,476	0.19	0.00	0.14	0.00	0.22	0.00	0.37	0.00	1.79	0.00	1.76	0.00	1.92	0.00	2.05	0.00	1.84	0.00
IG1	IG1-3	0.13	0.10	3,777,315	0.22	0.00	0.25	0.00	0.16	0.00	0.25	0.00	1.95	0.00	1.82	0.00	1.98	0.00	2.11	0.00	1.89	0.00
IG1	IG1-4	0.13	0.10	4,237,421	0.16	0.00	0.09	0.00	0.28	0.00	0.23	0.00	1.91	0.00	1.71	0.00	2.04	0.00	1.99	0.00	1.83	0.00
IG1	IG1-5	0.09	0.10	4,353,505	0.25	5.74	0.09	0.00	0.36	0.00	0.17	0.00	1.89	5.74	1.78	0.00	2.03	0.00	1.93	0.00	1.89	0.00
IG2	IG2-1	0.25	0.10	4,854,406	0.17	0.00	0.23	0.00	0.20	0.00	0.36	0.00	2.03	0.00	1.98	0.00	2.17	0.00	2.33	0.00	2.16	0.00
IG2	IG2-2	0.23	0.10	3,953,906	0.20	0.00	0.14	0.00	0.31	0.25	0.31	0.25	2.07	0.00	2.03	0.00	2.34	0.25	2.32	0.25	2.07	0.25
IG2	IG2-3	0.22	0.10	3,741,404	0.14	7.69	0.23	7.69	0.36	0.00	0.39	0.00	2.27	7.69	2.32	7.69	2.41	0.00	2.40	0.00	2.10	0.00
IG2	IG2-4	0.25	0.10	4,470,052	0.17	1.45	0.17	0.00	0.27	0.00	0.28	0.00	2.20	1.45	1.97	0.00	2.29	0.00	2.32	0.00	2.06	0.00
IG2	IG2-5	0.27	0.10	3,959,135	0.16	0.00	0.16	0.00	0.27	0.00	0.22	0.00	2.00	0.00	1.99	0.00	2.30	0.00	2.28	0.00	2.10	0.00
IG3	IG3-1	7.83	0.10	4,265,921	0.27	4.36	0.24	0.00	0.33	0.00	0.23	0.00	2.26	4.36	2.38	0.00	2.48	0.00	2.58	0.00	2.40	0.00
IG3	IG3-2	3.56	0.10	4,089,375	0.23	10.04	0.14	10.04	0.20	0.00	0.30	0.00	2.22	10.04	2.16	10.04	2.36	0.00	2.54	0.00	2.47	0.00
IG3	IG3-3	4.13	0.10	4,362,484	0.09	20.12	0.14	0.00	0.30	0.00	0.23	0.00	2.19	20.12	2.12	0.00	2.55	0.00	2.47	0.00	2.42	0.00
IG3	IG3-4	3.59	0.10	4,531,804	0.17	0.00	0.25	0.00	0.28	0.00	0.30	0.00	2.19	0.00	2.22	0.00	2.40	0.00	2.42	0.00	2.36	0.00
IG3	IG3-5	6.31	0.10	4,255,258	0.17	14.46	0.19	0.00	0.28	0.00	0.37	0.00	2.75	14.46	2.29	0.00	2.54	0.00	2.70	0.00	2.38	0.00
IG4	IG4-1	35.16	0.10	4,434,085	0.17	0.00	0.23	0.00	0.36	2.55	0.19	2.55	2.48	0.00	2.39	0.00	2.94	2.55	2.91	2.55	2.48	0.00
IG4	IG4-2	22.17	0.10	3,673,906	0.06	6.56	0.13	6.56	0.34	0.00	0.33	0.00	2.29	6.56	2.42	6.56	2.78	0.00	2.78	0.00	2.54	0.00
IG4	IG4-3	33.22	0.10	4,239,826	0.16	0.00	0.22	0.00	0.41	0.00	0.30	0.00	2.36	0.00	2.39	0.00	2.73	0.00	2.73	0.00	2.58	0.00
IG4	IG4-4	24.38	0.10	3,965,068	0.19	2.05	0.11	2.05	0.17	2.05	0.41	2.05	2.45	2.05	2.41	2.05	2.45	2.05	2.90	2.05	2.54	0.00
IG4	IG4-5	35.17	0.10	4,291,573	0.16	3.08	0.19	0.00	0.28	0.00	0.27	0.00	2.49	3.08	2.41	0.00	2.66	0.00	2.62	0.00	2.40	0.00
IG5	IG5-1	84.81	0.10	3,978,757	0.11	5.68	0.17	5.68	0.41	0.00	0.39	0.00	2.51	5.68	2.57	5.68	2.83	0.00	2.90	0.00	2.59	0.00
IG5	IG5-2	51.34	0.10	3,935,648	0.17	0.00	0.20	0.00	0.41	0.00	0.36	0.00	2.60	0.00	2.57	0.00	2.99	0.00	3.01	0.00	2.62	0.00
IG5	IG5-3	127.39	0.10	4,308,944	0.09	7.86	0.09	0.00	0.28	7.86	0.24	0.00	2.54	7.86	2.45	0.00	2.86	7.86	2.87	0.00	2.57	0.00
IG5	IG5-4	37.05	0.10	3,741,123	0.09	0.00	0.10	0.00	0.39	0.00	0.34	0.00	2.48	0.00	2.52	0.00	2.91	0.00	3.00	0.00	2.60	0.00
IG5	IG5-5	97.31	0.10	4,339,741	0.19	-0.04	0.28	-0.04	0.28	-0.04	0.25	-0.04	2.54	-0.04	2.62	-0.04	2.97	-0.04	2.74	-0.04	2.52	-0.04
IG6	IG6-1	1,724.53	0.10	4,287,253	0.22	6.17	0.16	6.17	0.41	0.00	0.35	0.00	2.76	6.17	2.73	6.17	3.04	0.00	3.00	0.00	2.74	0.00
IG6	IG6-2	2,341.78	0.10	4,456,767	0.34	0.00	0.36	0.00	0.39	0.00	0.37	0.00	2.77	0.00	2.66	0.00	2.99	0.00	2.97	0.00	2.83	0.00
IG6	IG6-3	2,381.34	0.10	4,608,080	0.14	5.37	0.25	0.00	0.28	5.37	0.31	0.00	2.67	5.37	2.76	0.00	2.94	5.37	3.06	0.00	2.75	0.00
IG6	IG6-4	1,921.48	0.10	4,035,724	0.31	5.08	0.30	0.88	0.25	0.88	0.42	0.88	2.68	5.08	2.84	0.88	3.00	0.88	3.23	0.88	2.90	0.00
IG6	IG6-5	850.09	0.10	3,972,268	0.20	22.20	0.35	0.00	0.41	0.00	0.37	0.00	2.66	22.20	2.74	0.00	3.06	0.00	3.08	0.00	2.72	0.00
IG7	IG7-1	4,158.31	0.10	4,259,947	0.31	9.80	0.20	0.00	0.22	9.80	0.34	0.00	2.91	9.80	2.88	0.00	3.01	9.80	3.09	0.00	3.06	0.00
IG7	IG7-2	10,800.00	37.95	5,361,219	0.33	0.00	0.31	0.00	0.53	0.00	0.47	0.00	2.85	0.00	2.90	0.00	3.28	0.00	3.24	0.00	2.99	0.00
IG7	IG7-3	2,381.67	0.10	4,007,612	0.28	0.00	0.37	0.00	0.41	0.00	0.31	0.00	2.95	0.00	2.94	0.00	3.21	0.00	3.14	0.00	3.15	0.00
IG7	IG7-4	1,957.30	0.10	3,663,014	0.28	0.00	0.22	0.00	0.45	0.00	0.22	0.00	2.92	0.00	2.84	0.00	3.17	0.00	3.12	0.00	3.08	0.00
IG7	IG7-5	8,108.19	0.10	4,883,305	0.34	0.00	0.13	0.00	0.44	0.00	0.34	0.00	2.92	0.00	2.88	0.00	3.19	0.00	3.30	0.00	3.16	0.00
IG8	IG8-1	10,800.00	31.50	4,036,635	0.20	2.00	0.33	-1.36	0.38	2.00	0.34	-1.36	3.00	2.00	3.29	-1.36	3.44	2.00	3.63	-1.36	3.60	-1.36
IG8	**IG8-1***	**10,800.00**	**0.10**	**3,981,885**	0.20	3.40	0.33	0.00	0.38	3.40	0.34	0.00	3.00	3.40	3.29	0.00	3.44	3.40	3.63	0.00	3.60	0.00
IG8	IG8-2	10,800.00	33.44	3,878,734	0.39	19.19	0.45	-2.68	0.49	-2.68	0.44	-2.68	2.96	19.19	3.12	-2.68	3.42	-2.68	3.42	-2.68	3.31	-2.68
IG8	IG8-3	10,800.00	29.36	3,676,518	0.42	-0.50	0.49	-0.50	0.52	-0.50	0.64	-0.50	2.97	-0.50	3.13	-0.50	3.30	-0.50	3.49	-0.50	3.33	-0.50
IG8	IG8-4	10,800.00	37.41	4,604,959	0.30	-0.46	0.19	-1.35	0.38	-1.35	0.39	-1.35	3.03	-0.46	2.97	-1.35	3.58	-1.35	3.34	-1.35	3.15	-0.05
IG8	IG8-5	10,800.01	31.52	3,815,299	0.14	-2.15	0.25	-2.15	0.27	-2.15	0.28	-2.15	2.92	-2.15	3.04	-2.15	3.35	-2.15	3.36	-2.15	3.31	-2.15
IG9	IG9-1	10,800.00	35.29	4,338,402	0.47	20.32	0.25	7.54	0.45	20.32	0.55	-1.05	3.15	20.32	3.09	7.54	3.42	20.32	3.38	-1.05	3.44	-1.05
IG9	**IG9-1***	**432,000.00**	**35.09**	**4,325,627**	0.47	20.67	0.25	7.86	0.45	20.67	0.55	-0.76	3.15	20.67	3.09	7.86	3.42	20.67	3.38	-0.76	3.44	-0.76
IG9	IG9-2	10,800.00	42.09	4,613,262	0.47	-0.32	0.39	-0.87	0.53	-0.87	0.56	-0.87	3.23	-0.32	3.17	-0.87	3.41	-0.87	3.41	-0.87	3.33	-0.87
IG9	IG9-3	10,800.00	42.51	5,052,869	0.27	-1.99	0.36	-1.99	0.36	-1.99	0.33	-1.99	3.23	-1.99	3.29	-1.99	3.44	-1.99	3.40	-1.99	3.48	-1.99
IG9	IG9-4	10,800.00	34.53	3,850,465	0.28	1.90	0.23	-2.61	0.42	1.90	0.52	-2.61	3.08	1.90	3.11	-2.61	3.44	1.90	3.29	-2.61	3.51	-2.61
IG9	IG9-5	10,800.01	33.57	3,975,344	0.33	19.11	0.30	19.11	0.28	19.11	0.39	19.11	3.10	19.11	3.14	19.11	3.48	19.11	3.31	19.11	3.48	-1.97
IG10	IG10-1	10,800.00	36.30	3,947,471	0.44	18.01	0.36	-1.11	0.70	-1.11	0.55	-1.11	3.47	18.01	3.39	-1.11	3.91	-1.11	3.71	-1.11	3.75	-0.53
IG10	**IG10-1***	**432,000.00**	**36.30**	**3,947,471**	0.44	18.01	0.36	-1.11	0.70	-1.11	0.55	-1.11	3.47	18.01	3.39	-1.11	3.91	-1.11	3.71	-1.11	3.75	-0.53
IG10	IG10-2	10,800.01	34.17	3,885,664	0.27	-2.87	0.28	-2.87	0.44	-2.87	0.39	-2.87	3.54	-2.87	3.41	-2.87	3.70	-2.87	3.89	-2.87	3.81	-2.87
IG10	IG10-3	10,800.00	41.82	4,843,756	0.31	-1.92	0.28	-1.92	0.56	-1.92	0.42	-1.92	3.62	-1.92	3.46	-1.92	3.93	-1.92	3.83	-1.92	3.80	-14.01
IG10	IG10-4	10,800.00	42.87	4,485,461	0.42	-1.34	0.36	-1.34	0.38	-1.34	0.58	-1.34	3.61	-1.34	3.52	-1.34	3.98	-1.34	3.85	-1.34	4.19	-1.34
IG10	IG10-5	10,800.00	39.38	4,526,793	0.11	-4.07	0.16	-4.07	0.31	-4.07	0.20	-4.07	3.46	-4.07	3.53	-4.07	3.93	-4.07	3.67	-4.07	4.04	-4.07

* Indicates that the corresponding problem instance is solved using the CPU time limitation of 120 hours.

** Gap (%) = ((“Objective function value obtained by the corresponding solution method”-“objective function value obtained by Optimal Solution Method”)/ (“Solution obtained by Optimal Solution Method”))*100. Blue highlighted cells correspond to negative gap values (a lower objective function value) and green highlighted cells correspond to positive gap values (higher objective function value).

*** Relative Gap (%): (“lower bound”-“objective function value obtained by optimal solution method”)/ “lower bound”)*100.

Table 5. cont'd

Instance Group	Test Instance	Optimal Solution Method			DH1		DH2		DH3		DH4		HH1		HH2		HH3		HH4		SA	
		CPU Time (Seconds)	Relative Gap (%) ***	Objective Function Value	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **
IG11	IG11-1	10,800.00	49.49	5,306,704	0.78	-20.31	0.91	-25.37	1.17	-20.31	1.08	-25.37	3.72	-20.31	3.58	-25.37	4.34	-20.31	3.90	-25.37	4.12	-25.37
IG11	**IG11-1***	**432,000.00**	**38.57**	**4,363,794**	0.78	-3.09	0.91	-9.25	1.17	-3.09	1.08	-9.25	3.72	-3.09	3.58	-9.25	4.34	-3.09	3.90	-9.25	4.12	-9.25
IG11	IG11-2	10,800.00	35.21	3,964,147	0.50	0.35	0.42	-3.59	0.92	0.35	0.61	-3.59	3.70	0.35	3.82	-3.59	4.23	0.35	4.17	-3.59	4.12	-3.59
IG11	IG11-3	10,800.01	35.69	4,210,994	0.38	-4.16	0.56	11.86	0.63	-4.16	0.80	11.86	3.95	-4.16	3.77	11.86	4.48	-4.16	4.03	11.86	4.63	-4.16
IG11	IG11-4	10,800.00	46.03	4,913,315	0.61	2.53	0.67	-0.34	1.02	-3.65	0.89	-3.65	3.77	2.53	3.79	-0.34	4.22	-3.65	3.78	-3.65	4.08	-3.65
IG11	IG11-5	10,800.01	38.38	4,182,513	1.20	-4.49	1.30	-4.49	1.67	-4.49	1.52	-4.49	3.59	-4.41	3.69	-4.41	4.44	-4.49	4.07	-4.49	4.29	-4.49
IG12	IG12-1	10,800.00	36.37	4,627,397	1.08	-4.10	0.89	-8.71	1.19	-8.71	1.09	-8.71	4.23	-4.10	4.12	-8.71	4.57	-8.64	4.34	-8.68	4.59	-8.71
IG12	**IG12-1***	**432,000.00**	**35.82**	**4,587,247**	1.08	-3.26	0.89	-7.92	1.19	-7.92	1.09	-7.92	4.23	-3.26	4.12	-7.92	4.57	-7.84	4.34	-7.88	4.59	-7.92
IG12	IG12-2	10,800.00	37.91	4,189,622	0.66	-1.83	1.16	2.43	0.94	-1.83	1.30	2.43	4.11	-1.79	3.94	2.43	4.67	-1.83	4.20	2.43	4.67	-1.83
IG12	IG12-3	10,800.01	50.29	5,078,301	0.39	-13.54	0.41	-13.54	1.53	-20.23	1.47	-20.23	4.05	-13.50	4.13	-13.54	4.27	-20.23	4.15	-20.20	4.37	-20.23
IG12	IG12-4	10,800.00	44.44	4,807,414	0.59	3.78	1.14	-4.66	1.25	-4.66	1.38	-4.66	3.82	3.82	3.87	-4.66	4.24	-4.66	4.24	-4.54	4.38	-4.54
IG12	IG12-5	10,800.00	51.44	5,355,350	1.49	-15.79	1.56	-15.79	1.67	-15.79	1.69	-15.79	3.86	-15.79	4.07	-15.79	4.11	-15.79	4.15	-15.79	4.44	-15.79
IG13	IG13-1	10,800.00	48.44	5,945,330	5.28	-18.74	4.48	-20.74	5.67	-18.74	4.66	-20.74	4.36	-18.74	4.15	-20.71	4.58	-18.74	4.36	-20.74	4.79	-22.09
IG13	**IG13-1***	**432,000.00**	**48.13**	**5,910,655**	5.28	-18.27	4.48	-20.27	5.67	-18.27	4.66	-20.27	4.36	-18.27	4.15	-20.24	4.58	-18.27	4.36	-20.27	4.79	-22.03
IG13	IG13-2	10,800.00	38.80	4,248,580	5.08	5.31	5.33	5.31	5.45	5.31	5.50	5.31	4.29	5.31	4.18	5.40	4.69	5.48	4.48	5.31	4.71	-1.72
IG13	IG13-3	10,800.00	43.77	4,483,565	2.05	9.95	1.83	-3.54	2.25	9.95	1.63	-3.54	4.17	9.95	4.44	-3.54	4.62	9.95	4.62	-3.54	4.83	-3.46
IG13	IG13-4	10,800.00	40.48	4,277,079	1.55	20.28	1.48	20.28	1.60	20.28	1.70	20.28	4.22	20.28	4.27	20.28	4.47	20.28	4.78	20.28	4.63	-10.00
IG13	IG13-5	10,800.01	58.94	6,514,624	1.20	-22.51	1.61	-35.13	1.53	-35.13	1.66	-35.13	4.09	-22.51	4.50	-35.13	4.61	-35.13	4.64	-35.13	4.73	-35.13
IG14	IG14-1	10,800.00	52.51	5,363,083	4.91	-18.99	2.05	-17.95	4.89	-18.99	2.33	-17.95	4.50	-18.99	4.44	-17.95	4.90	-18.99	4.64	-17.81	4.72	-22.89
IG14	**IG14-1***	**432,000.00**	**43.06**	**4,473,019**	4.91	-2.88	2.05	-1.62	4.89	-2.88	2.33	-1.62	4.50	-2.88	4.44	-1.62	4.90	-2.88	4.64	-1.46	4.72	-7.55
IG14	IG14-2	10,800.00	60.34	6,380,986	1.80	-15.82	3.08	-12.55	1.74	-15.82	2.00	-23.28	4.56	-15.82	4.60	-12.55	4.76	-15.82	4.68	-23.05	4.81	-23.28
IG14	IG14-3	10,800.00	64.81	7,282,661	1.91	-37.00	2.00	-39.50	2.11	-37.00	2.22	-39.50	4.49	-37.00	4.67	-39.50	4.77	-37.00	4.91	-39.50	4.89	-39.45
IG14	IG14-4	10,800.00	37.63	4,230,293	3.27	-4.62	3.38	-4.62	3.49	-4.62	3.50	-4.62	4.42	-4.57	4.66	-4.49	4.86	-4.57	4.57	-4.57	4.80	-4.62
IG14	IG14-5	10,800.00	65.19	7,405,965	3.75	-44.81	3.70	-44.81	3.67	-44.81	3.73	-44.81	4.62	-44.81	4.66	-44.73	5.17	-44.78	4.77	-44.81	5.22	-44.76
IG15	IG15-1	14,400.06	50.20	5,371,104	4.42	-6.22	11.86	-3.49	4.30	-6.22	12.05	-3.49	5.25	-5.84	5.02	-3.29	5.58	-6.01	5.26	-3.49	5.79	-13.59
IG15	**IG15-1***	**432,000.00**	**49.16**	**5,261,604**	4.42	-4.27	11.86	-1.48	4.30	-4.27	12.05	-1.48	5.25	-3.88	5.02	-1.28	5.58	-4.06	5.26	-1.48	5.79	-11.79
IG15	IG15-2	14,400.06	67.70	8,188,568	114.72	-27.24	139.36	-50.21	107.83	-27.24	138.94	-50.21	5.21	-27.08	5.45	-50.21	5.39	-27.21	5.68	-50.21	5.56	-50.21
IG15	IG15-3	14,400.00	69.50	8,304,352	9.56	-45.98	9.20	-45.98	9.22	-45.98	9.45	-45.98	5.42	-45.91	5.39	-45.89	5.82	-45.89	5.99	-45.65	5.90	-45.83
IG15	IG15-4	14,400.00	57.33	5,710,740	21.86	-29.46	26.17	-29.45	28.80	-29.46	26.01	-29.45	5.15	-29.30	5.17	-29.04	5.61	-29.46	5.62	-29.20	5.59	-29.27
IG15	IG15-5	14,400.00	56.98	6,367,656	6.19	0.02	600.20	-27.01	30.27	-17.23	600.28	-27.01	5.13	0.22	5.20	-26.75	5.66	-17.00	5.45	-27.01	5.35	-26.78
IG16	IG16-1	28,800.00	55.08	6,124,478	14.38	-27.94	24.47	-28.72	18.59	-27.94	24.99	-28.72	6.04	-27.74	6.00	-28.28	6.36	-27.77	6.43	-28.31	6.02	-28.28
IG16	**IG16-1***	**432,000.00**	**55.08**	**6,124,478**	14.38	-27.94	24.47	-28.72	18.59	-27.94	24.99	-28.72	6.04	-27.74	6.00	-28.28	6.36	-27.77	6.43	-28.31	6.02	-28.28
IG16	IG16-2	28,800.00	58.51	7,130,902	28.11	-15.82	107.17	-29.77	148.05	-29.77	110.03	-29.77	6.08	-15.51	6.05	-29.57	6.17	-29.49	6.21	-29.51	6.26	-29.46
IG16	IG16-3	28,800.00	69.34	8,852,790	73.95	-36.55	73.59	-39.22	114.58	-42.92	24.33	-45.64	5.91	-36.40	6.03	-39.05	6.02	-42.84	6.30	-45.58	5.98	-43.40
IG16	IG16-4	28,800.00	52.23	5,326,207	6.92	-2.27	14.09	-5.85	600.27	-22.89	14.60	-5.85	5.92	-2.06	5.72	-5.68	5.91	-22.71	6.22	-5.33	5.96	-22.85
IG16	IG16-5	28,800.00	51.89	5,307,215	600.39	-24.72	8.77	-27.47	600.66	-24.72	600.39	-24.72	5.94	-24.85	6.01	-27.40	6.25	-24.68	6.18	-24.58	6.28	-27.12
IG17	IG17-1	28,800.00	49.06	5,061,509	287.44	-4.67	225.39	-0.28	389.39	-4.67	226.42	-0.28	6.54	-4.12	6.62	0.22	6.94	-4.38	7.37	-0.03	6.90	-8.33
IG17	**IG17-1***	**432,000.00**	**49.06**	**5,061,509**	287.44	-4.67	225.39	-0.28	389.39	-4.67	226.42	-0.28	6.54	-4.12	6.62	0.22	6.94	-4.38	7.37	-0.03	6.90	-8.33
IG17	IG17-2	28,800.00	63.72	7,237,484	600.30	-	16.13	-36.44	23.97	-36.44	16.20	-36.44	9.19	-10.34	6.58	-36.21	7.04	-36.31	7.19	-36.33	7.06	-36.18
IG17	IG17-3	28,800.09	75.85	10,467,168	600.41	-	9.63	-58.82	556.66	-57.77	368.53	-57.77	9.02	-39.17	6.68	-58.61	6.88	-57.48	6.95	-57.69	7.15	-58.63
IG17	IG17-4	28,800.00	57.98	6,129,912	169.55	0.56	60.58	-9.42	87.75	-9.42	62.72	-9.42	7.01	0.89	6.97	-9.27	7.20	-9.03	7.36	-9.03	6.88	-15.78
IG17	IG17-5	28,800.00	79.85	12,943,273	600.39	-	600.45	-	600.31	-	600.62	-	9.46	-51.26	9.38	-51.38	9.22	-51.46	10.01	-51.44	6.98	-59.71
IG18	IG18-1	36,000.02	58.45	6,574,943	600.45	-	332.66	-23.89	600.59	-	600.64	-	9.75	0.56	7.47	-23.44	10.21	-11.07	10.16	-10.99	7.58	-25.53
IG18	**IG18-1***	**432,000.00**	**58.45**	**6,574,943**	600.45	-	332.66	-23.89	600.59	-	600.64	-	9.75	0.56	7.47	-23.44	10.21	-11.07	10.16	-10.99	7.58	-25.53
IG18	IG18-2	36,000.02	61.54	7,067,675	600.28	-	600.42	-	600.41	-	600.72	-	9.90	-2.61	9.60	-6.86	9.81	-9.76	10.11	-9.86	7.62	-23.10
IG18	IG18-3	36,000.00	61.97	7,399,048	145.89	-27.37	99.49	-40.34	11.61	-33.14	600.55	-	7.43	-26.90	7.54	-39.88	8.15	-32.52	10.63	-27.01	7.86	-40.04
IG18	IG18-4	36,000.08	71.22	8,741,718	600.33	-18.99	164.03	-40.54	600.31	-	164.94	-40.54	9.61	-20.49	7.77	-40.27	10.05	-39.04	8.42	-40.29	7.67	-48.02
IG18	IG18-5	36,000.04	77.48	12,096,555	600.30	-	600.27	-61.68	600.58	-61.64	600.41	-61.68	9.69	-39.20	7.54	-61.55	8.31	-61.29	7.96	-61.50	7.75	-61.44
IG19	IG19-1	43,200.02	66.27	7,686,996	600.49	-	600.53	-35.58	600.72	-36.83	600.70	-36.15	10.58	-5.60	8.50	-35.89	8.88	-37.49	8.58	-36.04	8.68	-37.30
IG19	**IG19-1***	**432,000.00**	**66.27**	**7,686,996**	600.49	-	600.53	-35.58	600.72	-36.83	600.70	-36.15	10.58	-5.60	8.50	-35.89	8.88	-37.49	8.58	-36.04	8.68	-37.30
IG19	IG19-2	43,200.02	67.01	7,718,163	600.37	-	600.72	-40.44	194.28	-38.92	600.70	-40.20	10.29	1.13	9.16	-40.09	8.28	-38.42	8.81	-40.20	8.84	-40.13
IG19	IG19-3	43,200.14	63.51	6,825,822	600.33	-	600.64	-	100.11	-36.27	600.81	-	10.39	-16.99	10.88	-10.97	8.73	-35.92	11.34	-23.86	8.30	-37.83
IG19	IG19-4	43,200.02	66.84	7,587,277	600.20	-	600.42	-31.63	600.36	-31.56	600.44	-31.63	10.26	-14.47	8.53	-31.58	8.64	-31.48	8.63	-31.44	8.54	-31.48
IG19	IG19-5	43,200.00	73.71	9,945,634	600.45	-	177.60	-40.28	600.73	-47.27	600.50	-	10.19	-33.84	8.23	-39.91	8.84	-48.94	10.87	-31.81	8.41	-49.04
IG20	IG20-1	86,400.02	77.69	11,936,761	600.31	-	600.58	-	600.64	-	600.87	-	11.66	-46.27	11.43	-44.61	12.52	-46.27	11.94	-48.81	9.13	-57.82
IG20	**IG20-1***	**432,000.00**	**77.69**	**11,936,761**	600.31	-	600.58	-	600.64	-	600.87	-	11.66	-46.27	11.43	-44.61	12.52	-46.27	11.94	-48.81	9.13	-57.82
IG20	IG20-2	86,400.05	74.55	10,189,182	600.44	-	600.56	-53.62	600.50	-	600.59	-53.14	11.43	-18.39	9.60	-54.11	11.34	-30.68	9.39	-54.27	9.19	-54.32
IG20	IG20-3	86,400.13	73.14	9,295,995	600.58	-	600.53	-	600.72	-	211.02	-51.80	12.09	-28.19	11.74	-36.65	12.03	-37.01	9.55	-51.37	9.44	-51.45
IG20	IG20-4	86,400.02	68.43	8,394,730	600.38	-	214.97	-42.07	600.67	-24.29	212.13	-42.07	11.70	-25.93	9.46	-41.33	11.98	-30.60	9.21	-41.38	9.40	-41.23
IG20	IG20-5	86,400.00	81.36	13,761,874	600.28	-	600.52	-	206.95	-62.04	600.45	-	11.23	-51.65	11.30	-59.57	9.43	-61.73	11.58	-59.61	9.25	-66.55

* Indicates that the corresponding problem instance is solved using the CPU time limitation of 120 hours.

** Gap (%) = ((“Objective function value obtained by the corresponding solution method”-“objective function value obtained by Optimal Solution Method”)/ (“Solution obtained by Optimal Solution Method”))*100. Blue highlighted cells correspond to negative gap values (a lower objective function value) and green highlighted cells correspond to positive gap values (higher objective function value).

*** Relative Gap (%): (“lower bound”-“objective function value obtained by optimal solution method”)/ “lower bound”)*100.

SA performs better than the optimal solution method for all medium-sized problem instances. Other heuristics also provide negative percentage gap values when compared to the solutions obtained by the optimal solution method for most of the medium-sized problem instances. However, there are still some exceptional instances for which other heuristics have positive percentage gap values up to 20.67%. For medium-sized problem instances, except the ones for which DHs cannot provide integer solutions within the specified time limits, HH1, HH2, HH3, and HH4 also present nearly the same performances as DH1, DH2, DH3, and DH4, respectively.

CPU times of the proposed heuristics are quite acceptable for small and medium-sized problem instances except DHs. CPU times of DHs are also acceptable for the problem instances belonging to IGs from 1 to 15. However, as the problem size increases, CPU times of DHs increase rapidly, and for some instances DHs cannot even provide any integer solution within the specified time limits.

The distinction between the performance of the proposed solution methods and the optimal solution method turns out to be more obvious when we analyze the mean percentage gap and standard deviation values reported in Table 6. It can be easily depicted from Table 6 that all heuristics have acceptable positive mean percentage gap values for small-sized problem instances, and for the medium-sized ones, all heuristics result in negative mean percentage gap values. The main drawback of all heuristics, except SA, is that they have sometimes results with large deviations which correspond explicitly to varying performances among problem instances. Inability to obtain integer solutions due to increasing CPU times for some of the medium-sized problem instances is another disadvantage of DHs. However, it is clear that SA outperforms the optimal solution method for all small and medium-sized problem instances, except only one for which it has a small percentage gap value of 0.25%.

As discussed in the previous sections, four hybrid heuristics called HH1, HH2, HH3, and HH4 are the modified versions of the decomposition heuristics called DH1, DH2, DH3, and DH4, respectively. For each of the Hybrid Heuristics, instead of solving vehicle routing subproblem optimally by using an optimization software package, it is solved by using a simulated annealing procedure presented in the previous sections. In order to evaluate the performance of the simulated annealing (SA) procedure developed for the vehicle routing subproblem, solutions obtained by each HH are compared as pairs with the ones obtained by the corresponding DH. The results of this comparison are summarized in Table 7. As it can be depicted from the table, for more than 70% of the problem instances, HHs find exactly the same solution as DHs, and percentage gap values are lower than 1% for almost all of the remaining instances. In addition to that, CPU times of DHs are dramatically lowered by using the simulated annealing procedure. Therefore, the problem instances, for which DHs cannot provide integer solutions, are solved by HHs in quite reasonable CPU times.

In order to analyze the performances of the proposed solution methods from a different perspective, the best (minimum) objective function value obtained among all heuristics for each problem instance is determined, and this value (instead of the value obtained by optimal solution method) is used as a base for the comparisons presented in Tables 8 and 9. As it can be seen from the tables, SA finds the best solution for more than 60% of the problem instances, and has a percentage gap value lower than 1% for almost all of the remaining instances. Other methods have deviating performances in finding the best or near-best solutions; however, SA obviously performs better than the optimal solution method in terms of both solution time and solution quality for medium-sized problem instances.

7.2.2. Results of Large-Sized Problem Instances

Optimal solution method and DHs cannot generate any feasible integer solutions for large-sized test problem instances; the solution procedure cannot be started due to solver error stating that memory is insufficient. Therefore, only the performances of HHs and SA method can be reported and compared for large-sized problem instances. Summary of runs representing performance comparisons of these methods is given in Table 10, and comparisons of average values by instance groups are presented in Table 11.

Table 6. Comparison of the Average Performances of the Heuristic Solution Methods with the Optimal Solution Method for Small and Medium-Sized Instance Groups

Solution Method	**Basic Performance Indicators**	**Intance Groups**																			
		IG1	**IG2**	**IG3**	**IG4**	**IG5**	**IG6**	**IG7**	**IG8**	**IG9**	**IG10**	**IG11**	**IG12**	**IG13**	**IG14**	**IG15**	**IG16**	**IG17**	**IG18**	**IG19**	**IG20**
DH1	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	1/5	2/5	0/5	0/5
	Mean Gap (%) **	**1.15**	**1.83**	**9.80**	**2.34**	**2.70**	**7.76**	**1.96**	**3.90**	**7.88**	**1.56**	**-1.78**	**-6.13**	**-1.05**	**-21.02**	**-21.39**	**-21.46**	**-2.05**	**-23.18**	-	-
	Standard Deviation	2.30	2.98	7.13	2.43	3.40	7.54	3.92	7.86	9.90	8.28	2.75	7.39	16.57	17.01	17.06	11.67	2.61	4.19	-	-
	Coefficient of Variation	2.00	1.63	0.73	1.04	1.26	0.97	2.00	2.02	1.26	5.30	-1.55	-1.21	-15.82	-0.81	-0.80	-0.54	-1.27	-0.18	-	-
DH2	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	4/5	4/5	4/5	2/5
	Mean Gap (%) **	**0.00**	**1.54**	**2.01**	**1.72**	**1.13**	**1.41**	**0.00**	**-1.34**	**4.30**	**-2.26**	**-1.16**	**-7.89**	**-6.67**	**-20.62**	**-30.83**	**-26.20**	**-26.24**	**-41.61**	**-36.98**	**-47.85**
	Standard Deviation	0.00	3.08	4.02	2.55	2.28	2.40	0.00	1.00	8.32	1.09	7.11	6.50	19.36	18.02	17.22	10.99	23.03	13.41	3.66	5.78
	Coefficient of Variation	-	2.00	2.00	1.48	2.02	1.71	-	-0.75	1.93	-0.48	-6.12	-0.82	-2.90	-0.87	-0.56	-0.42	-0.88	-0.32	-0.10	-0.12
DH3	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	4/5	2/5	5/5	2/5
	Mean Gap (%) **	**0.31**	**0.05**	**0.00**	**0.92**	**1.56**	**1.25**	**1.96**	**-0.65**	**7.76**	**-2.26**	**-3.01**	**-10.08**	**-3.57**	**-21.02**	**-24.84**	**-29.65**	**-27.07**	**-47.39**	**-38.17**	**-43.16**
	Standard Deviation	0.62	0.10	0.00	1.14	3.15	2.09	3.92	2.16	9.99	1.09	1.74	6.90	20.21	17.01	13.82	7.06	21.47	14.25	5.15	18.87
	Coefficient of Variation	2.00	2.00	-	1.24	2.01	1.67	2.00	-3.30	1.29	-0.48	-0.58	-0.68	-5.66	-0.81	-0.56	-0.24	-0.79	-0.30	-0.13	-0.44
DH4	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	4/5	2/5	3/5	3/5
	Mean Gap (%) **	**0.31**	**0.05**	**0.00**	**0.92**	**-0.01**	**0.18**	**0.00**	**-1.34**	**2.58**	**-2.26**	**-1.82**	**-9.23**	**-6.67**	**-22.76**	**-30.83**	**-26.94**	**-25.98**	**-51.11**	**-36.00**	**-49.00**
	Standard Deviation	0.62	0.10	0.00	1.14	0.02	0.35	0.00	1.00	8.30	1.09	7.16	8.03	19.36	17.57	17.22	12.73	22.67	10.57	3.50	4.93
	Coefficient of Variation	2.00	2.00	-	1.24	-2.00	2.00	-	-0.75	3.22	-0.48	-3.93	-0.87	-2.90	-0.77	-0.56	-0.47	-0.87	-0.21	-0.10	-0.10
HH1	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**1.15**	**1.83**	**9.80**	**2.34**	**2.70**	**7.76**	**1.96**	**3.90**	**7.88**	**1.56**	**-1.76**	**-6.10**	**-1.05**	**-21.02**	**-21.19**	**-21.31**	**-20.80**	**-17.73**	**-13.96**	**-34.09**
	Standard Deviation	2.30	2.98	7.13	2.43	3.40	7.54	3.92	7.86	9.90	8.28	2.73	7.40	16.57	17.02	17.15	11.71	20.61	14.94	11.85	12.69
	Coefficient of Variation	2.00	1.63	0.73	1.04	1.26	0.97	2.00	2.02	1.26	5.30	-1.55	-1.21	-15.82	-0.81	-0.81	-0.55	-0.99	-0.84	-0.85	-0.37
HH2	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**0.00**	**1.54**	**2.01**	**1.72**	**1.13**	**1.41**	**0.00**	**-1.34**	**4.30**	**-2.26**	**-1.14**	**-7.89**	**-6.65**	**-20.58**	**-30.63**	**-25.99**	**-31.05**	**-34.38**	**-31.69**	**-47.25**
	Standard Deviation	0.00	3.08	4.02	2.55	2.28	2.40	0.00	1.00	8.32	1.09	7.10	6.50	19.37	18.02	17.29	10.98	23.03	18.33	10.82	8.40
	Coefficient of Variation	-	2.00	2.00	1.48	2.02	1.71	-	-0.75	1.93	-0.48	-6.21	-0.82	-2.91	-0.88	-0.56	-0.42	-0.74	-0.53	-0.34	-0.18
HH3	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**0.31**	**0.05**	**0.00**	**0.92**	**1.56**	**1.25**	**1.96**	**-0.65**	**7.76**	**-2.26**	**-3.01**	**-10.07**	**-3.54**	**-21.01**	**-24.73**	**-29.50**	**-31.73**	**-30.74**	**-38.45**	**-41.26**
	Standard Deviation	0.62	0.10	0.00	1.14	3.15	2.09	3.92	2.16	9.99	1.09	1.74	6.90	20.23	17.01	13.88	7.07	21.62	19.14	5.76	11.73
	Coefficient of Variation	2.00	2.00	-	1.24	2.01	1.67	2.00	-3.30	1.29	-0.48	-0.58	-0.69	-5.72	-0.81	-0.56	-0.24	-0.68	-0.62	-0.15	-0.28
HH4	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**0.31**	**0.05**	**0.00**	**0.92**	**-0.01**	**0.18**	**0.00**	**-1.34**	**2.58**	**-2.26**	**-1.82**	**-9.19**	**-6.67**	**-22.68**	**-30.71**	**-26.66**	**-30.90**	**-29.93**	**-32.67**	**-51.09**
	Standard Deviation	0.62	0.10	0.00	1.14	0.02	0.35	0.00	1.00	8.30	1.09	7.16	8.04	19.36	17.61	17.17	12.87	22.80	19.36	5.44	6.04
	Coefficient of Variation	2.00	2.00	-	1.24	-2.00	2.00	-	-0.75	3.22	-0.48	-3.93	-0.87	-2.90	-0.78	-0.56	-0.48	-0.74	-0.65	-0.17	-0.12
SA	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**0.00**	**0.05**	**0.00**	**0.00**	**-0.01**	**0.00**	**0.00**	**-1.08**	**-1.64**	**-4.56**	**-5.03**	**-10.06**	**-14.47**	**-23.93**	**-32.78**	**-30.62**	**-35.73**	**-39.63**	**-39.16**	**-54.27**
	Standard Deviation	0.00	0.10	0.00	0.00	0.02	0.00	0.00	1.12	0.71	4.88	2.14	6.92	12.55	16.23	13.88	7.72	21.21	14.27	5.70	8.26
	Coefficient of Variation	-	2.00	-	-	-2.00	-	-	-1.04	-0.43	-1.07	-0.42	-0.69	-0.87	-0.68	-0.42	-0.25	-0.59	-0.36	-0.15	-0.15

* S/P: Number of problem instances for which a feasible solution is obtained by the proposed solution method within the time limits/Total number of problems in the instance group.

** Mean Gap (%): Mean of gap values of the problem instances belonging to the related instance group. Gap (%) = ((“Objective function value obtained by the corresponding solution method”-“ Objective function value obtained by the Optimal Solution Method”)/ (“Objective function value obtained the by Optimal Solution Method”))*100. Green highlighted cells indicate the lowest mean gap values for the corresponding instance group.

Table 7. Comparison of the Performances of the DHs with the Related HHs

Instance Group	Test Instance	DH1		HH1		Gap (%) DH1 vs HH1 *	DH2		HH2		Gap (%) DH2 vs HH2 *	DH3		HH3		Gap (%) DH3 vs HH3 *	DH4		HH4		Gap (%) DH4 vs HH4 *
		CPU Time (Seconds)	Objective Function Value	CPU Time (Seconds)	Objective Function Value		CPU Time (Seconds)	Objective Function Value	CPU Time (Seconds)	Objective Function Value		CPU Time (Seconds)	Objective Function Value	CPU Time (Seconds)	Objective Function Value		CPU Time (Seconds)	Objective Function Value	CPU Time (Seconds)	Objective Function Value	
IG1	IG1-1	0.20	3,861,134	1.85	3,861,134	0.00	0.20	3,861,134	1.77	3,861,134	0.00	0.34	3,920,643	2.14	3,920,643	0.00	0.50	3,920,643	2.48	3,920,643	0.00
IG1	IG1-2	0.19	4,698,476	1.79	4,698,476	0.00	0.14	4,698,476	1.76	4,698,476	0.00	0.22	4,698,476	1.92	4,698,476	0.00	0.37	4,698,476	2.05	4,698,476	0.00
IG1	IG1-3	0.22	3,777,315	1.95	3,777,315	0.00	0.25	3,777,315	1.82	3,777,315	0.00	0.16	3,777,315	1.98	3,777,315	0.00	0.25	3,777,315	2.11	3,777,315	0.00
IG1	IG1-4	0.16	4,237,421	1.91	4,237,421	0.00	0.09	4,237,421	1.71	4,237,421	0.00	0.28	4,237,421	2.04	4,237,421	0.00	0.23	4,237,421	1.99	4,237,421	0.00
IG1	IG1-5	0.25	4,603,569	1.89	4,603,569	0.00	0.09	4,353,505	1.78	4,353,505	0.00	0.36	4,353,505	2.03	4,353,505	0.00	0.17	4,353,505	1.93	4,353,505	0.00
IG2	IG2-1	0.17	4,854,406	2.03	4,854,406	0.00	0.23	4,854,406	1.98	4,854,406	0.00	0.20	4,854,406	2.17	4,854,406	0.00	0.36	4,854,406	2.33	4,854,406	0.00
IG2	IG2-2	0.20	3,953,906	2.07	3,953,906	0.00	0.14	3,953,906	2.03	3,953,906	0.00	0.31	3,963,962	2.34	3,963,962	0.00	0.31	3,963,962	2.32	3,963,962	0.00
IG2	IG2-3	0.14	4,029,161	2.27	4,029,161	0.00	0.23	4,029,161	2.32	4,029,161	0.00	0.36	3,741,404	2.41	3,741,404	0.00	0.39	3,741,404	2.40	3,741,404	0.00
IG2	IG2-4	0.17	4,534,677	2.20	4,534,677	0.00	0.17	4,470,052	1.97	4,470,052	0.00	0.27	4,470,052	2.29	4,470,052	0.00	0.28	4,470,052	2.32	4,470,052	0.00
IG2	IG2-5	0.16	3,959,135	2.00	3,959,135	0.00	0.16	3,959,135	1.99	3,959,135	0.00	0.27	3,959,135	2.30	3,959,135	0.00	0.22	3,959,135	2.28	3,959,135	0.00
IG3	IG3-1	0.27	4,451,845	2.26	4,451,845	0.00	0.24	4,265,921	2.38	4,265,921	0.00	0.33	4,265,921	2.48	4,265,921	0.00	0.23	4,265,921	2.58	4,265,921	0.00
IG3	IG3-2	0.23	4,499,989	2.22	4,499,989	0.00	0.14	4,499,989	2.16	4,499,989	0.00	0.20	4,089,375	2.36	4,089,375	0.00	0.30	4,089,375	2.54	4,089,375	0.00
IG3	IG3-3	0.09	5,240,332	2.19	5,240,332	0.00	0.14	4,362,484	2.12	4,362,484	0.00	0.30	4,362,484	2.55	4,362,484	0.00	0.23	4,362,484	2.47	4,362,484	0.00
IG3	IG3-4	0.17	4,531,804	2.19	4,531,804	0.00	0.25	4,531,804	2.22	4,531,804	0.00	0.28	4,531,804	2.40	4,531,804	0.00	0.30	4,531,804	2.42	4,531,804	0.00
IG3	IG3-5	0.17	4,870,501	2.75	4,870,501	0.00	0.19	4,255,258	2.29	4,255,258	0.00	0.28	4,255,258	2.54	4,255,258	0.00	0.37	4,255,258	2.70	4,255,258	0.00
IG4	IG4-1	0.17	4,434,085	2.48	4,434,085	0.00	0.23	4,434,085	2.39	4,434,085	0.00	0.36	4,547,177	2.94	4,547,177	0.00	0.19	4,547,177	2.91	4,547,177	0.00
IG4	IG4-2	0.06	3,915,012	2.29	3,915,012	0.00	0.13	3,915,012	2.42	3,915,012	0.00	0.34	3,673,906	2.78	3,673,906	0.00	0.33	3,673,906	2.78	3,673,906	0.00
IG4	IG4-3	0.16	4,239,826	2.36	4,239,826	0.00	0.22	4,239,826	2.39	4,239,826	0.00	0.41	4,239,826	2.73	4,239,826	0.00	0.30	4,239,826	2.73	4,239,826	0.00
IG4	IG4-4	0.19	4,046,442	2.45	4,046,442	0.00	0.11	4,046,442	2.41	4,046,442	0.00	0.17	4,046,442	2.45	4,046,442	0.00	0.41	4,046,442	2.90	4,046,442	0.00
IG4	IG4-5	0.16	4,423,742	2.49	4,423,742	0.00	0.19	4,291,573	2.41	4,291,573	0.00	0.28	4,291,573	2.66	4,291,573	0.00	0.27	4,291,573	2.62	4,291,573	0.00
IG5	IG5-1	0.11	4,204,870	2.51	4,204,870	0.00	0.17	4,204,870	2.57	4,204,870	0.00	0.41	3,978,757	2.83	3,978,757	0.00	0.39	3,978,757	2.90	3,978,757	0.00
IG5	IG5-2	0.17	3,935,648	2.60	3,935,648	0.00	0.20	3,935,648	2.57	3,935,648	0.00	0.41	3,935,648	2.99	3,935,648	0.00	0.36	3,935,648	3.01	3,935,648	0.00
IG5	IG5-3	0.09	4,647,683	2.54	4,647,683	0.00	0.09	4,308,944	2.45	4,308,944	0.00	0.28	4,647,683	2.86	4,647,683	0.00	0.24	4,308,944	2.87	4,308,944	0.00
IG5	IG5-4	0.09	3,741,123	2.48	3,741,123	0.00	0.10	3,741,123	2.52	3,741,123	0.00	0.39	3,741,123	2.91	3,741,123	0.00	0.34	3,741,123	3.00	3,741,123	0.00
IG5	IG5-5	0.19	4,337,916	2.54	4,337,916	0.00	0.28	4,337,916	2.62	4,337,916	0.00	0.28	4,337,916	2.97	4,337,916	0.00	0.25	4,337,916	2.74	4,337,916	0.00
IG6	IG6-1	0.22	4,551,599	2.76	4,551,599	0.00	0.16	4,551,599	2.73	4,551,599	0.00	0.41	4,287,253	3.04	4,287,253	0.00	0.35	4,287,253	3.00	4,287,253	0.00
IG6	IG6-2	0.34	4,456,767	2.77	4,456,767	0.00	0.36	4,456,767	2.66	4,456,767	0.00	0.39	4,456,767	2.99	4,456,767	0.00	0.37	4,456,767	2.97	4,456,767	0.00
IG6	IG6-3	0.14	4,855,588	2.67	4,855,588	0.00	0.25	4,608,080	2.76	4,608,080	0.00	0.28	4,855,588	2.94	4,855,588	0.00	0.31	4,608,080	3.06	4,608,080	0.00
IG6	IG6-4	0.31	4,240,794	2.68	4,240,794	0.00	0.30	4,071,150	2.84	4,071,150	0.00	0.25	4,071,150	3.00	4,071,150	0.00	0.42	4,071,150	3.23	4,071,150	0.00
IG6	IG6-5	0.20	4,854,129	2.66	4,854,129	0.00	0.35	3,972,268	2.74	3,972,268	0.00	0.41	3,972,268	3.06	3,972,268	0.00	0.37	3,972,268	3.08	3,972,268	0.00
IG7	IG7-1	0.31	4,677,391	2.91	4,677,391	0.00	0.20	4,259,947	2.88	4,259,947	0.00	0.22	4,677,391	3.01	4,677,391	0.00	0.34	4,259,947	3.09	4,259,947	0.00
IG7	IG7-2	0.33	5,361,219	2.85	5,361,219	0.00	0.31	5,361,219	2.90	5,361,219	0.00	0.53	5,361,219	3.28	5,361,219	0.00	0.47	5,361,219	3.24	5,361,219	0.00
IG7	IG7-3	0.28	4,007,612	2.95	4,007,612	0.00	0.37	4,007,612	2.94	4,007,612	0.00	0.41	4,007,612	3.21	4,007,612	0.00	0.31	4,007,612	3.14	4,007,612	0.00
IG7	IG7-4	0.28	3,663,014	2.92	3,663,014	0.00	0.22	3,663,014	2.84	3,663,014	0.00	0.45	3,663,014	3.17	3,663,014	0.00	0.22	3,663,014	3.12	3,663,014	0.00
IG7	IG7-5	0.34	4,883,305	2.92	4,883,305	0.00	0.13	4,883,305	2.88	4,883,305	0.00	0.44	4,883,305	3.19	4,883,305	0.00	0.34	4,883,305	3.30	4,883,305	0.00
IG8	IG8-1	0.20	4,117,419	3.00	4,117,419	0.00	0.33	3,981,885	3.29	3,981,885	0.00	0.38	4,117,419	3.44	4,117,419	0.00	0.34	3,981,885	3.63	3,981,885	0.00
IG8	IG8-2	0.39	4,623,133	2.96	4,623,133	0.00	0.45	3,774,709	3.12	3,774,709	0.00	0.49	3,774,709	3.42	3,774,709	0.00	0.44	3,774,709	3.42	3,774,709	0.00
IG8	IG8-3	0.42	3,658,268	2.97	3,658,268	0.00	0.49	3,658,268	3.13	3,658,268	0.00	0.52	3,658,268	3.30	3,658,268	0.00	0.64	3,658,268	3.49	3,658,268	0.00
IG8	IG8-4	0.30	4,583,549	3.03	4,583,549	0.00	0.19	4,542,909	2.97	4,542,909	0.00	0.38	4,542,909	3.58	4,542,909	0.00	0.39	4,542,909	3.34	4,542,909	0.00
IG8	IG8-5	0.14	3,733,174	2.92	3,733,174	0.00	0.25	3,733,174	3.04	3,733,174	0.00	0.27	3,733,174	3.35	3,733,174	0.00	0.28	3,733,174	3.36	3,733,174	0.00
IG9	IG9-1	0.47	5,219,791	3.15	5,219,791	0.00	0.25	4,665,499	3.09	4,665,499	0.00	0.45	5,219,791	3.42	5,219,791	0.00	0.55	4,292,777	3.38	4,292,777	0.00
IG9	IG9-2	0.47	4,598,619	3.23	4,598,619	0.00	0.39	4,573,112	3.17	4,573,112	0.00	0.53	4,573,112	3.41	4,573,112	0.00	0.56	4,573,112	3.41	4,573,112	0.00
IG9	IG9-3	0.27	4,952,494	3.23	4,952,494	0.00	0.36	4,952,494	3.29	4,952,494	0.00	0.36	4,952,494	3.44	4,952,494	0.00	0.33	4,952,494	3.40	4,952,494	0.00
IG9	IG9-4	0.28	3,923,530	3.08	3,923,530	0.00	0.23	3,750,090	3.11	3,750,090	0.00	0.42	3,923,530	3.44	3,923,530	0.00	0.52	3,750,090	3.29	3,750,090	0.00
IG9	IG9-5	0.33	4,735,073	3.10	4,735,073	0.00	0.30	4,735,073	3.14	4,735,073	0.00	0.28	4,735,073	3.48	4,735,073	0.00	0.39	4,735,073	3.31	4,735,073	0.00
IG10	IG10-1	0.44	4,658,423	3.47	4,658,423	0.00	0.36	3,903,671	3.39	3,903,671	0.00	0.70	3,903,671	3.91	3,903,671	0.00	0.55	3,903,671	3.71	3,903,671	0.00
IG10	IG10-2	0.27	3,774,339	3.54	3,774,339	0.00	0.28	3,774,339	3.41	3,774,339	0.00	0.44	3,774,339	3.70	3,774,339	0.00	0.39	3,774,339	3.89	3,774,339	0.00
IG10	IG10-3	0.31	4,750,681	3.62	4,750,681	0.00	0.28	4,750,681	3.46	4,750,681	0.00	0.56	4,750,681	3.93	4,750,681	0.00	0.42	4,750,681	3.83	4,750,681	0.00
IG10	IG10-4	0.42	4,425,236	3.61	4,425,236	0.00	0.36	4,425,236	3.52	4,425,236	0.00	0.38	4,425,236	3.98	4,425,236	0.00	0.58	4,425,236	3.85	4,425,236	0.00
IG10	IG10-5	0.11	4,342,468	3.46	4,342,468	0.00	0.16	4,342,468	3.53	4,342,468	0.00	0.31	4,342,468	3.93	4,342,468	0.00	0.20	4,342,468	3.67	4,342,468	0.00
IG11	IG11-1	0.78	4,228,744	3.72	4,228,744	0.00	0.91	3,960,353	3.58	3,960,353	0.00	1.17	4,228,744	4.34	4,228,744	0.00	1.08	3,960,353	3.90	3,960,353	0.00
IG11	IG11-2	0.50	3,977,875	3.70	3,977,875	0.00	0.42	3,821,797	3.82	3,821,797	0.00	0.92	3,977,875	4.23	3,977,875	0.00	0.61	3,821,797	4.17	3,821,797	0.00
IG11	IG11-3	0.38	4,035,794	3.95	4,035,794	0.00	0.56	4,710,559	3.77	4,710,559	0.00	0.63	4,035,794	4.48	4,035,794	0.00	0.80	4,710,559	4.03	4,710,559	0.00
IG11	IG11-4	0.61	5,037,399	3.77	5,037,399	0.00	0.67	4,896,727	3.79	4,896,727	0.00	1.02	4,734,164	4.22	4,734,164	0.00	0.89	4,734,164	3.78	4,734,164	0.00
IG11	IG11-5	1.20	3,994,538	3.59	3,998,188	0.09	1.30	3,994,538	3.69	3,998,188	0.09	1.67	3,994,538	4.44	3,994,538	0.00	1.52	3,994,538	4.07	3,994,538	0.00
IG12	IG12-1	1.08	4,437,597	4.23	4,437,597	0.00	0.89	4,224,125	4.12	4,224,125	0.00	1.19	4,224,125	4.57	4,227,776	0.09	1.09	4,224,125	4.34	4,225,951	0.04
IG12	IG12-2	0.66	4,112,972	4.11	4,114,797	0.04	1.16	4,291,579	3.94	4,291,579	0.00	0.94	4,112,972	4.67	4,112,972	0.00	1.30	4,291,579	4.20	4,291,579	0.00
IG12	IG12-3	0.39	4,390,875	4.05	4,392,700	0.04	0.41	4,390,875	4.13	4,390,875	0.00	1.53	4,050,894	4.27	4,050,894	0.00	1.47	4,050,894	4.15	4,052,719	0.05
IG12	IG12-4	0.59	4,989,157	3.82	4,990,982	0.04	1.14	4,583,627	3.87	4,583,627	0.00	1.25	4,583,627	4.24	4,583,627	0.00	1.38	4,583,627	4.24	4,589,102	0.12
IG12	IG12-5	1.49	4,509,606	3.86	4,509,606	0.00	1.56	4,509,606	4.07	4,509,606	0.00	1.67	4,509,606	4.11	4,509,606	0.00	1.69	4,509,606	4.15	4,509,606	0.00
IG13	IG13-1	5.28	4,831,064	4.36	4,831,064	0.00	4.48	4,712,353	4.15	4,714,178	0.04	5.67	4,831,064	4.58	4,831,064	0.00	4.66	4,712,353	4.36	4,712,353	0.00
IG13	IG13-2	5.08	4,474,155	4.29	4,474,155	0.00	5.33	4,474,155	4.18	4,477,805	0.08	5.45	4,474,155	4.69	4,481,462	0.16	5.50	4,474,155	4.48	4,474,155	0.00
IG13	IG13-3	2.05	4,929,602	4.17	4,929,602	0.00	1.83	4,324,790	4.44	4,324,790	0.00	2.25	4,929,602	4.62	4,929,602	0.00	1.63	4,324,790	4.62	4,324,790	0.00
IG13	IG13-4	1.55	5,144,454	4.22	5,144,454	0.00	1.48	5,144,454	4.27	5,144,454	0.00	1.60	5,144,454	4.47	5,144,454	0.00	1.70	5,144,454	4.78	5,144,454	0.00
IG13	IG13-5	1.20	5,048,107	4.09	5,048,107	0.00	1.61	4,225,749	4.50	4,225,749	0.00	1.53	4,225,749	4.61	4,225,749	0.00	1.66	4,225,749	4.64	4,225,749	0.00
IG14	IG14-1	4.91	4,344,414	4.50	4,344,414	0.00	2.05	4,400,567	4.44	4,400,567	0.00	4.89	4,344,414	4.90	4,344,414	0.00	2.33	4,400,567	4.64	4,407,867	0.17
IG14	IG14-2	1.80	5,371,626	4.56	5,371,626	0.00	3.08	5,580,311	4.60	5,580,311	0.00	1.74	5,371,626	4.76	5,371,626	0.00	2.00	4,895,644	4.68	4,910,251	0.30
IG14	IG14-3	1.91	4,587,743	4.49	4,587,743	0.00	2.00	4,406,031	4.67	4,406,031	0.00	2.11	4,587,743	4.77	4,587,743	0.00	2.22	4,406,031	4.91	4,406,031	0.00
IG14	IG14-4	3.27	4,035,018	4.42	4,036,843	0.05	3.38	4,035,018	4.66	4,040,493	0.14	3.49	4,035,018	4.86	4,036,843	0.05	3.50	4,035,018	4.57	4,036,843	0.05
IG14	IG14-5	3.75	4,087,587	4.62	4,087,587	0.00	3.70	4,087,587	4.66	4,093,062	0.13	3.67	4,087,587	5.17	4,089,412	0.04	3.73	4,087,587	4.77	4,087,587	0.00
IG15	IG15-1	4.42	5,037,129	5.25	5,057,204	0.40	11.86	5,183,546	5.02	5,194,496	0.21	4.30	5,037,129	5.58	5,048,079	0.22	12.05	5,183,546	5.26	5,183,546	0.00
IG15	IG15-2	114.72	5,958,259	5.21	5,971,036	0.21	139.36	4,077,161	5.45	4,077,161	0.00	107.83	5,958,259	5.39	5,960,086	0.03	138.94	4,077,161	5.68	4,077,161	0.00
IG15	IG15-3	9.56	4,486,041	5.42	4,491,516	0.12	9.20	4,486,041	5.39	4,493,341	0.16	9.22	4,486,041	5.82	4,493,341	0.16	9.45	4,486,041	5.99	4,513,416	0.61
IG15	IG15-4	21.86	4,028,092	5.15	4,037,217	0.23	26.17	4,028,729	5.17	4,052,454	0.59	28.80	4,028,092	5.61	4,028,092	0.00	26.01	4,028,729	5.62	4,043,329	0.36
IG15	IG15-5	6.19	6,369,039	5.13	6,381,814	0.20	600.20	4,647,800	5.20	4,664,225	0.35	30.27	5,270,258	5.66	5,284,858	0.28	600.28	4,647,800	5.45	4,647,800	0.00
IG16	IG16-1	14.38	4,413,028	6.04	4,425,821	0.29	24.47	4,365,359	6.00	4,392,734	0.63	18.59	4,413,028	6.36	4,423,996	0.25	24.99	4,365,359	6.43	4,390,909	0.59
IG16	IG16-2	28.11	6,003,144	6.08	6,025,044	0.36	107.17	5,007,972	6.05	5,022,572	0.29	148.05	5,007,972	6.17	5,028,047	0.40	110.03	5,007,972	6.21	5,026,222	0.36
IG16	IG16-3	73.95	5,617,390	5.91	5,630,165	0.23	73.59	5,381,149	6.03	5,395,760	0.27	114.58	5,053,359	6.02	5,060,670	0.14	24.33	4,812,006	6.30	4,817,492	0.11
IG16	IG16-4	6.92	5,205,447	5.92	5,216,397	0.21	14.09	5,014,716	5.72	5,023,841	0.18	600.27	4,107,296	5.91	4,116,421	0.22	14.60	5,014,716	6.22	5,042,091	0.55
IG16	IG16-5	600.39	3,995,430	5.94	3,988,130	-0.18	8.77	3,849,569	6.01	3,853,219	0.09	600.66	3,995,430	6.25	3,997,255	0.05	600.39	3,995,430	6.18	4,002,730	0.18
IG17	IG17-1	287.44	4,825,353	6.54	4,852,728	0.57	225.39	5,047,236	6.62	5,072,786	0.51	389.39	4,825,353	6.94	4,839,953	0.30	226.42	5,047,236	7.37	5,060,011	0.25
IG17	IG17-2	600.30	-	9.19	6,489,170		16.13	4,600,472	6.58	4,616,897	0.36	23.97	4,600,472	7.04	4,609,597	0.20	16.20	4,600,472	7.19	4,607,772	0.16
IG17	IG17-3	600.41	-	9.02	6,366,897		9.63	4,310,443	6.68	4,332,346	0.51	556.66	4,419,803	6.88	4,450,834	0.70	368.53	4,419,803	6.95	4,428,934	0.21
IG17	IG17-4	169.55	6,164,200	7.01	6,184,275	0.33	60.58	5,552,562	6.97	5,561,687	0.16	87.75	5,552,562	7.20	5,576,287	0.43	62.72	5,552,562	7.36	5,576,287	0.43
IG17	IG17-5	600.39	-	9.46	6,308,979		600.45	-	9.38	6,293,261		600.31	-	9.22	6,283,187		600.62	-	10.01	6,285,012	
IG18	IG18-1	600.45	-	9.75	6,611,761		332.66	5,004,369	7.47	5,033,569	0.58	600.59	-	10.21	5,846,814		600.64	-	10.16	5,852,289	
IG18	IG18-2	600.28	-	9.90	6,883,039		600.42	-	9.60	6,582,866		600.41	-	9.81	6,377,916		600.72	-	10.11	6,370,616	
IG18	IG18-3	145.89	5,373,793	7.43	5,408,468	0.65	99.49	4,414,251	7.54	4,454,401	0.91	11.61	4,947,028	8.15	4,992,653	0.92	600.55	-	10.63	5,400,707	
IG18	IG18-4	600.33	7,081,833	9.61	6,950,442	-1.86	164.03	5,197,622	7.77	5,221,347	0.46	600.31	-	10.05	5,328,717		164.94	5,197,622	8.42	5,219,522	0.42
IG18	IG18-5	600.30	-	9.69	7,354,890		600.27	4,634,891	7.54	4,651,320	0.35	600.58	4,640,366	8.31	4,682,345	0.90	600.41	4,634,891	7.96	4,656,795	0.47
IG19	IG19-1	600.49	-	10.58	7,256,709		600.53	4,951,632	8.50	4,927,907	-0.48	600.72	4,855,906	8.88	4,804,806	-1.05	600.70	4,907,832	8.58	4,916,957	0.19
IG19	IG19-2	600.37	-	10.29	7,805,290		600.72	4,596,924	9.16	4,624,299	0.60	194.28	4,714,272	8.28	4,752,597	0.81	600.70	4,615,174	8.81	4,615,174	0.00
IG19	IG19-3	600.33	-	10.39	5,665,950		600.64	-	10.88	6,076,843		100.11	4,349,979	8.73	4,373,704	0.55	600.81	-	11.34	5,197,391	
IG19	IG19-4	600.20	-	10.26	6,489,254		600.42	5,187,606	8.53	5,191,260	0.07	600.36	5,193,081	8.64	5,198,556	0.11	600.44	5,187,606	8.63	5,202,206	0.28
IG19	IG19-5	600.45	-	10.19	6,579,591		177.60	5,939,696	8.23	5,976,196	0.61	600.73	5,243,969	8.84	5,077,894	-3.17	600.50	-	10.87	6,781,823	
IG20	IG20-1	600.31	-	11.66	6,413,224		600.58	-	11.43	6,611,717		600.64	-	12.52	6,413,224		600.87	-	11.94	6,110,349	
IG20	IG20-2	600.44	-	11.43	8,315,824		600.56	4,725,244	9.60	4,675,969	-1.04	600.50	-	11.34	7,062,992		600.59	4,774,519	9.39	4,659,544	-2.41
IG20	IG20-3	600.58	-	12.09	6,675,097		600.53	-	11.74	5,888,865		600.72	-	12.03	5,856,002		211.02	4,480,673	9.55	4,520,826	0.90
IG20	IG20-4	600.38	-	11.70	6,217,647		214.97	4,862,975	9.46	4,925,041	1.28	600.67	6,355,538	11.98	5,826,288	-8.33	212.13	4,862,975	9.21	4,921,391	1.20
IG20	IG20-5	600.28	-	11.23	6,653,269		600.52	-	11.30	5,563,693		206.95	5,224,505	9.43	5,266,480	0.80	600.45	-	11.58	5,558,192	

* Gap (%) = ((“Objective function value obtained by the corresponding HH”-“Objective function value obtained by the corresponding DH”)/(“Objective function value obtained by the corresponding DH”))*100. Green highlighted cells correspond to positive gap values (higher objective function value). Blue highlighted cells correspond to negative gap values (lower objective function value).

Table 8. Comparison of the Results of the Proposed Solution Methods with the Best Objective Function Values Obtained for Small and Medium-Sized Problem Instances

Instance Group	**Test Instance**	Best Objective Function Value	**Optimal Solution**		**DH1**		**DH2**		**DH3**		**DH4**		**HH1**		**HH2**		**HH3**		**HH4**		**SA**	
			CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **
IG1	IG1-1	3,861,134	0.06	0.00	0.20	0.00	0.20	0.00	0.34	1.54	0.50	1.54	1.85	0.00	1.77	0.00	2.14	1.54	2.48	1.54	2.01	0.00
IG1	IG1-2	4,698,476	0.08	0.00	0.19	0.00	0.14	0.00	0.22	0.00	0.37	0.00	1.79	0.00	1.76	0.00	1.92	0.00	2.05	0.00	1.84	0.00
IG1	IG1-3	3,777,315	0.11	0.00	0.22	0.00	0.25	0.00	0.16	0.00	0.25	0.00	1.95	0.00	1.82	0.00	1.98	0.00	2.11	0.00	1.89	0.00
IG1	IG1-4	4,237,421	0.03	0.00	0.16	0.00	0.09	0.00	0.28	0.00	0.23	0.00	1.91	0.00	1.71	0.00	2.04	0.00	1.99	0.00	1.83	0.00
IG1	IG1-5	4,353,505	0.11	0.00	0.25	5.74	0.09	0.00	0.36	0.00	0.17	0.00	1.89	5.74	1.78	0.00	2.03	0.00	1.93	0.00	1.89	0.00
IG2	IG2-1	4,854,406	0.09	0.00	0.17	0.00	0.23	0.00	0.20	0.00	0.36	0.00	2.03	0.00	1.98	0.00	2.17	0.00	2.33	0.00	2.16	0.00
IG2	IG2-2	3,953,906	0.11	0.00	0.20	0.00	0.14	0.00	0.31	0.25	0.31	0.25	2.07	0.00	2.03	0.00	2.34	0.25	2.32	0.25	2.07	0.25
IG2	IG2-3	3,741,404	0.03	0.00	0.14	7.69	0.23	7.69	0.36	0.00	0.39	0.00	2.27	7.69	2.32	7.69	2.41	0.00	2.40	0.00	2.10	0.00
IG2	IG2-4	4,470,052	0.03	0.00	0.17	1.45	0.17	0.00	0.27	0.00	0.28	0.00	2.20	1.45	1.97	0.00	2.29	0.00	2.32	0.00	2.06	0.00
IG2	IG2-5	3,959,135	0.02	0.00	0.16	0.00	0.16	0.00	0.27	0.00	0.22	0.00	2.00	0.00	1.99	0.00	2.30	0.00	2.28	0.00	2.10	0.00
IG3	IG3-1	4,265,921	0.11	0.00	0.27	4.36	0.24	0.00	0.33	0.00	0.23	0.00	2.26	4.36	2.38	0.00	2.48	0.00	2.58	0.00	2.40	0.00
IG3	IG3-2	4,089,375	0.11	0.00	0.23	10.04	0.14	10.04	0.20	0.00	0.30	0.00	2.22	10.04	2.16	10.04	2.36	0.00	2.54	0.00	2.47	0.00
IG3	IG3-3	4,362,484	0.05	0.00	0.09	20.12	0.14	0.00	0.30	0.00	0.23	0.00	2.19	20.12	2.12	0.00	2.55	0.00	2.47	0.00	2.42	0.00
IG3	IG3-4	4,531,804	0.05	0.00	0.17	0.00	0.25	0.00	0.28	0.00	0.30	0.00	2.19	0.00	2.22	0.00	2.40	0.00	2.42	0.00	2.36	0.00
IG3	IG3-5	4,255,258	0.02	0.00	0.17	14.46	0.19	0.00	0.28	0.00	0.37	0.00	2.75	14.46	2.29	0.00	2.54	0.00	2.70	0.00	2.38	0.00
IG4	IG4-1	4,434,085	0.03	0.00	0.17	0.00	0.23	0.00	0.36	2.55	0.19	2.55	2.48	0.00	2.39	0.00	2.94	2.55	2.91	2.55	2.48	0.00
IG4	IG4-2	3,673,906	0.02	0.00	0.06	6.56	0.13	6.56	0.34	0.00	0.33	0.00	2.29	6.56	2.42	6.56	2.78	0.00	2.78	0.00	2.54	0.00
IG4	IG4-3	4,239,826	0.06	0.00	0.16	0.00	0.22	0.00	0.41	0.00	0.30	0.00	2.36	0.00	2.39	0.00	2.73	0.00	2.73	0.00	2.58	0.00
IG4	IG4-4	3,965,068	0.11	0.00	0.19	2.05	0.11	2.05	0.17	2.05	0.41	2.05	2.45	2.05	2.41	2.05	2.45	2.05	2.90	2.05	2.54	0.00
IG4	IG4-5	4,291,573	0.06	0.00	0.16	3.08	0.19	0.00	0.28	0.00	0.27	0.00	2.49	3.08	2.41	0.00	2.66	0.00	2.62	0.00	2.40	0.00
IG5	IG5-1	3,978,757	0.03	0.00	0.11	5.68	0.17	5.68	0.41	0.00	0.39	0.00	2.51	5.68	2.57	5.68	2.83	0.00	2.90	0.00	2.59	0.00
IG5	IG5-2	3,935,648	0.02	0.00	0.17	0.00	0.20	0.00	0.41	0.00	0.36	0.00	2.60	0.00	2.57	0.00	2.99	0.00	3.01	0.00	2.62	0.00
IG5	IG5-3	4,308,944	0.02	0.00	0.09	7.86	0.09	0.00	0.28	7.86	0.24	0.00	2.54	7.86	2.45	0.00	2.86	7.86	2.87	0.00	2.57	0.00
IG5	IG5-4	3,741,123	0.05	0.00	0.09	0.00	0.10	0.00	0.39	0.00	0.34	0.00	2.48	0.00	2.52	0.00	2.91	0.00	3.00	0.00	2.60	0.00
IG5	IG5-5	4,337,916	0.05	0.04	0.19	0.00	0.28	0.00	0.28	0.00	0.25	0.00	2.54	0.00	2.62	0.00	2.97	0.00	2.74	0.00	2.52	0.00
IG6	IG6-1	4,287,253	0.11	0.00	0.22	6.17	0.16	6.17	0.41	0.00	0.35	0.00	2.76	6.17	2.73	6.17	3.04	0.00	3.00	0.00	2.74	0.00
IG6	IG6-2	4,456,767	0.08	0.00	0.34	0.00	0.36	0.00	0.39	0.00	0.37	0.00	2.77	0.00	2.66	0.00	2.99	0.00	2.97	0.00	2.83	0.00
IG6	IG6-3	4,608,080	0.03	0.00	0.14	5.37	0.25	0.00	0.28	5.37	0.31	0.00	2.67	5.37	2.76	0.00	2.94	5.37	3.06	0.00	2.75	0.00
IG6	IG6-4	4,035,724	0.02	0.00	0.31	5.08	0.30	0.88	0.25	0.88	0.42	0.88	2.68	5.08	2.84	0.88	3.00	0.88	3.23	0.88	2.90	0.00
IG6	IG6-5	3,972,268	0.05	0.00	0.20	22.20	0.35	0.00	0.41	0.00	0.37	0.00	2.66	22.20	2.74	0.00	3.06	0.00	3.08	0.00	2.72	0.00
IG7	IG7-1	4,259,947	0.08	0.00	0.31	9.80	0.20	0.00	0.22	9.80	0.34	0.00	2.91	9.80	2.88	0.00	3.01	9.80	3.09	0.00	3.06	0.00
IG7	IG7-2	5,361,219	0.09	0.00	0.33	0.00	0.31	0.00	0.53	0.00	0.47	0.00	2.85	0.00	2.90	0.00	3.28	0.00	3.24	0.00	2.99	0.00
IG7	IG7-3	4,007,612	0.02	0.00	0.28	0.00	0.37	0.00	0.41	0.00	0.31	0.00	2.95	0.00	2.94	0.00	3.21	0.00	3.14	0.00	3.15	0.00
IG7	IG7-4	3,663,014	0.03	0.00	0.28	0.00	0.22	0.00	0.45	0.00	0.22	0.00	2.92	0.00	2.84	0.00	3.17	0.00	3.12	0.00	3.08	0.00
IG7	IG7-5	4,883,305	0.09	0.00	0.34	0.00	0.13	0.00	0.44	0.00	0.34	0.00	2.92	0.00	2.88	0.00	3.19	0.00	3.30	0.00	3.16	0.00
IG8	IG8-1	3,981,885	0.03	1.37	0.20	3.40	0.33	0.00	0.38	3.40	0.34	0.00	3.00	3.40	3.29	0.00	3.44	3.40	3.63	0.00	3.60	0.00
IG8	**IG8-1***	3,981,885	0.03	0.00	0.20	3.40	0.33	0.00	0.38	3.40	0.34	0.00	3.00	3.40	3.29	0.00	3.44	3.40	3.63	0.00	3.60	0.00
IG8	IG8-2	3,774,709	0.05	2.76	0.39	22.48	0.45	0.00	0.49	0.00	0.44	0.00	2.96	22.48	3.12	0.00	3.42	0.00	3.42	0.00	3.31	0.00
IG8	IG8-3	3,658,268	0.11	0.50	0.42	0.00	0.49	0.00	0.52	0.00	0.64	0.00	2.97	0.00	3.13	0.00	3.30	0.00	3.49	0.00	3.33	0.00
IG8	IG8-4	4,542,909	0.11	1.37	0.30	0.89	0.19	0.00	0.38	0.00	0.39	0.00	3.03	0.89	2.97	0.00	3.58	0.00	3.34	0.00	3.15	1.31
IG8	IG8-5	3,733,174	0.05	2.20	0.14	0.00	0.25	0.00	0.27	0.00	0.28	0.00	2.92	0.00	3.04	0.00	3.35	0.00	3.36	0.00	3.31	0.00
IG9	IG9-1	4,292,777	0.09	1.06	0.47	21.59	0.25	8.68	0.45	21.59	0.55	0.00	3.15	21.59	3.09	8.68	3.42	21.59	3.38	0.00	3.44	0.00
IG9	**IG9-1***	4,292,777	0.09	0.77	0.47	21.59	0.25	8.68	0.45	21.59	0.55	0.00	3.15	21.59	3.09	8.68	3.42	21.59	3.38	0.00	3.44	0.00
IG9	IG9-2	4,573,112	0.05	0.88	0.47	0.56	0.39	0.00	0.53	0.00	0.56	0.00	3.23	0.56	3.17	0.00	3.41	0.00	3.41	0.00	3.33	0.00
IG9	IG9-3	4,952,494	0.02	2.03	0.27	0.00	0.36	0.00	0.36	0.00	0.33	0.00	3.23	0.00	3.29	0.00	3.44	0.00	3.40	0.00	3.48	0.00
IG9	IG9-4	3,750,090	0.08	2.68	0.28	4.62	0.23	0.00	0.42	4.62	0.52	0.00	3.08	4.62	3.11	0.00	3.44	4.62	3.29	0.00	3.51	0.00
IG9	IG9-5	3,896,869	0.06	2.01	0.33	21.51	0.30	21.51	0.28	21.51	0.39	21.51	3.10	21.51	3.14	21.51	3.48	21.51	3.31	21.51	3.48	0.00
IG10	IG10-1	3,903,671	0.06	1.12	0.44	19.33	0.36	0.00	0.70	0.00	0.55	0.00	3.47	19.33	3.39	0.00	3.91	0.00	3.71	0.00	3.75	0.59
IG10	**IG10-1***	3,903,671	0.06	1.12	0.44	19.33	0.36	0.00	0.70	0.00	0.55	0.00	3.47	19.33	3.39	0.00	3.91	0.00	3.71	0.00	3.75	0.59
IG10	IG10-2	3,774,339	0.06	2.95	0.27	0.00	0.28	0.00	0.44	0.00	0.39	0.00	3.54	0.00	3.41	0.00	3.70	0.00	3.89	0.00	3.81	0.00
IG10	IG10-3	4,165,250	0.03	16.29	0.31	14.06	0.28	14.06	0.56	14.06	0.42	14.06	3.62	14.06	3.46	14.06	3.93	14.06	3.83	14.06	3.80	0.00
IG10	IG10-4	4,425,236	0.05	1.36	0.42	0.00	0.36	0.00	0.38	0.00	0.58	0.00	3.61	0.00	3.52	0.00	3.98	0.00	3.85	0.00	4.19	0.00
IG10	IG10-5	4,342,468	0.02	4.24	0.11	0.00	0.16	0.00	0.31	0.00	0.20	0.00	3.46	0.00	3.53	0.00	3.93	0.00	3.67	0.00	4.04	0.00

* Indicates that the corresponding problem instance is solved using the CPU time limitation of 120 hours.

** Gap (%) = ((“Objective function value obtained by the corresponding solution method”-“Minimum of the objective function values obtained by all proposed solution methods”)/ (“Minimum of the objective function values obtained by all proposed solution methods”))*100. Green highlighted cells correspond to positive gap values (higher objective function value).

Table 8. Cont'd

Instance Group	Test Instance	Best Objective Function Value	Optimal Solution		DH1		DH2		DH3		DH4		HH1		HH2		HH3		HH4		SA	
			CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **	CPU Time (Seconds)	Gap (%) **
IG11	IG11-1	3,960,353	0.03	34.00	0.78	6.78	0.91	0.00	1.17	6.78	1.08	0.00	3.72	6.78	3.58	0.00	4.34	6.78	3.90	0.00	4.12	0.00
IG11	**IG11-1***	3,960,353	0.03	10.19	0.78	6.78	0.91	0.00	1.17	6.78	1.08	0.00	3.72	6.78	3.58	0.00	4.34	6.78	3.90	0.00	4.12	0.00
IG11	IG11-2	3,821,797	0.08	3.72	0.50	4.08	0.42	0.00	0.92	4.08	0.61	0.00	3.70	4.08	3.82	0.00	4.23	4.08	4.17	0.00	4.12	0.00
IG11	IG11-3	4,035,794	0.08	4.34	0.38	0.00	0.56	16.72	0.63	0.00	0.80	16.72	3.95	0.00	3.77	16.72	4.48	0.00	4.03	16.72	4.63	0.00
IG11	IG11-4	4,734,164	0.08	3.78	0.61	6.41	0.67	3.43	1.02	0.00	0.89	0.00	3.77	6.41	3.79	3.43	4.22	0.00	3.78	0.00	4.08	0.00
IG11	IG11-5	3,994,538	0.02	4.71	1.20	0.00	1.30	0.00	1.67	0.00	1.52	0.00	3.59	0.09	3.69	0.09	4.44	0.00	4.07	0.00	4.29	0.00
IG12	IG12-1	4,224,125	0.11	9.55	1.08	5.05	0.89	0.00	1.19	0.00	1.09	0.00	4.23	5.05	4.12	0.00	4.57	0.09	4.34	0.04	4.59	0.00
IG12	**IG12-1***	4,224,125	0.11	8.60	1.08	5.05	0.89	0.00	1.19	0.00	1.09	0.00	4.23	5.05	4.12	0.00	4.57	0.09	4.34	0.04	4.59	0.00
IG12	IG12-2	4,112,972	0.03	1.86	0.66	0.00	1.16	4.34	0.94	0.00	1.30	4.34	4.11	0.04	3.94	4.34	4.67	0.00	4.20	4.34	4.67	0.00
IG12	IG12-3	4,050,894	0.05	25.36	0.39	8.39	0.41	8.39	1.53	0.00	1.47	0.00	4.05	8.44	4.13	8.39	4.27	0.00	4.15	0.05	4.37	0.00
IG12	IG12-4	4,583,627	0.05	4.88	0.59	8.85	1.14	0.00	1.25	0.00	1.38	0.00	3.82	8.89	3.87	0.00	4.24	0.00	4.24	0.12	4.38	0.12
IG12	IG12-5	4,509,606	0.05	18.75	1.49	0.00	1.56	0.00	1.67	0.00	1.69	0.00	3.86	0.00	4.07	0.00	4.11	0.00	4.15	0.00	4.44	0.00
IG13	IG13-1	4,608,402	0.06	29.01	5.28	4.83	4.48	2.26	5.67	4.83	4.66	2.26	4.36	4.83	4.15	2.30	4.58	4.83	4.36	2.26	4.79	0.00
IG13	**IG13-1***	4,608,402	0.06	28.26	5.28	4.83	4.48	2.26	5.67	4.83	4.66	2.26	4.36	4.83	4.15	2.30	4.58	4.83	4.36	2.26	4.79	0.00
IG13	IG13-2	4,175,580	0.02	1.75	5.08	7.15	5.33	7.15	5.45	7.15	5.50	7.15	4.29	7.15	4.18	7.24	4.69	7.33	4.48	7.15	4.71	0.00
IG13	IG13-3	4,324,790	0.02	3.67	2.05	13.98	1.83	0.00	2.25	13.98	1.63	0.00	4.17	13.98	4.44	0.00	4.62	13.98	4.62	0.00	4.83	0.08
IG13	IG13-4	3,849,344	0.11	11.11	1.55	33.64	1.48	33.64	1.60	33.64	1.70	33.64	4.22	33.64	4.27	33.65	4.47	33.64	4.78	33.64	4.63	0.00
IG13	IG13-5	4,225,749	0.02	54.16	1.20	19.46	1.61	0.00	1.53	0.00	1.66	0.00	4.09	19.46	4.50	0.00	4.61	0.00	4.64	0.00	4.73	0.00
IG14	IG14-1	4,135,219	0.11	29.69	4.91	5.06	2.05	6.42	4.89	5.06	2.33	6.42	4.50	5.06	4.44	6.42	4.90	5.06	4.64	6.59	4.72	0.00
IG14	**IG14-1***	4,135,219	0.11	8.17	4.91	5.06	2.05	6.42	4.89	5.06	2.33	6.42	4.50	5.06	4.44	6.42	4.90	5.06	4.64	6.59	4.72	0.00
IG14	IG14-2	4,895,644	0.08	30.34	1.80	9.72	3.08	13.99	1.74	9.72	2.00	0.00	4.56	9.72	4.60	13.99	4.76	9.72	4.68	0.30	4.81	0.00
IG14	IG14-3	4,406,031	0.02	65.29	1.91	4.12	2.00	0.00	2.11	4.12	2.22	0.00	4.49	4.12	4.67	0.00	4.77	4.12	4.91	0.00	4.89	0.08
IG14	IG14-4	4,035,018	0.03	4.84	3.27	0.00	3.38	0.00	3.49	0.00	3.50	0.00	4.42	0.05	4.66	0.14	4.86	0.05	4.57	0.05	4.80	0.00
IG14	IG14-5	4,087,587	0.06	81.18	3.75	0.00	3.70	0.00	3.67	0.00	3.73	0.00	4.62	0.00	4.66	0.13	5.17	0.04	4.77	0.00	5.22	0.09
IG15	IG15-1	4,641,011	0.05	15.73	4.42	8.54	11.86	11.69	4.30	8.54	12.05	11.69	5.25	8.97	5.02	11.93	5.58	8.77	5.26	11.69	5.79	0.00
IG15	**IG15-1***	4,641,011	0.05	13.37	4.42	8.54	11.86	11.69	4.30	8.54	12.05	11.69	5.25	8.97	5.02	11.93	5.58	8.77	5.26	11.69	5.79	0.00
IG15	IG15-2	4,077,161	0.13	100.84	114.72	46.14	139.36	0.00	107.83	46.14	138.94	0.00	5.21	46.45	5.45	0.00	5.39	46.18	5.68	0.00	5.56	0.00
IG15	IG15-3	4,486,041	0.06	85.12	9.56	0.00	9.20	0.00	9.22	0.00	9.45	0.00	5.42	0.12	5.39	0.16	5.82	0.16	5.99	0.61	5.90	0.28
IG15	IG15-4	4,028,092	0.06	41.77	21.86	0.00	26.17	0.02	28.80	0.00	26.01	0.02	5.15	0.23	5.17	0.60	5.61	0.00	5.62	0.38	5.59	0.27
IG15	IG15-5	4,647,800	0.08	37.00	6.19	37.03	600.20	0.00	30.27	13.39	600.28	0.00	5.13	37.31	5.20	0.35	5.66	13.71	5.45	0.00	5.35	0.31
IG16	IG16-1	4,365,359	0.05	40.30	14.38	1.09	24.47	0.00	18.59	1.09	24.99	0.00	6.04	1.39	6.00	0.63	6.36	1.34	6.43	0.59	6.02	0.63
IG16	**IG16-1***	4,365,359	0.05	40.30	14.38	1.09	24.47	0.00	18.59	1.09	24.99	0.00	6.04	1.39	6.00	0.63	6.36	1.34	6.43	0.59	6.02	0.63
IG16	IG16-2	5,007,972	0.11	42.39	28.11	19.87	107.17	0.00	148.05	0.00	110.03	0.00	6.08	20.31	6.05	0.29	6.17	0.40	6.21	0.36	6.26	0.44
IG16	IG16-3	4,812,006	0.06	83.97	73.95	16.74	73.59	11.83	114.58	5.02	24.33	0.00	5.91	17.00	6.03	12.13	6.02	5.17	6.30	0.11	5.98	0.46
IG16	IG16-4	4,107,296	0.09	29.68	6.92	26.74	14.09	22.09	600.27	0.00	14.60	22.09	5.92	27.00	5.72	22.32	5.91	0.22	6.22	22.76	5.96	0.04
IG16	IG16-5	3,849,569	0.11	37.87	600.39	3.79	8.77	0.00	600.66	3.79	600.39	3.79	5.94	3.60	6.01	0.09	6.25	3.84	6.18	3.98	6.28	0.47
IG17	IG17-1	4,639,934	0.11	9.09	287.44	4.00	225.39	8.78	389.39	4.00	226.42	8.78	6.54	4.59	6.62	9.33	6.94	4.31	7.37	9.05	6.90	0.00
IG17	**IG17-1***	4,639,934	0.11	9.09	287.44	4.00	225.39	8.78	389.39	4.00	226.42	8.78	6.54	4.59	6.62	9.33	6.94	4.31	7.37	9.05	6.90	0.00
IG17	IG17-2	4,600,472	0.11	57.32	600.30	-	16.13	0.00	23.97	0.00	16.20	0.00	9.19	41.05	6.58	0.36	7.04	0.20	7.19	0.16	7.06	0.40
IG17	IG17-3	4,310,443	0.06	142.83	600.41	-	9.63	0.00	556.66	2.54	368.53	2.54	9.02	47.71	6.68	0.51	6.88	3.26	6.95	2.75	7.15	0.47
IG17	IG17-4	5,162,316	0.02	18.74	169.55	19.41	60.58	7.56	87.75	7.56	62.72	7.56	7.01	19.80	6.97	7.74	7.20	8.02	7.36	8.02	6.88	0.00
IG17	IG17-5	5,214,312	0.08	148.23	600.39	-	600.45	-	600.31	-	600.62	-	9.46	20.99	9.38	20.69	9.22	20.50	10.01	20.53	6.98	0.00
IG18	IG18-1	4,896,359	0.03	34.28	600.45	-	332.66	2.21	600.59	-	600.64	-	9.75	35.03	7.47	2.80	10.21	19.41	10.16	19.52	7.58	0.00
IG18	**IG18-1***	4,896,359	0.03	34.28	600.45	-	332.66	2.21	600.59	-	600.64	-	9.75	35.03	7.47	2.80	10.21	19.41	10.16	19.52	7.58	0.00
IG18	IG18-2	5,435,046	0.11	30.04	600.28	-	600.42	-	600.41	-	600.72	-	9.90	26.64	9.60	21.12	9.81	17.35	10.11	17.21	7.62	0.00
IG18	IG18-3	4,414,251	0.11	67.62	145.89	21.74	99.49	0.00	11.61	12.07	600.55	-	7.43	22.52	7.54	0.91	8.15	13.10	10.63	22.35	7.86	0.50
IG18	IG18-4	4,544,128	0.03	92.37	600.33	55.85	164.03	14.38	600.31	-	164.94	14.38	9.61	52.95	7.77	14.90	10.05	17.27	8.42	14.86	7.67	0.00
IG18	IG18-5	4,634,891	0.05	160.99	600.30	-	600.27	0.00	600.58	0.12	600.41	0.00	9.69	58.69	7.54	0.35	8.31	1.02	7.96	0.47	7.75	0.63
IG19	IG19-1	4,804,806	0.11	59.99	600.49	-	600.53	3.06	600.72	1.06	600.70	2.14	10.58	51.03	8.50	2.56	8.88	0.00	8.58	2.33	8.68	0.30
IG19	**IG19-1***	4,804,806	0.11	59.99	600.49	-	600.53	3.06	600.72	1.06	600.70	2.14	10.58	51.03	8.50	2.56	8.88	0.00	8.58	2.33	8.68	0.30
IG19	IG19-2	4,596,924	0.06	67.90	600.37	-	600.72	0.00	194.28	2.55	600.70	0.40	10.29	69.79	9.16	0.60	8.28	3.39	8.81	0.40	8.84	0.52
IG19	IG19-3	4,243,403	0.06	60.86	600.33	-	600.64	-	100.11	2.51	600.81	-	10.39	33.52	10.88	43.21	8.73	3.07	11.34	22.48	8.30	0.00
IG19	IG19-4	5,187,606	0.02	46.26	600.20	-	600.42	0.00	600.36	0.11	600.44	0.00	10.26	25.09	8.53	0.07	8.64	0.21	8.63	0.28	8.54	0.21
IG19	IG19-5	5,068,769	0.05	96.21	600.45	-	177.60	17.18	600.73	3.46	600.50	-	10.19	29.81	8.23	17.90	8.84	0.18	10.87	33.80	8.41	0.00
IG20	IG20-1	5,034,573	0.02	137.10	600.31	-	600.58	-	600.64	-	600.87	-	11.66	27.38	11.43	31.33	12.52	27.38	11.94	21.37	9.13	0.00
IG20	**IG20-1***	5,034,573	0.02	137.10	600.31	-	600.58	-	600.64	-	600.87	-	11.66	27.38	11.43	31.33	12.52	27.38	11.94	21.37	9.13	0.00
IG20	IG20-2	4,654,069	0.02	118.93	600.44	-	600.56	1.53	600.50	-	600.59	2.59	11.43	78.68	9.60	0.47	11.34	51.76	9.39	0.12	9.19	0.00
IG20	IG20-3	4,480,673	0.13	107.47	600.58	-	600.53	-	600.72	-	211.02	0.00	12.09	48.98	11.74	31.43	12.03	30.69	9.55	0.90	9.44	0.73
IG20	IG20-4	4,862,975	0.03	72.63	600.38	-	214.97	0.00	600.67	30.69	212.13	0.00	11.70	27.86	9.46	1.28	11.98	19.81	9.21	1.20	9.40	1.46
IG20	IG20-5	4,603,701	0.02	198.93	600.28	-	600.52	-	206.95	13.48	600.45	-	11.23	44.52	11.30	20.85	9.43	14.40	11.58	20.73	9.25	0.00

* Indicates that the corresponding problem instance is solved using the CPU time limitation of 120 hours.

** Gap (%) = ((“Objective function value obtained by the corresponding solution method”-“Minimum of the objective function values obtained by all proposed solution methods”)/ (“Minimum of the objective function values obtained by all proposed solution methods”))*100. Green highlighted cells correspond to positive gap values (higher objective function value).

Table 9. Comparison of the Average Performances of the Proposed Solution Methods with the Best Objective Function Values Obtained for Small and Medium-Sized IGs

Solution		Intance Groups																			
Method	Basic Performance Indicators	IG1	IG2	IG3	IG4	IG5	IG6	IG7	IG8	IG9	IG10	IG11	IG12	IG13	IG14	IG15	IG16	IG17	IG18	IG19	IG20
Optimal Solution Method	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**0.00**	**0.00**	**0.00**	**0.00**	**0.01**	**0.00**	**0.00**	**1.36**	**1.67**	**5.19**	**5.35**	**11.89**	**19.79**	**37.96**	**55.62**	**46.84**	**75.24**	**77.06**	**66.24**	**127.01**
	Standard Deviation	0.00	0.00	0.00	0.00	0.02	0.00	0.00	1.02	0.74	5.66	2.45	8.82	19.57	30.52	32.37	19.06	59.64	47.77	16.54	41.66
	Coefficient of Variation	-	-	-	-	2.00	-	-	0.75	0.44	1.09	0.46	0.74	0.99	0.80	0.58	0.41	0.79	0.62	0.25	0.33
DH1	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	1/5	2/5	0/5	0/5
	Mean Gap (%) **	**1.15**	**1.83**	**9.80**	**2.34**	**2.71**	**7.76**	**1.96**	**5.35**	**9.66**	**6.68**	**3.45**	**4.46**	**15.81**	**3.78**	**18.34**	**13.65**	**11.70**	**38.79**	-	-
	Standard Deviation	2.30	2.98	7.13	2.43	3.39	7.54	3.92	8.65	9.84	8.35	2.97	3.87	10.30	3.62	19.45	9.74	7.71	17.05	-	-
	Coefficient of Variation	2.00	1.63	0.73	1.04	1.25	0.97	2.00	1.62	1.02	1.25	0.86	0.87	0.65	0.96	1.06	0.71	0.66	0.44	-	-
DH2	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	4/5	4/5	4/5	2/5
	Mean Gap (%) **	**0.00**	**1.54**	**2.01**	**1.72**	**1.14**	**1.41**	**0.00**	**0.00**	**6.04**	**2.81**	**4.03**	**2.55**	**8.61**	**4.08**	**2.34**	**6.78**	**4.08**	**4.15**	**5.06**	**0.76**
	Standard Deviation	0.00	3.08	4.02	2.55	2.27	2.40	0.00	0.00	8.43	5.62	6.48	3.37	12.79	5.54	4.67	8.92	4.11	5.98	7.11	0.76
	Coefficient of Variation	-	2.00	2.00	1.48	2.00	1.71	-	-	1.40	2.00	1.61	1.32	1.49	1.36	2.00	1.31	1.01	1.44	1.41	1.00
DH3	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	4/5	2/5	5/5	2/5
	Mean Gap (%) **	**0.31**	**0.05**	**0.00**	**0.92**	**1.57**	**1.25**	**1.96**	**0.68**	**9.55**	**2.81**	**2.17**	**0.00**	**11.92**	**3.78**	**13.61**	**1.98**	**3.52**	**6.09**	**1.94**	**22.09**
	Standard Deviation	0.62	0.10	0.00	1.14	3.14	2.09	3.92	1.36	9.95	5.62	2.79	0.00	11.76	3.62	17.05	2.06	2.73	5.98	1.19	8.60
	Coefficient of Variation	2.00	2.00	-	1.24	2.00	1.67	2.00	2.00	1.04	2.00	1.29	-	0.99	0.96	1.25	1.04	0.78	0.98	0.62	0.39
DH4	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	4/5	2/5	3/5	3/5
	Mean Gap (%) **	**0.31**	**0.05**	**0.00**	**0.92**	**0.00**	**0.18**	**0.00**	**0.00**	**4.30**	**2.81**	**3.34**	**0.87**	**8.61**	**1.28**	**2.34**	**5.18**	**4.72**	**7.19**	**0.85**	**0.86**
	Standard Deviation	0.62	0.10	0.00	1.14	0.00	0.35	0.00	0.00	8.60	5.62	6.69	1.74	12.79	2.57	4.67	8.58	3.59	7.19	0.93	1.22
	Coefficient of Variation	2.00	2.00	-	1.24	-	2.00	-	-	2.00	2.00	2.00	2.00	1.49	2.00	2.00	1.66	0.76	1.00	1.10	1.41
HH1	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5				
	Mean Gap (%) **	**1.15**	**1.83**	**9.80**	**2.34**	**2.71**	**7.76**	**1.96**	**5.35**	**9.66**	**6.68**	**3.47**	**4.48**	**15.81**	**3.79**	**18.62**	**13.86**	**26.83**	**39.17**	**41.85**	**45.48**
	Standard Deviation	2.30	2.98	7.13	2.43	3.39	7.54	3.92	8.65	9.84	8.35	2.95	3.88	10.30	3.61	19.48	9.85	15.60	14.30	16.49	18.73
	Coefficient of Variation	2.00	1.63	0.73	1.04	1.25	0.97	2.00	1.62	1.02	1.25	0.85	0.86	0.65	0.95	1.05	0.71	0.58	0.37	0.39	0.41
HH2	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**0.00**	**1.54**	**2.01**	**1.72**	**1.14**	**1.41**	**0.00**	**0.00**	**6.04**	**2.81**	**4.05**	**2.55**	**8.64**	**4.13**	**2.61**	**7.09**	**7.72**	**8.02**	**12.87**	**17.07**
	Standard Deviation	0.00	3.08	4.02	2.55	2.27	2.40	0.00	0.00	8.43	5.62	6.47	3.37	12.78	5.50	4.66	8.88	7.44	8.43	16.53	13.77
	Coefficient of Variation	-	2.00	2.00	1.48	2.00	1.71	-	-	1.40	2.00	1.60	1.32	1.48	1.33	1.79	1.25	0.96	1.05	1.28	0.81
HH3	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**0.31**	**0.05**	**0.00**	**0.92**	**1.57**	**1.25**	**1.96**	**0.68**	**9.55**	**2.81**	**2.17**	**0.02**	**11.96**	**3.80**	**13.76**	**2.19**	**7.26**	**13.63**	**1.37**	**28.81**
	Standard Deviation	0.62	0.10	0.00	1.14	3.14	2.09	3.92	1.36	9.95	5.62	2.79	0.03	11.74	3.60	17.03	1.97	7.08	6.63	1.52	12.81
	Coefficient of Variation	2.00	2.00	-	1.24	2.00	1.67	2.00	2.00	1.04	2.00	1.29	2.00	0.98	0.95	1.24	0.90	0.98	0.49	1.11	0.44
HH4	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**0.31**	**0.05**	**0.00**	**0.92**	**0.00**	**0.18**	**0.00**	**0.00**	**4.30**	**2.81**	**3.34**	**0.91**	**8.61**	**1.39**	**2.54**	**5.56**	**8.10**	**14.88**	**11.86**	**8.86**
	Standard Deviation	0.62	0.10	0.00	1.14	0.00	0.35	0.00	0.00	8.60	5.62	6.69	1.72	12.79	2.61	4.58	8.71	7.03	7.62	13.79	9.96
	Coefficient of Variation	2.00	2.00	-	1.24	-	2.00	-	-	2.00	2.00	2.00	1.89	1.49	1.88	1.81	1.57	0.87	0.51	1.16	1.12
SA	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**0.00**	**0.05**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.26**	**0.00**	**0.12**	**0.00**	**0.02**	**0.02**	**0.03**	**0.17**	**0.41**	**0.17**	**0.23**	**0.21**	**0.44**
	Standard Deviation	0.00	0.10	0.00	0.00	0.00	0.00	0.00	0.53	0.00	0.24	0.00	0.05	0.03	0.04	0.14	0.19	0.21	0.28	0.20	0.58
	Coefficient of Variation	-	2.00	-	-	-	-	-	2.00	-	2.00	-	2.00	2.00	1.23	0.82	0.48	1.23	1.24	0.95	1.33

* S/P: Number of problem instances for which a feasible solution is obtained by the proposed solution method within the time limits/Total number of problem instances in the instance group.

** Mean Gap (%): Mean of gap values of the problem instances belonging to the related instance group. Gap (%) = ((“Objective function value obtained by the corresponding solution method”-“Minimum of the objective function values obtained by all proposed solution methods”)/ (“Minimum of the objective function values obtained by all proposed solution methods”))*100. Green highlighted cells indicates the lowest mean gap values for the corresponding IG.

Best (minimum) objective function value obtained among all heuristics for each problem instance is used as a base for the comparisons presented in Tables 10 and 11. As it can be seen from the tables, SA finds the best objective function value for 95 large-sized problem instances and provides quite acceptable percentage gap values for the remaining 5 instances, ranging from 0.48% to 8.66%. SA also has the lowest mean percentage gap value for all instance groups. Other heuristic methods have deviating performances in finding the best or near-best solutions.

Table 10. Comparison of the Results of the Proposed Solution Methods with the Best Objective Function Values Obtained for Large-Sized Problem Instances

Instance Group	Test Instance	Best Objective Function Value	HH1		HH2		HH3		HH4		SA	
			CPU Time (Seconds)	GAP (%) *	CPU Time (Seconds)	GAP (%) *	CPU Time (Seconds)	GAP (%) *	CPU Time (Seconds)	GAP (%) *	CPU Time (Seconds)	GAP (%) *
IG21	IG21-1	9,194,372	11.49	8.21	4.36	5.09	11.66	5.97	4.08	16.03	1.71	0.00
IG21	IG21-2	9,220,860	8.27	24.39	2.07	0.67	7.03	0.00	1.89	0.00	1.81	0.63
IG21	IG21-3	9,443,292	14.88	24.66	5.33	15.40	15.31	1.68	4.60	1.68	1.87	0.00
IG21	IG21-4	9,034,355	10.22	30.00	3.40	3.50	11.17	18.10	3.79	9.66	1.75	0.00
IG21	IG21-5	9,552,760	12.53	17.15	5.77	16.51	12.04	9.26	6.50	23.11	1.85	0.00
IG22	IG22-1	9,947,900	44.22	74.20	14.07	33.60	44.20	37.19	17.59	22.27	2.42	0.00
IG22	IG22-2	11,805,934	101.83	38.36	28.69	16.54	98.91	14.21	26.82	15.87	2.71	0.00
IG22	IG22-3	11,464,697	66.49	42.45	13.91	14.53	81.69	28.62	22.83	20.07	2.43	0.00
IG22	IG22-4	12,097,638	50.73	39.72	36.61	6.93	47.65	4.16	44.34	11.88	2.54	0.00
IG22	IG22-5	11,462,394	111.79	38.69	9.59	6.53	110.45	24.00	8.23	7.50	2.51	0.00
IG23	IG23-1	15,732,965	120.83	24.99	147.75	0.57	128.71	7.17	111.23	0.00	3.32	8.66
IG23	IG23-2	15,443,185	120.73	31.73	107.03	17.55	169.89	16.13	104.73	8.55	3.24	0.00
IG23	IG23-3	15,624,221	120.71	34.42	168.03	15.45	172.27	16.84	152.63	19.82	3.46	0.00
IG23	IG23-4	15,819,733	120.86	39.66	37.70	21.60	152.90	21.51	101.57	16.94	3.46	0.00
IG23	IG23-5	15,650,324	120.71	20.29	38.42	19.47	157.91	6.08	63.93	11.59	3.35	0.00
IG24	IG24-1	22,321,657	121.29	34.92	104.66	16.76	241.29	2.00	196.25	4.83	5.01	0.00
IG24	IG24-2	23,700,403	121.48	33.02	121.06	17.53	196.54	0.08	241.52	12.36	4.87	0.00
IG24	IG24-3	21,623,646	121.24	30.03	120.95	8.09	241.41	13.86	241.18	0.00	5.04	5.12
IG24	IG24-4	23,213,274	121.57	37.80	120.87	6.82	241.42	10.30	241.11	0.00	5.13	0.48
IG24	IG24-5	21,526,858	120.97	17.37	120.96	13.77	241.01	5.72	241.25	20.64	5.12	0.00
IG25	IG25-1	31,198,415	121.65	22.45	110.56	11.28	241.75	0.00	231.04	8.66	6.96	3.15
IG25	IG25-2	29,015,575	121.95	32.72	50.60	6.77	241.60	4.57	171.04	14.08	7.25	0.00
IG25	IG25-3	30,010,737	121.30	23.01	121.22	5.24	241.48	7.54	241.69	7.34	6.91	0.00
IG25	IG25-4	27,822,541	121.19	21.22	121.22	8.48	241.62	9.61	241.43	4.90	6.67	0.00
IG25	IG25-5	28,847,059	121.56	28.64	121.52	8.59	241.82	4.78	241.87	6.24	6.87	0.00
IG26	IG26-1	41,592,732	165.48	107.05	121.97	0.00	-	-	242.64	9.83	11.03	4.51
IG26	IG26-2	42,111,873	132.72	108.97	121.81	5.09	-	-	-	-	10.90	0.00
IG26	IG26-3	40,994,433	125.62	106.57	122.02	7.49	243.19	5.35	242.85	10.71	10.99	0.00
IG26	IG26-4	41,550,143	142.13	117.12	122.94	14.95	-	-	243.94	14.76	10.41	0.00
IG26	IG26-5	40,277,242	126.55	114.20	122.06	5.05	246.36	138.15	242.77	11.81	10.67	0.00
IG27	IG27-1	55,655,133	135.18	100.63	123.57	9.71	-	-	-	-	15.61	0.00
IG27	IG27-2	53,474,785	131.41	107.76	122.84	8.36	-	-	261.81	131.56	15.11	0.00
IG27	IG27-3	55,241,308	245.85	107.27	123.60	11.00	-	-	-	-	15.21	0.00
IG27	IG27-4	57,329,966	168.00	97.43	-	-	-	-	-	-	16.18	0.00
IG27	IG27-5	54,170,778	163.91	105.66	123.29	5.05	-	-	251.63	69.73	15.01	0.00
IG28	IG28-1	67,049,865	217.08	96.31	-	-	-	-	-	-	20.43	0.00
IG28	IG28-2	75,632,783	247.17	76.24	125.58	0.55	-	-	-	-	20.91	0.00
IG28	IG28-3	76,217,851	247.20	77.79	-	-	-	-	-	-	22.11	0.00
IG28	IG28-4	66,288,441	231.84	99.42	-	-	-	-	-	-	20.50	0.00
IG28	IG28-5	71,498,201	247.28	90.47	-	-	-	-	-	-	20.10	0.00
IG29	IG29-1	88,187,471	249.01	89.68	-	-	-	-	-	-	26.36	0.00
IG29	IG29-2	84,228,642	249.08	97.65	-	-	-	-	-	-	26.64	0.00
IG29	IG29-3	92,905,324	250.00	80.62	-	-	-	-	-	-	27.65	0.00
IG29	IG29-4	91,454,837	249.24	82.45	-	-	-	-	-	-	28.10	0.00
IG29	IG29-5	88,620,777	249.21	85.93	-	-	-	-	-	-	27.64	0.00
IG30	IG30-1	100,200,144	251.70	91.61	-	-	-	-	-	-	110.74	0.00
IG30	IG30-2	99,003,623	252.03	90.33	-	-	-	-	-	-	118.39	0.00
IG30	IG30-3	101,346,944	252.76	81.53	-	-	-	-	-	-	118.49	0.00
IG30	IG30-4	105,000,827	257.36	84.33	-	-	-	-	-	-	115.84	0.00
IG30	IG30-5	99,388,226	253.12	95.31	-	-	-	-	-	-	117.48	0.00

* Gap (%) = ((“Objective function value obtained by the corresponding solution method”-“Minimum of the objective function values obtained by all proposed solution methods”)/ (“Minimum of the objective function values obtained by all proposed solution methods”))*100. Green highlighted cells correspond to positive gap values (higher objective function value).

Table 11. Comparison of the Average Performances of the Proposed Solution Methods with the Best Objective Function Values Obtained for Large-Sized IGs

Solution Method	Basic Performance Indicators	Intance Groups									
		IG21	IG22	IG23	IG24	IG25	IG26	IG27	IG28	IG29	IG30
HH1	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**20.88**	**46.68**	**30.22**	**30.63**	**25.61**	**110.78**	**103.75**	**88.04**	**87.27**	**88.62**
	Standard Deviation	7.54	13.83	6.86	7.10	4.38	4.17	4.04	9.47	6.05	5.01
	Coefficient of Variation	0.36	0.30	0.23	0.23	0.17	0.04	0.04	0.11	0.07	0.06
HH2	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	4/5	1/5	0/5	0/5
	Mean Gap (%) **	**8.23**	**15.62**	**14.93**	**12.59**	**8.07**	**6.52**	**8.53**	**0.55**	**-**	**-**
	Standard Deviation	6.47	9.83	7.46	4.40	2.02	4.87	2.22	0.00	-	-
	Coefficient of Variation	0.79	0.63	0.50	0.35	0.25	0.75	0.26	0.00	-	-
HH3	S/P *	5/5	5/5	5/5	5/5	5/5	2/5	0/5	0/5	0/5	0/5
	Mean Gap (%) **	**7.00**	**21.64**	**13.55**	**6.39**	**5.30**	**71.75**	**-**	**-**	**-**	**-**
	Standard Deviation	6.43	11.46	5.96	5.11	3.24	66.40	-	-	-	-
	Coefficient of Variation	0.92	0.53	0.44	0.80	0.61	0.93	-	-	-	-
HH4	S/P *	5/5	5/5	5/5	5/5	5/5	4/5	2/5	0/5	0/5	0/5
	Mean Gap (%) **	**10.10**	**15.52**	**11.38**	**7.56**	**8.24**	**11.78**	**100.64**	**-**	**-**	**-**
	Standard Deviation	8.69	5.37	6.92	7.95	3.17	1.86	30.91	-	-	-
	Coefficient of Variation	0.86	0.35	0.61	1.05	0.38	0.16	0.31	-	-	-
SA	S/P *	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
	Mean Gap (%) **	**0.13**	**0.00**	**1.73**	**1.12**	**0.63**	**0.90**	**0.00**	**0.00**	**0.00**	**0.00**
	Standard Deviation	0.25	0.00	3.46	2.01	1.26	1.80	0.00	0.00	0.00	0.00
	Coefficient of Variation	2.00	-	2.00	1.79	2.00	2.00	-	-	-	-

* S/P: Number of problem instances for which a feasible solution is obtained by the proposed solution method within the time limits/Total number of problem instances in the instance group.

** Mean Gap (%): Mean of gap values of the problem instances belonging to the related instance group. Gap (%) = ((“Objective function value obtained by the corresponding solution method”-“Minimum of the objective function values obtained by all proposed solution methods”)/(“Minimum of the objective function values obtained by all proposed solution methods”))*100. Green highlighted cells indicate the lowest mean gap values for the corresponding instance group.

In addition to the deviating performances of HHs in general, HH2, HH3, and HH4 cannot generate any feasible integer solutions for some of the problem instances within the CPU time limits. HH1 generates feasible solutions for all of the large-sized problem instances, however, it has the worst performance in terms of solution quality. SA clearly outperforms other solution methods in terms of both solution quality and CPU time.

7.2.3. The Effects of Modeling Inventory Related Costs in RTC Location-Allocation Submodels

The inventory related costs are not taken into account in the submodels related to RTC location-allocation problems that are used in the proposed decomposition and hybrid heuristics; rather, for the sake of computational simplicity, they are considered later, that is, they are added to the objective function after the solution is obtained. In this section, we analyze the effects of this simplification on the quality of the solutions and CPU times. For this purpose, the selected problem instances are solved with the modified versions of the current heuristics taking into account the inventory related costs directly in the objective functions of RTC related submodels. The objective function values thus obtained are compared with the ones previously obtained by the current heuristics. In order to make these comparisons, all RTC location-allocation related submodels' objective functions are modified so as to consider the inventory related costs directly. In other words, the two terms presented below are added to the objective functions of the submodels:

$$\sum_{j \in J} \sqrt{2h_j p_j} \sqrt{\sum_{k \in K} \mu_k Z_{jk}}\text{, and } \sum_{j \in J} h_j z_\alpha \sqrt{lt \sum_{k \in K} \sigma_k^2 Z_{jk}}\text{.}$$

The results showing the effect of modeling inventory related costs directly in RTC location-allocation submodels are presented in Tables 12, 13, 14, 15, and 16. In these tables the modified versions of the current heuristics are named as "the name of current heuristics"-INV (i.e. DH1-INV). The green highlighted cells in the tables correspond to positive percentage values (higher cost values), while the blue highlighted cells correspond to negative percentage values (lower cost value).

Tables 12, 13, 14, and 15 present the results obtained by solving the instances selected from small and medium-sized problem instances using DHs, while Table 16 presents the results obtained by solving the instances selected from large-sized problem instances using HHs.

As it can be depicted from Tables 12, 13, 14, and 15, DHs and the corresponding DHs-INV provide exactly the same solution for more than 60% of the problem instances. Results obtained by solving the problem instances using DHs-INV provide lower inventory holding costs for the remaining instances; however, this reduction does not always result in a reduction in the total expected costs. The effect of modeling inventory related costs on CPU time is not clear enough for small and medium-sized instances, because total solution time mainly depends on the vehicle routing subproblem for small and medium-sized problem instances.

When we compare the performance of HHs-INV with the corresponding HHs based on the solutions obtained for the selected large-sized problem instances, it is clear that HHs-INV perform worse than the corresponding HHs in terms of both solution quality and CPU time for most of the cases presented in Table 16. In addition to that, HHs-INV, except HH1-INV, cannot reach feasible integer solutions within the solution time limits for the problem instance IG26-3. The main reason for not obtaining an integer solution or obtaining a lower quality one by using HHs-INV is the increasing CPU time due to the more complex structure of the submodels.

7.2.4. The Effects of Using the Solutions Obtained by the Other Heuristic Methods as an Initial Solution for SA

In order to analyze the effects of using the solutions obtained by other heuristic methods as an initial solution for SA, some randomly selected problem instances are re-solved using the Simulated Annealing Tool and the results are presented in Table 17. In this table, the results obtained by SA using randomly generated initial solutions are given as a base. The results obtained by using the solutions of the other heuristic methods as an initial solution for SA are compared with them in terms of solution quality and CPU time. As it can be depicted from Table 17, only small changes which can be explained by the randomness of the solution process are observed in the quality of the solutions for small and medium-sized problem instances. However, it can be stated that, significant improvements in solution quality can be achieved by using the solutions obtained by other heuristic methods as an initial solution for SA for large-sized problem instances. Nevertheless, it should be noted that CPU times for large-sized problem instances are much higher than the cases where randomly generated initial solutions are used.

Table 12. Comparison of the solutions obtained by solving the selected problem instances using DH1 and DH1-INV

Problem Instance	Heuristic Solution Method	CPU Time	Total Cost (Objective Funstion Value)	RBC Location Cost	RTC Location Cost	Routing Cost	Inventory and order cost at RTCs	Transportation Cost between DCs and RBCs	Transportation Cost between RBCs and RTCs
IG6-4	DH1	0.31	4,240,794	2,628,680	652,630	233,600	236,248	256,476	233,160
IG6-4	DH1-INV	0.30	4,240,794	2,628,680	652,630	233,600	236,248	256,476	233,160
Comparision of DH1 & DH1-INV		-5.13%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG9-1	DH1	0.47	5,219,791	2,952,920	648,410	235,425	344,271	125,565	913,200
IG9-1	DH1-INV	0.41	5,219,791	2,952,920	648,410	235,425	344,271	125,565	913,200
Comparision of DH1 & DH1-INV		-12.58%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG9-5	DH1	0.33	4,735,073	2,645,990	620,650	120,450	324,583	523,600	499,800
IG9-5	DH1-INV	0.46	4,735,073	2,645,990	620,650	120,450	324,583	523,600	499,800
Comparision of DH1 & DH1-INV		40.37%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG13-1	DH1	5.28	4,831,064	2,877,150	709,140	191,625	487,199	188,650	377,300
IG13-1	DH1-INV	4.91	4,712,353	2,954,210	648,180	198,925	297,068	339,570	274,400
Comparision of DH1 & DH1-INV		-7.02%	-2.46%	2.68%	-8.60%	3.81%	-39.03%	80.00%	-27.27%
IG14-1	DH1	4.91	4,344,414	2,368,990	652,590	198,925	333,637	266,112	524,160
IG14-1	DH1-INV	1.08	5,168,233	2,572,830	777,740	195,275	243,444	532,224	846,720
Comparision of DH1 & DH1-INV		-78.01%	18.96%	8.60%	19.18%	-1.83%	-27.03%	100.00%	61.54%
IG17-1	DH1	287.44	4,825,353	2,495,200	802,750	195,275	750,841	515,467	65,820
IG17-1	DH1-INV	93.08	4,619,859	2,495,200	827,730	189,800	394,202	515,467	197,460
Comparision of DH1 & DH1-INV		-67.62%	-4.26%	0.00%	3.11%	-2.80%	-47.50%	0.00%	200.00%

Table 13. Comparison of the solutions obtained by solving the selected problem instances using DH2 and DH2-INV

Problem Instance	Heuristic Solution Method	CPU Time	Total Cost (Objective Funstion Value)	RBC Location Cost	RTC Location Cost	Routing Cost	Inventory and order cost at RTCs	Transportation Cost between DCs and RBCs	Transportation Cost between RBCs and RTCs
IG6-4	DH2	0.30	4,071,150	2,597,360	685,000	235,425	234,713	85,492	233,160
IG6-4	DH2-INV	0.26	4,071,150	2,597,360	685,000	235,425	234,713	85,492	233,160
Comparision of DH2 & DH2-INV		-11.78%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG9-1	DH2	0.25	4,665,499	2,709,570	648,200	228,125	392,421	276,243	410,940
IG9-1	DH2-INV	0.53	4,292,777	2,709,570	694,850	244,550	299,074	276,243	68,490
Comparision of DH2 & DH2-INV		113.60%	-7.99%	0.00%	7.20%	7.20%	-23.79%	0.00%	-83.33%
IG9-5	DH2	0.30	4,735,073	2,645,990	620,650	120,450	324,583	523,600	499,800
IG9-5	DH2-INV	0.34	4,735,073	2,645,990	620,650	120,450	324,583	523,600	499,800
Comparision of DH2 & DH2-INV		14.43%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG13-1	DH2	4.48	4,712,353	2,954,210	648,180	198,925	297,068	339,570	274,400
IG13-1	DH2-INV	4.68	4,712,353	2,954,210	648,180	198,925	297,068	339,570	274,400
Comparision of DH2 & DH2-INV		4.33%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG14-1	DH2	2.05	4,400,567	2,572,830	712,440	191,625	270,488	532,224	120,960
IG14-1	DH2-INV	2.46	4,400,567	2,572,830	712,440	191,625	270,488	532,224	120,960
Comparision of DH2 & DH2-INV		20.03%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG17-1	DH2	225.39	5,047,236	2,431,910	903,660	197,100	559,948	625,518	329,100
IG17-1	DH2-INV	232.98	5,047,236	2,431,910	903,660	197,100	559,948	625,518	329,100
Comparision of DH2 & DH2-INV		3.37%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%

Table 14. Comparison of the solutions obtained by solving the selected problem instances using DH3 and DH3-INV

Problem Instance	Heuristic Solution Method	CPU Time	Total Cost (Objective Funtion Value)	RBC Location Cost	RTC Location Cost	Routing Cost	Inventory and order cost at RTCs	Transportation Cost between DCs and RBCs	Transportation Cost between RBCs and RTCs
IG6-4	DH3	0.25	4,071,150	2,597,360	685,000	235,425	234,713	85,492	233,160
IG6-4	DH3-INV	0.49	4,035,724	2,628,680	741,450	204,400	146,428	256,476	58,290
Comparision of DH3 & DH3-INV		95.18%	-0.87%	1.21%	8.24%	-13.18%	-37.61%	200.00%	-75.00%
IG9-1	DH3	0.45	5,219,791	2,952,920	648,410	235,425	344,271	125,565	913,200
IG9-1	DH3-INV	0.48	5,219,791	2,952,920	648,410	235,425	344,271	125,565	913,200
Comparision of DH3 & DH3-INV		6.61%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG9-5	DH3	0.28	4,735,073	2,645,990	620,650	120,450	324,583	523,600	499,800
IG9-5	DH3-INV	0.75	4,735,073	2,645,990	620,650	120,450	324,583	523,600	499,800
Comparision of DH3 & DH3-INV		167.26%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG13-1	DH3	5.67	4,831,064	2,877,150	709,140	191,625	487,199	188,650	377,300
IG13-1	DH3-INV	5.03	4,712,353	2,954,210	648,180	198,925	297,068	339,570	274,400
Comparision of DH3 & DH3-INV		-11.30%	-2.46%	2.68%	-8.60%	3.81%	-39.03%	80.00%	-27.27%
IG14-1	DH3	4.89	4,344,414	2,368,990	652,590	198,925	333,637	266,112	524,160
IG14-1	DH3-INV	2.57	4,400,567	2,572,830	712,440	191,625	270,488	532,224	120,960
Comparision of DH3 & DH3-INV		-47.53%	1.29%	8.60%	9.17%	-3.67%	-18.93%	100.00%	-76.92%
IG17-1	DH3	389.39	4,825,353	2,495,200	802,750	195,275	750,841	515,467	65,820
IG17-1	DH3-INV	88.02	4,619,859	2,495,200	827,730	189,800	394,202	515,467	197,460
Comparision of DH3 & DH3-INV		-77.40%	-4.26%	0.00%	3.11%	-2.80%	-47.50%	0.00%	200.00%

Table 15. Comparison of the solutions obtained by solving the selected problem instances using DH4 and DH4-INV

Problem Instance	Heuristic Solution Method	CPU Time	Total Cost (Objective Funstion Value)	RBC Location Cost	RTC Location Cost	Routing Cost	Inventory and order cost at RTCs	Transportation Cost between DCs and RBCs	Transportation Cost between RBCs and RTCs
IG6-4	DH4	0.42	4,071,150	2,597,360	685,000	235,425	234,713	85,492	233,160
IG6-4	DH4-INV	0.59	4,071,150	2,597,360	685,000	235,425	234,713	85,492	233,160
Comparision of DH4 & DH4-INV		38.30%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG9-1	DH4	0.55	4,292,777	2,709,570	694,850	244,550	299,074	276,243	68,490
IG9-1	DH4-INV	0.83	4,292,777	2,709,570	694,850	244,550	299,074	276,243	68,490
Comparision of DH4 & DH4-INV		51.10%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG9-5	DH4	0.39	4,735,073	2,645,990	620,650	120,450	324,583	523,600	499,800
IG9-5	DH4-INV	0.62	4,735,073	2,645,990	620,650	120,450	324,583	523,600	499,800
Comparision of DH4 & DH4-INV		57.69%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG13-1	DH4	4.66	4,712,353	2,954,210	648,180	198,925	297,068	339,570	274,400
IG13-1	DH4-INV	4.93	4,712,353	2,954,210	648,180	198,925	297,068	339,570	274,400
Comparision of DH4 & DH4-INV		5.91%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG14-1	DH4	2.33	4,400,567	2,572,830	712,440	191,625	270,488	532,224	120,960
IG14-1	DH4-INV	2.61	4,400,567	2,572,830	712,440	191,625	270,488	532,224	120,960
Comparision of DH4 & DH4-INV		11.99%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
IG17-1	DH4	226.42	5,047,236	2,431,910	903,660	197,100	559,948	625,518	329,100
IG17-1	DH4-INV	425.93	4,898,844	2,431,910	779,330	189,800	411,546	625,518	460,740
Comparision of DH4 & DH4-INV		88.11%	-2.94%	0.00%	-13.76%	-3.70%	-26.50%	0.00%	40.00%

Table 16. Comparison of the solutions obtained by solving the selected problem instances using HHs and HHs-INV

Problem Instance	Heuristic Solution Method	CPU Time	Total Cost (Objective Function Value)	RBC Location Cost	RTC Location Cost	Routing Cost	Inventory and order cost at RTCs	Transportation Cost between DCs and RBCs	Transportation Cost between RBCs and RTCs
IG23-1	HH1	120.83	19,664,770	7,869,300	3,972,240	1,845,075	2,069,210	1,091,405	2,817,540
IG23-1	HH1-INV	160.96	20,052,344	6,118,030	3,739,270	1,211,800	1,670,606	1,512,258	5,800,380
Comparision of HH1 & HH1-INV		33.21%	1.97%	-22.25%	-5.86%	-34.32%	-19.26%	38.56%	105.87%
IG23-1	HH2	147.75	15,822,955	6,269,290	3,651,990	1,582,275	1,840,439	1,238,131	1,240,830
IG23-1	HH2-INV	356.63	27,495,050	6,269,290	13,399,740	1,775,725	2,635,316	1,246,579	2,168,400
Comparision of HH2 & HH2-INV		141.37%	73.77%	0.00%	266.92%	12.23%	43.19%	0.68%	74.75%
IG23-1	HH3	128.71	16,860,913	7,869,300	3,581,660	1,368,750	2,097,928	1,273,175	670,100
IG23-1	HH3-INV	280.75	15,747,485	6,118,030	3,516,840	1,195,375	1,854,682	1,512,258	1,550,300
Comparision of HH3 & HH3-INV		118.12%	-6.60%	-22.25%	-1.81%	-12.67%	-11.59%	18.78%	131.35%
IG26-3	HH4-INV	111.23	15,732,965	6,269,290	3,588,510	1,573,150	1,930,197	1,169,698	1,202,120
IG26-3	HH4-INV	-	-	-	-	-	-	-	-
Comparision of HH4 & HH4-INV		-	-	-	-	-	-	-	-
IG26-3	HH1	125.62	84,681,926	15,603,530	43,414,170	2,878,025	12,271,483	3,732,588	6,782,130
IG26-3	HH1-INV	319.20	121,393,777	16,906,410	63,563,510	19,720,950	12,058,234	3,423,203	5,721,470
Comparision of HH1 & HH1-INV		154.09%	43.35%	8.35%	46.41%	585.23%	-1.74%	-8.29%	-15.64%
IG26-3	HH2	122.02	44,065,533	17,818,030	8,303,240	4,058,800	4,984,159	3,696,674	5,204,630
IG26-3	HH2-INV	-	-	-	-	-	-	-	-
Comparision of HH2 & HH2-INV		-	-	-	-	-	-	-	-
IG26-3	HH3	246.36	43,188,895	15,603,530	11,301,960	4,790,625	5,867,940	3,716,640	1,908,200
IG26-3	HH3-INV	-	-	-	-	-	-	-	-
Comparision of HH3 & HH3-INV		-	-	-	-	-	-	-	-
IG26-3	HH4	242.77	45,384,852	16,355,670	12,018,930	4,828,950	6,333,974	3,755,178	2,092,150
IG26-3	HH4-INV	-	-	-	-	-	-	-	-
Comparision of HH4 & HH4-INV		-	-	-	-	-	-	-	-

Table 17. Comparison of the results obtained by using the solutions of other heuristic methods as an initial solution for SA

Problem Instances	SA		SA-DH1		SA-DH2		SA-DH3		SA-DH4		SA-HH1		SA-HH2		SA-HH3		SA-HH4	
	CPU Time	Total Cost (Objective Function Value)	CPU Time	Gap(%)*	CPU Time	Gap(%)*	CPU Time	Gap(%)*	CPU Time	Gap(%)*	CPU Time	Gap(%)*	CPU Time	Gap(%)*	CPU Time	Gap(%)*	CPU Time	Gap(%)*
IG10-1	3.75	3,926,614	5.53	0.00%	5.55	0.00%	6.01	0.00%	5.47	0.00%	5.57	0.00%	5.65	0.00%	5.76	0.00%	5.67	0.00%
IG10-2	3.81	3,774,339	5.60	0.00%	5.81	0.00%	6.21	0.00%	6.07	0.00%	5.94	0.00%	6.04	0.00%	5.86	0.00%	5.96	0.00%
IG13-4	4.63	3,849,344	7.16	0.00%	6.87	0.09%	7.01	0.00%	6.97	0.00%	7.19	0.00%	7.06	0.00%	6.90	0.00%	7.08	0.00%
IG14-1	4.72	4,135,219	7.29	-0.26%	7.76	-0.26%	7.43	-0.26%	7.69	-0.09%	7.65	-0.26%	8.22	-0.09%	7.34	-0.09%	7.67	-0.09%
IG17-1	6.90	4,639,934	10.62	-0.08%	13.19	-0.08%	10.93	0.08%	10.63	-0.31%	11.63	0.08%	11.35	0.16%	10.56	0.24%	11.10	0.20%
IG19-4	8.54	5,198,556	14.02	0.07%	14.42	-0.14%	13.96	0.11%	13.70	-0.28%	14.24	-0.18%	14.24	-0.35%	14.01	-0.07%	13.93	0.18%
IG26-5	10.67	40,277,242	-	-	-	-	-	-	-	-	179.34	-0.90%	198.04	-3.32%	181.44	-6.69%	178.16	-5.98%

* Gap (%) = ((“Objective function value obtained by using the solutions of corresponding heuristic method as an initial solution for SA”-“Minimum of the objective function values obtained by SA without using any initial solutions”)/ (“Minimum of the objective function values obtained by SA without using any initial solutions”))*100. Green highlighted cells correspond to positive gap values (higher objective function value). Blue highlighted cells correspond to negative gap values (lower objective function value).

7.2.5. The Effects of Ignoring Perishability of Blood

Blood is a perishable product, as the shelf-life of red blood cells is 42 days. We do not consider the perishability of blood for computational simplicity while modelling our problem. In this section, we analyze the effects of this simplification on the resulting values of order quantities obtained by solving problem instances. In order to analyze these effects, the order quantities at RTCs are calculated and they are compared with the total demand of the TCs assigned to that respective RTCs. The main goal is to calculate the number-of-days equivalence of the order quantities in terms of daily demand of RTCs. Table 18 presents the resulting order quantities and their equivalent days of inventory levels obtained by solving the instances selected from small and medium-sized problem instances using DH1. As it can be depicted from Table 18, order quantities at RTCs correspond to the days of inventory levels ranging from 2 to 9 days, which are quite acceptable when we consider that the shelf-life of red blood cells is 42 days. Therefore, we can conclude that resulting order quantities do not pose a significant risk of outdating, and ignoring the perishability of blood in our problem does not result in impractical solutions in terms of order quantities.

Table 18. Order Quantities and Their Equivalent Days of Inventory Levels Obtained by Solving the Instances

Test Instance	**Opened RTCs**	**Order Quantity**	**Total Yearly Demand at RTCs**	**Order Quantity in Terms of "Days of Inventory" (*)**
IG1-1	RTC1	233	13,500	6.300
IG3-1	RTC1	447	19,150	8.520
IG5-1	RTC2	423	17,760	8.693
IG7-1	RTC1	148	18,380	2.939
IG9-1	RTC3	383	22,830	6.123
IG11-1	RTC1	396	27,890	5.183
IG13-1	RTC1	438	34,300	4.661
IG15-1	RTC1	791	44,170	6.536
IG17-1	RTC1	740	65,820	4.104

* Order Quantity in Terms of "Days of Inventory" = (Order Quantity at RTC/Total Yearly Demand of TCs that are assigned to that RTC)*365

CHAPTER 8

CONCLUSIONS AND FURTHER RESEARCH ISSUES

Main motivation of our study stems from a real life problem faced by the decision makers in developing new strategies for improving the Turkish Blood Supply System. One of these new strategies is to centralize the transfusion services, by adding a new type of facility called Regional Transfusion Center (RTC) to the blood supply chain. RTC is a unit that is planned to be operated as a central transfusion laboratory and a distribution center as well. In the presence of RTCs, an additional echelon will be included in the blood supply chain, and thus, locations and allocations of other facilities in the chain will also be affected. This situation brings in the location and allocation decisions of the two different types of facilities to be made by the decision makers. In our study, we intend to propose an integrated approach aiming to determine locations and allocations of more than one type of facilities by simultaneously taking into account also the other main decisions of the blood supply chain, such as inventory management, and distribution and routing of blood and blood components. We therefore consider a joint location-inventory-routing problem with multiple location layers for a distinctive blood supply chain structure, which we formulate as a mixed-integer nonlinear programming model. We show that subcases of the problem, under the predetermined parameter settings, are equivalent to the well-known problems (Multi-Depot Vehicle Routing Problem, Single Source Capacitated Facility Location Problem, and Capacitated Vehicle Routing Problem) in the literature all of which have already been shown to be NP-hard.

We present two different types of solution methods for the problem. First we develop an optimal solution method, by transforming the problem to a mixed-integer convex program which can be optimally solved by using branch and bound methods. However, solving medium and large-sized problems for the optimal solution turns out to be impractical and sometimes even impossible. Therefore, we also try to develop heuristic solution methods as alternative solution methods. We select decomposition and simulated annealing techniques as the basis for our solution development efforts and propose nine different heuristic solution methods. Four of these methods (called DH1, DH2, DH3, and DH4) are based on decomposition techniques, one of them is a simulated annealing heuristic (SA) combined with a Tabu list, and four of them are hybrid heuristics (called HH1, HH2, HH3, and HH4) that incorporate the decomposition and simulated annealing techniques. We develop computer codes for the implementation of the proposed heuristics. Both models and computer codes of the heuristics are verified and validated by using conceptual validity, model verification, and operational validity techniques. In order to evaluate the performance of the solution methods proposed, we conduct extensive computational studies on the test problems including small, medium, and large-sized instances. The main findings of the computational studies can be summarized as follows:

- Performance of the proposed solution methods for small-sized test problems
    - Optimal solution method reaches the optimal solution in acceptable CPU times.
    - SA finds the optimal solutions for the small-sized problem instances, except the one for which it has a small percentage gap value of 0.25%.
    - DH1 finds the optimal solution only for 50% of the problem instances and percentage gap values are found to range from 1.45% to 22.20% for the remaining instances.
    - DH2, DH3, and DH4 find the optimal solution for more than 75% of the small-sized problem instances (percentage gap values ranging from 0.88% to 10.04%, from 0.25% to 9.80%, and from 0.25% to 2.55% for the remaining instances, respectively).
    - HH1, HH2, HH3, and HH4 present exactly the same performances as DH1, DH2, DH3 and DH4, respectively.
    - CPU times of the proposed heuristics are quite acceptable.

- Performance of the proposed solution methods for medium-sized test problem instances
    - The quality of the solutions obtained by the optimal solution method deteriorates.
    - SA performs better than the optimal solution method for all of the problem instances.
    - DHs and HHs also provide negative percentage gap values (perform better) when compared to the optimal solution method for most of the problem instances; however, there are still exceptional instances having positive percentage gap values up to 20%.
    - CPU times of the proposed heuristics are quite acceptable in general; however, after some point, as the problem size increases, CPU times of DHs increase rapidly.
    - DHs cannot provide any integer solutions within the specified time limits for some instances for which HHs are able to provide. Except for those instances, HH1, HH2, HH3, and HH4 present nearly the same performances as DH1, DH2, DH3, and DH4, respectively
- Performance of the proposed solution methods for large-sized test problem instances
    - Optimal solution method and DHs cannot generate any feasible integer solutions.
    - SA finds the best solution for 95 large-sized problem instances and provides quite acceptable percentage gap values for the remaining 5 instances.
    - Other heuristic methods have deviating performances in finding the best or near-best solutions.
    - HH2, HH3, and HH4 cannot generate any feasible integer solutions for some of the problem instances within the CPU time limits.
- Overall performances
    - SA clearly outperforms other solution methods in terms of both solution quality and CPU time. Performance of SA is consistent, and

the changes in problem parameters do not have a major effect on its performance.

  - DHs and HHs have deviating performances. They perform better than the optimal solution method for most of the instances. However, their performances may be affected by the problem parameters. They also have limitations in terms of solution time, especially, for medium-to-large, and large-sized problems. However, performance of HHs in terms of solution time is much better than DHs, as expected.
  - For more than 70% of the problem instances, HHs find exactly the same solution as the corresponding DHs, and percentage gap values are lower than 1% for almost all of the remaining instances. Therefore, we can conclude that Simulated annealing (SA) method used in hybrid heuristics for solving vehicle routing subproblem performs quite well.

Based on the experience we obtained by the computational studies, we can also make some recommendations which can be helpful for decision makers in implementing the proposed solution approaches for the real life problems:

- One or more of the recommendations listed below can be applied to reduce the problem size:
  - Applying clustering techniques for the blood demand (TCs) and/or blood supply (DCs): Clustering techniques (i.e. k-means clustering) can be effectively used to obtain approximate optimal solutions for the problem instances including a large number of demand and/or supply points. Problem size can be dramatically reduced by constructing clusters especially for TCs, since, in real life applications, the number of TCs is much higher than the number of other blood establishments in the blood supply chain. When the size of the problem is reduced, most of the proposed solution approaches in our study can be applied effectively and efficiently. While applying some clustering techniques for the real life problem instances, the most critical point is to determine

the level of aggregation by considering the trade-off between computational simplicity and any potential errors.

    - Eliminating undesirable assignments between different facility pairs as listed below (i.e., eliminate the decision variables corresponding to the assignments between two different types of facilities having a cost-weighted distance greater than a threshold value)
        - RTC-TC
        - RTC-RBC
        - RBC-DC

- As it is not so practical to develop lower bounds or to solve the problem for the optimal solution for large-sized real life instances, the main objective will be obtaining the best reachable solution. Therefore, trying to solve the problem by using all applicable solution approaches and selecting the solution having the lowest objective function value will help to make better decisions.
    - Solve the problem using all proposed solution approaches
        - Optimal Solution Method
        - Decomposition Heuristics
        - Hybrid Heuristics
        - SA
    - Solve the problem by changing the parameters (target temperature, cooling rate, maximum number of iterations at each temperature, etc.) of SA to obtain improved solutions
    - Use the solutions of the other proposed solution approaches as an initial solution for both SA and the optimal solution method
- Due to the uncertainty in blood demand, solving the problem under different possible demand scenarios and checking the robustness of the solutions obtained can bring in more value for the analysis.

The main contribution of our study is to propose a modelling framework and alternative solution methods for the joint location (with multiple location layers)-inventory-routing problem which considers a specific problem environment having distinctive characteristics. Although our study is motivated by the blood supply chain, the proposed modelling approach and the solution methods can also be applied to supply chains of other products having similar supply chain characteristics.

Further Research Issues

A mobile blood collection planning problem can be modelled which can use the resulting values of the amounts sent from DCs to RBCs (Annual blood collection targets for DCs) obtained after solving the joint location-inventory-routing problem as input.

Various different cases of the problem environment can also be analyzed:

- Multi-product case in which different blood groups and different blood components are considered without aggregation
- Multi-period case
- Robust optimization case considering the uncertainty of blood demand
- The case in which RBCs' inventory costs are considered
- The cases in which special routing constraints (i.e. time windows) are considered
- The cases in which alternative inventory management policies are considered for RTCs

Alternative solution methods or new techniques to improve the proposed solution methods can also be investigated:

- Using some valid inequalities to improve the proposed solution methods
- Alternative solution methods
    - Lagrangian relaxation based heuristic methods to solve the joint location-inventory-routing problem with multiple location layers
    - Genetic algorithms
    - Methods for reducing the solution space

REFERENCES

Ambrosino, D., Scutella, M. G., 2005. ‘Distribution network design: New problems and related models’, *European Journal of Operational Research*, 165, 610–624

Andersson, H., Hoff, A., Christiansen, M., Hasle, G., Løkketangen, A., 2010. ‘Industrial aspects and literature survey: Combined inventory management and routing’, *Computers & Operations Research*, 37, 1515–1536.

AuBuchon, J. P., Linauts, S., Vaughan,M., Wagner, F., Delaney, M., Nester, T., 2011. 'Evolution in a centralized transfusion service', *Transfusion,* (51), 2750-2757.

Axsater, S., Olsson, F., Tydesjo, P., 2007. 'Heuristics For Handling Direct Upstream Demand In Two-Echelon Distribution Inventory Systems', *International Journal of Production Economics*, 108(1-2), 266-270.

Badri, H., Bashiri, M., Hejazi T. H., 2013.’ Integrated strategic and tactical planning in a supply chain network design with a heuristic solution method’, *Computers & Operations Research*, 40, 1143–1154.

Baita, F., Ukovich, W., Pesenti, R., Favaretto, D., 1998. 'Dynamic Routing-And-Inventory Problems: A Review', *Transportation Research Part A: Policy and Practice*, 32(8), 585-598.

Beliën, J., Forcé, H., 2012. 'Supply Chain Management Of Blood Products: A Literature Review', *European Journal of Operational Research*, 217, 1–16.

Boccia, M., Crainic, T., Sforza, A., & Sterle, C. 2010. ‘A metaheuristic for a two echelon location-routing problem’, *In P. Festa (Ed.), Symposium on experimental algorithms (SEA 2010).* Lecture notes in computer science (Vol. 6049, pp. 288–301). Berlin: Springer-Verlag.

Bodin, L.,Golden, B., Assad, A.,Ball, M., 1983. "Routing and scheduling of vehicles and crews: The state of the art’, *Computers and Operations Research*, (10).

Bortfeldt A., 2012. ‘A hybrid algorithm for the capacitated vehicle routing problem with three-dimensional loading constraints’, *Computers & Operations Research*, 39, 2248–2257.

Brodheim, E., Prastacos, G. P., 1979. 'The Long Island Blood Distribution System as A Prototype for Regional Blood Management', *Interfaces*, 9 (5), 3–20.

Chao, I.-M., 2002. ‘A tabu search method for the truck and trailer routing problem’, *Computers and Operations Research*, 29, 33–51.

Chen, F., Federgruen, A., Zheng, Y., 2001. 'Coordination mechanisms for a distribution system with one supplier and multiple retailers', *Management Science*, 693-708.

Christiansen C. H., Lysgaard J. 2007. ‘A branch-and-price algorithm for the capacitated vehicle routing problem with stochastic demands’, *Operations Research Letters* 35, 773 – 781.

Contartdo, C., Hemmelmayr, V., & Crainic, T. G. 2012. ‘Lower and upper bounds for the two-echelon capacitated location-routing problem’, *Computers and Operations Research*, 39(12), 3185–3199.

Contartdo C., Martinelli R. 2015. ‘A new exact algorithm for the multi-depot vehicle routing problem under capacity and route length constraints’, *Discrete Optimization* 12, 129–146.

Cortinhal M. J., Captivo M. E. 2003. ‘Upper and lower bounds for the single source capacitated location problem’, *European Journal of Operational Research* 151, 333–351.

Cumming, P.D., Kendall, K. E., Pegels, C. C., and Seagle, J. P, Shubsda J.F. 1976a. 'A Collections Planning Model for Regional Blood Suppliers: Description And Validation', *Management Science*, 22 (9), 962–971.

Cumming, P.D., Kendall, K. E., Pegels, C. C., and Seagle, J. P., 1976b. ‘Cost Effectiveness of Use of Frozen Blood to Alleviate Blood Shortages’, *Transfusion*, 17 (6), 602-606.

Custer, B., Johnson, E. S., Sullivan, S. D., Hazlet, T. K., Ramsey, S.D., Murphy, E. L., Busch M.R., 2005. 'Community Blood Supply Model: Development Of A New Model To Assess The Safety, Sufficiency, And Cost Of The Blood Supply', *Medical Decision Making*, 25 (5), 571–582.

Çetin, E., Sarul, L. S., (2009). 'A Blood Bank Location Model: A Multiobjective Approach', *European Journal Of Pure And Applied Mathematics*, 2 (1), 112-124

Daskin, M., Coullard, C., Shen, Z., 2002. 'An Inventory-Location Model: Formulation, Solution Algorithm and Computational Results', *Annals of Operations Research*, 110(1), 83-106.

Denesiuk, L., Richardson, T., Nahirniak, S.,Clarke G., 2006. 'Implementation of A Redistribution System for Near-Outdate Red Blood Cell Units', *Archives of Pathology and Laboratory Medicine*, 130 (8), 1178–1183.

Drezner, Z., Scott, C., 2010. 'Optimizing the Location of a Production Firm’, *Networks and Spatial Economics*, 1-15.

Dumas, M. B., and Rabınowitz, M., 1977. ‘Policies for Reducing Blood Wastage In Hospital Blood Banks’, *Management Science,* 23 (10), 1124-1132

Eksioglu, B., Vural, A. V., Reisman, A., 2009. 'The Vehicle Routing Problem: A Taxonomic Review', *Computers & Industrial Engineering*, 57, 1472–1483.

Elston, R. C., and Pickrel, J.C., 1965. ‘Guide To Inventory Levels For A Hospital Blood Bank Determined By Electronic Computer Simulation’, *Transfusion,* 5 (5), 465-470.

Eppen, G. D., 1979.’Effects of Centralization on Expected Costs in a Multi-Location Newsboy Problem’, Management Science, 25 (5), 498-501.

Erickson, M. L., Champion, M. H., Klein, R., Ross, R. L., Neal, Z., M., Snyder, E. L., 2008. 'Management Of Blood Shortages In A Tertiary Care Academic Medical Center: The Yale-New Haven Hospital Frozen Blood Reserve', *Transfusion*, 48 (10), 2252–2263.

Fontaine, M. J., Chung, Y. T., Rogers, W. M., Sussmann, H. D., Quach, P., Galel, S. A., Goodnough, L. T., Erhun, F., 2009.'Improving platelet supply chains through collaborations between blood centers and transfusion services', *Transfusion*, 49 (10), 2040–2047.

Frankfurter, G. M., Kendall, K. E., and Pegels, C. C., 1974. ‘Management Control of Blood through A Short-Term Supply-Demand Forecast System’, *Management Science,* 28 (4), 444-452.

Friedman, B.A., Abbott, R.D., and Williams, G.W., 1982. ‘A Blood Ordering Strategy for Hospital Blood Banks Derived from a Computer Simulation’, *American Journal of Clinical Pathology*, 78, 154–160.

Giosa I. D., Tansini I.L., Viera I.O.2002. ‘New assignment algorithms for the multi-depot vehicle routing problem’, *J. Oper. Res. Soc*. 53, 977–984

Guerrero W. J., Prodhon C., Velasco N., Amaya C. A. 2013. ‘Hybrid heuristic for the inventory location-routing problem with deterministic demand’, *Int. J. Production Economics*, 146, 359–370.

Gulczynski D., GoldenB., Wasil E. 2011. ‘The multi-depot split delivery vehicle routing problem: An integerprogramming-based heuristic, new test problems, and computational results’, *Computers & Industrial Engineering*, 61, 794–804.

Haijema, R.,Wal, J., and Dijk, N. M., 2007. ‘Blood Platelet Production: Optimization by Dynamic Programming and Simulation’, *Computers & Operations Research*, 34, 760–779.

Hansen P.H., Hegedahl B., Hjortkjvr S., Obel B., (1994). ‘A heuristic solution to the warehouse location-routing problem’ *European Journal of Operational Research,* 27,76-111.

Heddle, N. M., Liu, Y., Barty, R., Webert, K.E., Whittaker, S., Gagliardi, K., Lauzon, D., Owens, W., 2009. 'Factors Affecting The Frequency Of Red Blood Cell Outdates: An Approach To Establish Benchmarking Targets', *Transfusion*, 49 (2), 219–226.

Hiassat, A., Diabat, A., 2011. ‘A Location-Inventory-Routing-Problem with Perishable Products’, *Proceedings of the 41st International Conference on Computers & Industrial Engineering*.

Hindi, K., Pienkosz, K., 1999. 'Efficient Solution of Large Scale, Single-Source, Capacitated Plant Location Problems', *Journal of the Operational Research Society*, 50(3), 268-274.

Hinojosa, Y., Puerto, J, Fernandez, F. R., 2000. ‘A multiperiod two-echelon multicommodity capacitated plant location problem’, *European Journal of Operational Research*, 123, 271-291.

Ho S. C. 2015. ‘An iterated tabu search heuristic for the Single Source Capacitated Facility Location Problem’, *Applied Soft Computing*, 27, 169–178.

Jacobsen, S.K., Madsen, O.B.G., 1980. ‘A comparative study of heuristics for a two-level routing-location problem’, *European Journal of Operational Research*, 5, 378–387.

Jagannathan, R. and Sen, T., 1991. ‘Storing Crossmatched Blood: A Perishable Inventory Prior Allocation’, *Management Science,* 37 (3), 251-266.

Javid, A. A., Azad, N., 2010. 'Incorporating Location, Routing and Inventory Decisions in Supply Chain Network Design’, *Transportation Research*, Part E 46, 582–597.

Jayaraman, V. 1998. 'An Efficient Heuristic Procedure for Practical-Sized Capacitated Warehouse Design and Management', *Decision Sciences*, 29(3), 729-745.

Jayaraman, V., Pirkul, H., 2001. ‘Planning and coordination of production and distribution facilities for multiple commodities’, *European Journal of Operational Research*, 133, 394–408

Jennings, J. B., 1968. ‘An Analysis of Hospital Blood Bank Whole Blood Inventory Control Policies’, Transfusion 8, 335-342

Jennings, J. B., 1973. ‘Blood Bank Inventory Control’, *Management Science*, 19, 637-645.

Jin J., Crainic T. G., Lokkentangen A. 2014. ‘A cooperative parallel metaheuristic for the capacitated vehicle routing problem’, *Computers & Operations Research*, 44, 33–41.

Juan A. A., Faulin J., Ruiz R., Barrios B., Caballe ´ S. 2010. ‘The SR-GCWS hybrid algorithm for solving the capacitated vehicle routing problem’, *Applied Soft Computing*, 10, 215–224.

Kamp, C., Heiden, M., Henseler, O., Seitz, R. 2010. 'Management of blood supplies during an influenza pandemic', *Transfusion*, 50 (1).

Katsaliaki, K., Brailsford, S.C. 2007. 'Using Simulation To Improve The Blood Supply Chain', *Journal of the Operational Research Society*, 58 (2), 219–227.

Katz, A.J., Carter C.W., Saxton P., Blutt J., and Kakaiya, R.M., 1983. ‘Simulation Analysis of Platelet Production and Inventory Management’, *Vox Sanguinis*, 44, 31–36.

Kaufman, L., Eede, M. V., Hansen, P., 1977. ‘A Plant and Warehouse Location Problem’, *Opl Res. Q.*, 28(3), 547-554

Kendall, K. E., 1980. ‘Multiple Objective Planning for Regional Blood Centers’, *Long Range Planning*, 13 (4), 88-94.

Kendall, K. E., and Lee, S. M., 1980. ‘Formulating Blood Rotation Policies with Multiple Objectives’, *Management Science*, 26 (11), 1145-1157.

Kopach, R., 2008. 'Tutorial On Constructing A Red Blood Cell Inventory Management System With Two Demand Rates', *European Journal of Operational Research*, 185 (3), 1051–1059.

Kuo, Y., Wang, C. 2012. ‘A variable neighborhood search for the multi-depot vehicle routing problem with loading cost’, *Expert Systems with Applications*, 39, 6949–6954.

Laporte, G., 1992. ‘The vehicle routing problem: an overview of exact and approximate algorithms’, *European Journal of Operational Research*, 59(3):345–358.

Lenstra, J., Kan, A. K., 1981. ‘Complexity of vehicle routing and scheduling problems". *Networks*, (11), 221-228

Li J., Pardalos P. M., Sun H., Pei J., Zhang Y. 2015. ‘Iterated local search embedded adaptive neighborhood selection approach for the multi-depot vehicle routing problem with simultaneous deliveries and pickups’, *Expert Systems with Applications*, 42, 3551–3561.

Lin, J. R., & Lei, H.-C. 2009. ‘Distribution systems design with two-level routing considerations’, *Annals of Operations Research*, 172, 329–347. ISSN 0254-533.

Liu, S. C., Lee, S. B., 2003. ‘A two-phase heuristic method for the multi-depot location routing problem taking inventory control decisions into consideration’, *International Journal of Advanced Manufacturing Technology*, 22, 941–950

Liu, S., Lin, C., 2005. ‘A heuristic method for the combined location routing and inventory problem’, *International Journal of Advanced Manufacturing Technology*, 26(4), 372–381.

Lmariouh, J., Bouami, D., Jamali, A., Mozher, A., 2016. ‘Solving a multi-depot inventory routing problem arising in the moroccan food market’, *Journal of Theoretical and Applied Information Technology*, 84, 1.

Ma, H., Davidrajuh, R., 2005. ‘An iterative approach for distribution chain design in agile virtual environment’, *Industrial Management and Data Systems*, 105(6), 815–834.

Madsen, O.B.G., 1983. ‘Methods for solving combined two level location-routing problems of realistic dimensions’, *European Journal of Operational Research*, 12, 295–301.

Melechovsky´, J., Prins, C., Wolfler Calvo, R., 2005. ‘A metaheuristic to solve a location-routing problem with non-linear costs’, *Journal of Heuristics*, 11, 375–391.

Melkote,S., Daskin, M.S., 2001. 'Capacitated facility location/network design problems', *European Journal of Operational Research*, 481–495.

Melnyk, S.A., Pagell, M., Jorae, G., Sharpe, A.S., 1995.'Applying Survival Analysis to Operations Management: Analyzing The Differences in Donor Classes in the Blood Donation Process', *Journal of Operations Management*, 13 (4), 339–356.

Melo, M. T., Nickel, S., Gama, F. S., 2006. 'Dynamic multi-commodity capacitated facility location: A mathematical modeling framework for strategic supply chain planning', *Computers & Operations Research*, 181–208.

Melo, M.T., Nickel, S., Saldanha-da-Gama F., 2005.’ Dynamic multi-commodity capacitated facility location: amathematical modeling framework for strategic supply chain planning’, *Computers & Operations Research*, 33, 181–208

Melo, M.T., Nickel, S., Saldanha-da-Gama F., 2009. ‘Facility location and supply chain management – A review’, *European Journal of Operational Research*, 196, 401–412

Mirabi M., Ghomi F. S. M. T., Jolai F. 2010. ‘Efficient stochastic hybrid heuristics for the multi-depot vehicle routing problem’, *Robotics and Computer-Integrated Manufacturing*, 26, 564–569.

Moghaddam R. T., Safaei N., Gholipour Y. 2006. ‘A hybrid simulated annealing for capacitated vehicle routing problems with the independent route length’, *Applied Mathematics and Computation*, 176, 445–454.

Moin, N., Salhi, S., 2006. 'Inventory Routing Problems: A Logistical Overview', *Journal of the Operational Research Society*, 58(9), 1185-1194.

Nagurney, A., Masoumi, A. H., (2011). ' Supply Chain Network Design of a Sustainable Blood Banking System', *In Sustainable Supply Chains: Models, Methods and Public Policy Implications* T. Boone, V. Jayaraman, and R. Ganeshan, Editors, Springer, London, England, in press.

Nagy, G., Salhi, S., 2007. 'Location-Routing: Issues, Models and Methods', *European Journal of Operational Research*, 177(2), 649-672.

Nahmias S., 1982. 'Perishable Inventory Theory: A Review', *Operations Research*, 30 (4), 680-708.

Nekooghadirli N.,Moghaddam R. T., Ghezavati V. R., Javanmard S. 2014. 'Solving a new bi-objective location-routing-inventory problem in a distribution network by meta-heuristics', *Computers & Industrial Engineering*, 76, 204–221.

Nguyen, V.-P., Prins, C., & Prodhon, C. 2012. 'Solving the two-echelon location routing problem by a GRASP reinforced by a learning process and path relinking', *European Journal of Operational Research*, 216(1), 113–126.

Nozick, L. K., Turnquist, M. A., 2001. 'A two-echelon inventory allocation and distribution center location analysis', *Transportation Research Part E*, 2001, 425–441

Or, I., and Pierskalla, W. P., 1979. 'A Tranportation Location-Allocation Model for Regional Blood Banking', *AIEE Transactions*, 11 (2), 86-95

Pegels, C. C., Seagle, J. P., Cumming, D., and Shubsda, J. F., 1977. 'An Analysis of Selected Blood Service Policy Changes', *Medical Care*, 15 (1), 147-157.

Perl, J., Daskin, M.S., 1985. 'A warehouse location–routing problem', *Transportation Research B*, 19, 381–396.

Pierskalla, W.P., 2004. 'Supply chain management of blood banks, in: M.L. Brandeau, F. Sainfort, and W.P. Pierskalla (Eds.), *Operations Research and Health Care: A Handbook of Methods and Applications*, Kluwer Academic Publishers, 103–145.

Pirkul, H., and Jayaraman, V., 1997. 'A Multi-Commodity, Multi-Plant, Capacitated Facility Location Problem: Formulation and Efficient Heuristic Solution', *Computers Ops. Res*, 25(10), 869-878.

Popovsky, M. A., 1997. "Should Hospitals Collect Blood Components? No", *Transfusion Science*, 18 (4), 545-551.

Prastacos, G.P., 1978.'Optimal Myopic Allocation of a Product with Fixed Lifetime', *Journal of the Operational Research Society*, 29 (9), 905–913.

Prodhon, C., Prins, C., 2014.' A survey of recent research on location-routing problems', *European Journal of Operational Research*, 238, 1–17

Rabinowitz, M., 1973. 'Blood Bank Inventory Policies: A Computer Simulation', *Health Services Research*, 8 (4), 271–282.

Rahmani, A., MirHassani, S. A. 2014. ‘A hybrid Firefly-Genetic Algorithm for the capacitated facility location problem’, *Information Sciences*, 283, 70–78.

Ramkumar, N., Subramanian, P., Narendran, 2012. ‘Mixed-integer linear programming model for multi-commodity multi-depot inventory routing problem’, *OPSEARCH*, 49, 413.

Razavi, K. R., Nik, E. R., 2013. ‘Meta heuristic for multi depot inventory routing problem backlogging’, *J. Basic. Appl. Sci. Res.*, 3, 273-280.

Rönnqvist, M., Tragantalerngsak, S., Holt J. 1999. ‘A repeated matching heuristic for the single-source capacitated facility location problem’, *European Journal of Operational Research*, 116, 51-68.

Sadjady, H, Davoudpour, H., 2012. ‘ Two-echelon, multi-commodity supply chain network design with mode selection, lead-times and inventory costs’, *Computers & Operations Research*, 39, 1345–1354.

Sargent, R., G., 1998. ‘Verification and validation of simulation models’, *Proceedings of the 1998 Winter Simulation Conference*, 121-130.

Schreiber, G.B., Sharma, U.K., Wright, D.J., Glynn, S.A., Ownby, H.E., Tu, Y., Garratty, G., Piliavin, J., Zuck, T., Gilcher, R., 2005. 'First Year Donation Patterns Predict Long-Term Commitment for First-Time Donors', *Vox Sanguinis*, 88 (2), 114–121.

Semet, F., Taillard, E., 1993. ‘Solving real-life vehicle routing problems efficiently using tabu search’, *Annals of Operations Research*, 41, 469–488.

Shen, Z. M., Qi, L., 2007. 'Incorporating Inventory And Routing Costs In Strategic Location Models', *European Journal of Operational Research*, 179(2), 372- 389.

Shen, Z., Coullard, C., Daskin, M., 2003. 'A joint location-inventory model', *Transportation Science*, 37(1), 40-55.

Silva, F. J. F., Figuera, D. S., 2007. ‘A Capacitated Facility Location Problem with Constrained Backlogging Probabilities’, *International Journal of Production Research*, 45 (21), 5117-5134

Silver, E. A., 2007. ‘An overview of heuristic solution methods’, *Journal of the operational research society*, 55, 936-956.

Sirelson, V., and Brodheim, E., 1991. ‘A Computer Planning Model for Blood Platelet Production and Distribution’, *Computer Methods and Programs in Biomedicine*, 35, 279–291.

Sumichrast R. T., Markham S. 1995. ‘A heuristic and lower bound for a multi-depot routing problem’, *Computers and Operations Research*. 22(10), 1047-1056.

Surekha, P., Sumathi, S., 2011. ‘Solution to Multi-Depot Vehicle Routing Problem Using Genetic Algorithms’, *World Applied Programming,* 1 (3), 118-131

Synder, L. V., Daskin, M. S., Teo, C. P., 2007. ‘The Stochastic Location Model with Risk Pooling’, *European Journal of Operational Research,* 179(3), 1221-1238

Szeto W. Y., Wu Y., Ho S. C. 2011. ‘An artificial bee colony algorithm for the capacitated vehicle routing problem’, *European Journal of Operational Research,* 215, 126–135.

Şahin, G., Süral, H., Meral, S., 2007. ‘Locational Analysis for Regionalization of Turkish Red Crescent Blood Services’, *Computers & Operations Research*, 34, 692–704

Tragantalerngsak S., Holt J., Rönnqvist M. 1997. ‘Lagrangian heuristics for the two-echelon, single-source, capacitated facility location problem’, *European Journal of Operational Research*, 102, 611-625.

Tragantalerngsak S., Holt J., Rönnqvist M. 2000. ‘An exact method for the two-echelon, single-source, capacitated facility location problem’, *European Journal of Operational Research*, 123, 473-489.

Triulzi, D. J., (1997). 'Advantages of Outsourcing the Transfusion Service', *Transfusion,* (18) 4, 559-563

Wu T. H., Low C., Bai J. W. 2002. ‘Heuristic solutions to multi-depot location-routing problem’, *Computers & Operations Research*, 29, 1393-1415.

Xuefeng, W., 2010. 'An Integrated Multi-depot Location- inventory-routing Problem for Logistics Distribution System Planning of a Chain Enterprise', *International Conference on Logistics Systems and Intelligent Management ICLSIM 2010*, 3, 1427-1431.

Yegül, M., 2007. “Simulation analysis of the blood supply chain and a case study”. *Master’s thesis, Middle East Technical University*.

Zhang Y., Qi M., Miao L., Liu E. 2014. ‘Hybrid metaheuristic solutions to inventory location routing problem’, *Transportation Research Part E,* 70, 305–323.

APPENDIX A.

INPUTS AND RESULTS OF THE BASELINE PROBLEM

A.1. Input Parameters of Baseline Problem

- Set of Vehicles
  - Vehicle1
  - Vehicle2
- Set of TCs
  - TC1
  - TC2
- Set of RTCs
  - RTC1
  - RTC2
- Set of RBCs
  - RBC1
  - RBC2
- Two different capacity levels for RTBCs and RTCs
  - Capacity Level 1
  - Capacity Level 2
- Mean annual demand at TCs
  - TC1 – 500 units
  - TC2 – 600 units
- Variance of annual demand at TCs
  - TC1 – 25
  - TC2 – 25
- Capacities for DCs

    - DC1 – 20,000 units
    - DC2 – 20,000 units

- Annual inventory holding costs per unit of product at RTCs
    - RTC1 – 1 TL
    - RTC2 – 2 TL
- Fixed cost of placing an order to RBCs by RTCs
    - RTC1 – 2 TL
    - RTC2 – 4 TL
- Fixed annual costs of opening and operating RTCs for different capacity levels
    - RTC1
        - 125,000 TL for capacity level 1
        - 250,000 TL for capacity level 2
    - RTC2
        - 125,000 TL for capacity level 1
        - 250,000 TL for capacity level 2
- Fixed annual costs of opening and operating RBCs for different capacity levels
    - RBC1
        - 270,000 TL for capacity level 1
        - 420,000 TL for capacity level 2
    - RBC2
        - 270,000 TL for capacity level 1
        - 420,000 TL for capacity level 2
- Maximum capacities for different capacity levels for RTCs
    - RTC1
        - 25,000 units for capacity level 1
        - 35.000 units for capacity level 2
    - RTC2
        - 25,000 units for capacity level 1

        - 35.000 units for capacity level 2
- Maximum capacities for different capacity levels for RBCs
    - RBC1
        - 125,000 units for capacity level 1
        - 275.000 units for capacity level 2
    - RBC2
        - 125,000 units for capacity level 1
        - 275.000 units for capacity level 2
- Weighted distances between DCs and RBCs
    - DC1 – RBC1 : 7 TL/unit
    - DC1 – RBC2 : 2 TL/unit
    - DC2 – RBC1 : 2 TL/unit
    - DC2 – RBC2 : 8 TL/unit
- Weighted distances between RBCs and RTCs
    - RBC1 – RBC1 : 11 TL/unit
    - RBC1 – RBC2 : 2 TL/unit
    - RBC2 – RBC1 : 2 TL/unit
    - RBC2 – RBC2 : 8 TL/unit
- Transportation costs between TCs and RTCs and between different TCs
    - RTC1 – RTC2 : 2 TL
    - RTC1 – TC1 : 6 TL
    - RTC1 – TC2 : 7 TL
    - RTC2 – RTC1 : 2 TL
    - RTC2 – TC1 : 8 TL
    - RTC2 – TC2 : 10 TL
    - TC1 – RTC1 : 6 TL
    - TC1 – RTC2 : 8 TL
    - TC1 – TC2 : 6 TL
    - TC2 – RTC1 : 7 TL
    - TC2 – RTC2 : 10 TL
    - TC2 – TC1 : 6 TL

- Blood Disposal Rate: 0.1
- Fill rate : 0.95
- Lead Time : 0.03 years
- Annual number of visits a vehicle: 250
- Annual delivery capacity of a vehicle: 250,000 blood units
- α-percentile of standard normal distribution:1.645

A.2. Results of Baseline Problem

- Total Cost: 404,437 TL
- DC- RBC Assignments
    - DC1-RBC2
    - DC2-RBC2
- TC-RTC Assignments
    - TC1-RTC1
    - TC2-RTC1
- Vehicle Routes
    - Vehicle1
        - RTC1-TC2-TC1-RTC1
- RTC-RBC Assignments
    - RBC2-RTC1
- Opened RBCs and their capacity levels
    - RBC2 with capacity level 1
- Opened RTCs and their capacity levels
    - RTC1 with capacity level 1
- Amounts sent from DCs to RBCs
    - DC1 – RBC2 : 1,120 units
    - DC2 – RBC2 : 0
- Amount sent from RBCs to RTCs
    - RBC2 – RTC1 : 1,100 units

APPENDIX B.

SUMMARY OF THE SOLUTIONS OBTAINED BY APPLYING THE PROPOSED SOLUTION METHODS TO CTPs

B.1. Optimal Solution Method

Table 19. Summary of the solutions obtained by applying optimal solution method to CTPs

Scenarios (Problem Instances)	Size of instances										Optimal Solution Method				
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity	Number of RTC Capacity	Number of Variables	Number of discrete Variables	Number of Equations	CPU Time(seconds)	Objective Function Value	Best estimate	Absolute Gap	Relative Gap
CTP1	2	2	2	2	2	2	2	57	44	71	0.08	1,359,538.03	1,358,179.85	1,358.18	0.001
CTP2	2	2	2	4	4	2	2	177	152	185	3,600.00	3,284,589.63	3,276,818.37	7,771.26	0.002
CTP3	4	2	2	4	4	2	2	185	156	197	43.47	2,566,589.63	2,564,025.61	2,564.03	0.001
CTP4	3	3	3	3	3	3	3	154	126	157	3.09	1,998,957.60	1,996,960.64	1,996.96	0.001
CTP5	4	3	3	4	3	3	3	205	171	202	42.05	2,566,589.63	2,564,025.61	2,564.03	0.001
CTP6	4	4	4	4	4	4	4	321	272	293	460.52	1,978,057.22	1,976,081.14	1,976.08	0.001
CTP7	5	4	4	5	5	4	4	475	413	425	3,600.00	2,493,025.46	900,482.62	1,592,542.85	0.639
CTP8	5	3	3	5	5	4	4	388	338	363	3,600.00	3,368,948.58	1,109,307.43	2,259,641.15	0.671
CTP9	6	3	3	6	6	4	4	565	501	523	3,600.00	4,694,013.58	745,186.61	3,948,826.98	0.841
CTP10	6	4	4	6	6	4	4	677	600	599	3,600.00	3,362,748.88	672,937.52	2,689,811.36	0.800

- Objective Function Value: Objective function value of the best integer solution found by the solver at the end of the execution process.
- Best Estimate: Best theoretical objective function value (bound for the optimal solution).
- Absolute Gap: Difference between the “best estimate” and the “best integer solution”.
- Relative Gap: “best estimate”-“best integer solution”/ “best estimate”.

B.2. Decomposition Heuristic 1

Table 20. Summary of the solutions obtained by applying DH1 to CTPs

Scenarios (Problem Instances)	Size of instances										DH1	
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels	Number of Variables	Number of discrete Variables	Number of Equations	CPU Time (Seconds)	Objective Function Value
CTP1	2	2	2	2	2	2	2	57	44	71	0.28	1,359,538
CTP2	2	2	2	4	4	2	2	177	152	185	0.22	3,284,590
CTP3	4	2	2	4	4	2	2	185	156	197	0.19	2,566,590
CTP4	3	3	3	3	3	3	3	154	126	157	0.14	2,066,503
CTP5	4	3	3	4	3	3	3	205	171	202	0.13	2,566,590
CTP6	4	4	4	4	4	4	4	321	272	293	0.17	2,205,390
CTP7	5	4	4	5	5	4	4	475	413	425	0.17	2,840,219
CTP8	5	3	3	5	5	4	4	388	338	363	0.13	3,519,219
CTP9	6	3	3	6	6	4	4	565	501	523	0.47	4,602,465
CTP10	6	4	4	6	6	4	4	677	600	599	0.31	3,946,665

B.3. Decomposition Heuristic 2

Table 21. Summary of the solutions obtained by applying DH2 to CTPs

Scenarios (Problem Instances)	**Size of instances**										**DH2**	
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels	Number of Variables	Number of discrete Variables	Number of Equations	CPU Time (Seconds)	Objective Function Value
CTP1	2	2	2	2	2	2	2	57	44	71	0.14	1,359,538
CTP2	2	2	2	4	4	2	2	177	152	185	0.14	3,284,590
CTP3	4	2	2	4	4	2	2	185	156	197	0.13	2,566,590
CTP4	3	3	3	3	3	3	3	154	126	157	0.11	2,066,503
CTP5	4	3	3	4	3	3	3	205	171	202	0.27	2,566,590
CTP6	4	4	4	4	4	4	4	321	272	293	0.20	2,205,390
CTP7	5	4	4	5	5	4	4	475	413	425	0.19	2,840,219
CTP8	5	3	3	5	5	4	4	388	338	363	0.17	3,519,219
CTP9	6	3	3	6	6	4	4	565	501	523	0.36	4,602,465
CTP10	6	4	4	6	6	4	4	677	600	599	0.22	3,807,358

B.4. Decomposition Heuristic 3

Table 22. Summary of the solutions obtained by applying DH3 to CTPs

Scenarios (Problem Instances)	**Size of instances**										**DH3**	
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels	Number of Variables	Number of discrete Variables	Number of Equations	CPU Time (Seconds)	Objective Function Value
CTP1	2	2	2	2	2	2	2	57	44	71	0.48	1,359,538
CTP2	2	2	2	4	4	2	2	177	152	185	0.22	3,284,590
CTP3	4	2	2	4	4	2	2	185	156	197	0.30	2,566,590
CTP4	3	3	3	3	3	3	3	154	126	157	0.22	2,066,503
CTP5	4	3	3	4	3	3	3	205	171	202	0.34	2,566,590
CTP6	4	4	4	4	4	4	4	321	272	293	0.30	1,984,449
CTP7	5	4	4	5	5	4	4	475	413	425	0.23	2,493,025
CTP8	5	3	3	5	5	4	4	388	338	363	0.28	3,519,219
CTP9	6	3	3	6	6	4	4	565	501	523	0.37	4,949,658
CTP10	6	4	4	6	6	4	4	677	600	599	0.39	3,352,499

B.5. Decomposition Heuristic 4

Table 23. Summary of the solutions obtained by applying DH4 to CTPs

Scenarios (Problem Instances)	**Size of instances**										**DH4**	
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels	Number of Variables	Number of discrete Variables	Number of Equations	CPU Time (Seconds)	Objective Function Value
CTP1	2	2	2	2	2	2	2	57	44	71	0.09	1,359,538
CTP2	2	2	2	4	4	2	2	177	152	185	0.31	3,284,590
CTP3	4	2	2	4	4	2	2	185	156	197	0.19	2,566,590
CTP4	3	3	3	3	3	3	3	154	126	157	0.25	2,066,503
CTP5	4	3	3	4	3	3	3	205	171	202	0.23	2,566,590
CTP6	4	4	4	4	4	4	4	321	272	293	0.27	1,984,449
CTP7	5	4	4	5	5	4	4	475	413	425	0.35	2,493,025
CTP8	5	3	3	5	5	4	4	388	338	363	0.33	3,519,219
CTP9	6	3	3	6	6	4	4	565	501	523	0.39	4,949,658
CTP10	6	4	4	6	6	4	4	677	600	599	0.36	3,352,499

B.6. Hybrid Heuristic 1

Table 24**.** Summary of the solutions obtained by applying HH1 to CTPs

Scenarios (Problem Instances)	**Size of instances**										**HH1**	
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels	Number of Variables	Number of discrete Variables	Number of Equations	CPU Time (Seconds)	Objective Function Value
CTP1	2	2	2	2	2	2	2	57	44	71	1.89	1,359,538
CTP2	2	2	2	4	4	2	2	177	152	185	2.21	3,284,590
CTP3	4	2	2	4	4	2	2	185	156	197	2.21	2,566,732
CTP4	3	3	3	3	3	3	3	154	126	157	2.01	2,066,503
CTP5	4	3	3	4	3	3	3	205	171	202	2.16	2,566,732
CTP6	4	4	4	4	4	4	4	321	272	293	2.22	2,205,390
CTP7	5	4	4	5	5	4	4	475	413	425	2.50	2,840,219
CTP8	5	3	3	5	5	4	4	388	338	363	2.44	3,519,219
CTP9	6	3	3	6	6	4	4	565	501	523	3.99	4,602,465
CTP10	6	4	4	6	6	4	4	677	600	599	4.15	3,946,665

B.7. Hybrid Heuristic 2

Table 25. Summary of the solutions obtained by applying HH2 to CTPs

Scenarios (Problem Instances)	Size of instances										HH2	
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels	Number of Variables	Number of discrete Variables	Number of Equations	CPU Time (Seconds)	Objective Function Value
CTP1	2	2	2	2	2	2	2	57	44	71	1.72	1,359,538
CTP2	2	2	2	4	4	2	2	177	152	185	2.12	3,284,590
CTP3	4	2	2	4	4	2	2	185	156	197	2.15	2,566,732
CTP4	3	3	3	3	3	3	3	154	126	157	1.89	2,066,503
CTP5	4	3	3	4	3	3	3	205	171	202	2.24	2,566,732
CTP6	4	4	4	4	4	4	4	321	272	293	2.16	2,205,390
CTP7	5	4	4	5	5	4	4	475	413	425	2.35	2,840,219
CTP8	5	3	3	5	5	4	4	388	338	363	2.27	3,519,219
CTP9	6	3	3	6	6	4	4	565	501	523	3.84	4,602,465
CTP10	6	4	4	6	6	4	4	677	600	599	2.50	3,807,358

B.8. Hybrid Heuristic 3

Table 26. Summary of the solutions obtained by applying HH3 to CTPs

Scenarios (Problem Instances)	Size of instances										HH3	
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels	Number of Variables	Number of discrete Variables	Number of Equations	CPU Time (Seconds)	Objective Function Value
CTP1	2	2	2	2	2	2	2	57	44	71	2.10	1,359,538
CTP2	2	2	2	4	4	2	2	177	152	185	2.24	3,284,590
CTP3	4	2	2	4	4	2	2	185	156	197	2.31	2,566,732
CTP4	3	3	3	3	3	3	3	154	126	157	1.95	2,066,503
CTP5	4	3	3	4	3	3	3	205	171	202	2.35	2,566,732
CTP6	4	4	4	4	4	4	4	321	272	293	2.31	1,984,449
CTP7	5	4	4	5	5	4	4	475	413	425	2.43	2,493,025
CTP8	5	3	3	5	5	4	4	388	338	363	2.46	3,519,219
CTP9	6	3	3	6	6	4	4	565	501	523	2.70	4,949,658
CTP10	6	4	4	6	6	4	4	677	600	599	2.61	3,352,499

B.9. Hybrid Heuristic 4

Table 27. Summary of the solutions obtained by applying HH4 to CTPs

Scenarios (Problem Instances)	Size of instances										HH4	
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels	Number of Variables	Number of discrete Variables	Number of Equations	CPU Time (Seconds)	Objective Function Value
CTP1	2	2	2	2	2	2	2	57	44	71	1.75	1,359,538
CTP2	2	2	2	4	4	2	2	177	152	185	2.24	3,284,590
CTP3	4	2	2	4	4	2	2	185	156	197	2.19	2,566,732
CTP4	3	3	3	3	3	3	3	154	126	157	2.06	2,066,503
CTP5	4	3	3	4	3	3	3	205	171	202	2.27	2,566,732
CTP6	4	4	4	4	4	4	4	321	272	293	2.23	1,984,449
CTP7	5	4	4	5	5	4	4	475	413	425	2.52	2,493,025
CTP8	5	3	3	5	5	4	4	388	338	363	2.48	3,519,219
CTP9	6	3	3	6	6	4	4	565	501	523	2.62	4,949,658
CTP10	6	4	4	6	6	4	4	677	600	599	2.58	3,352,499

B.9. Simulated Annealing Heuristic

Table 28. Summary of the solutions obtained by applying SA to CTPs

Scenarios (Problem Instances)	**Size of instances**										**SA**	
	Number of DCs	Number of potential RBCs	Number of potential RTCs	Number of TCs	Number of Vehicles	Number of RBC Capacity Levels	Number of RTC Capacity Levels	Number of Variables	Number of discrete Variables	Number of Equations	CPU Time (Seconds)	Objective Function Value
CTP1	2	2	2	2	2	2	2	57	44	71	1.88	1,359,538
CTP2	2	2	2	4	4	2	2	177	152	185	2.20	3,284,590
CTP3	4	2	2	4	4	2	2	185	156	197	2.25	2,566,590
CTP4	3	3	3	3	3	3	3	154	126	157	2.09	1,998,958
CTP5	4	3	3	4	3	3	3	205	171	202	2.29	2,566,590
CTP6	4	4	4	4	4	4	4	321	272	293	2.27	1,984,449
CTP7	5	4	4	5	5	4	4	475	413	425	2.48	2,493,025
CTP8	5	3	3	5	5	4	4	388	338	363	2.47	3,519,219
CTP9	6	3	3	6	6	4	4	565	501	523	4.08	4,602,465
CTP10	6	4	4	6	6	4	4	677	600	599	2.66	3,359,919

APPENDIX C.

RESULTS OBTAINED BY THE OPTIMAL SOLUTION METHOD AND INDICATORS REPRESENTING THE PERFORMANCE OF THE METHOD

Table 29. Results Obtained By Solving Test Problems with Optimal Solution Method

Instance Group	Test Instance	Optimal Solution Method				
		CPU Time(seconds)	Objective Function Value	Best estimate	Absolute Gap	Relative Gap
IG1	IG1-1	0.090	3861133.908	3857276.631	3857.277	0.001
IG1	IG1-2	0.130	4698475.575	4693781.793	4693.782	0.001
IG1	IG1-3	0.130	3777314.564	3773541.023	3773.541	0.001
IG1	IG1-4	0.130	4237421.422	4233188.234	4233.188	0.001
IG1	IG1-5	0.090	4353505.430	4349156.273	4349.156	0.001
IG2	IG2-1	0.250	4854405.700	4849556.144	4849.556	0.001
IG2	IG2-2	0.230	3953905.884	3949955.928	3949.956	0.001
IG2	IG2-3	0.220	3741403.707	3737666.040	3737.666	0.001
IG2	IG2-4	0.250	4470052.441	4465586.855	4465.587	0.001
IG2	IG2-5	0.270	3959134.707	3955179.527	3955.180	0.001
IG3	IG3-1	7.830	4265920.833	4261659.174	4261.659	0.001
IG3	IG3-2	3.560	4089375.498	4085290.208	4085.290	0.001
IG3	IG3-3	4.130	4362484.277	4358126.151	4358.126	0.001
IG3	IG3-4	3.590	4531803.917	4527276.641	4527.277	0.001
IG3	IG3-5	6.310	4255258.398	4251007.390	4251.007	0.001
IG4	IG4-1	35.160	4434085.417	4429655.762	4429.656	0.001
IG4	IG4-2	22.170	3673906.243	3670236.007	3670.236	0.001
IG4	IG4-3	33.220	4239825.763	4235590.173	4235.590	0.001
IG4	IG4-4	24.380	3965067.576	3961106.469	3961.106	0.001
IG4	IG4-5	35.170	4291573.355	4287286.069	4287.286	0.001
IG5	IG5-1	84.810	3978756.744	3974781.962	3974.782	0.001
IG5	IG5-2	51.340	3935648.443	3931716.727	3931.717	0.001
IG5	IG5-3	127.390	4308943.607	4304638.968	4304.639	0.001
IG5	IG5-4	37.050	3741122.884	3737385.498	3737.386	0.001
IG5	IG5-5	97.310	4339741.418	4335406.012	4335.406	0.001
IG6	IG6-1	1724.530	4287253.461	4282970.490	4282.970	0.001
IG6	IG6-2	2341.780	4456766.817	4452314.503	4452.315	0.001
IG6	IG6-3	2381.340	4608080.151	4603476.675	4603.477	0.001
IG6	IG6-4	1921.480	4035723.620	4031691.928	4031.692	0.001
IG6	IG6-5	850.090	3972268.193	3968299.893	3968.300	0.001
IG7	IG7-1	4158.310	4259946.696	4255691.005	4255.691	0.001
IG7	IG7-2	10800.000	5361219.470	3326641.987	2034577.483	0.379
IG7	IG7-3	2381.670	4007612.192	4003608.583	4003.609	0.001
IG7	IG7-4	1957.300	3663014.231	3659354.876	3659.355	0.001
IG7	IG7-5	8108.190	4883304.587	4878426.160	4878.426	0.001

Table 29. (Continued)

Instance Group	Test Instance	Optimal Solution Method				
		CPU Time(seconds)	Objective Function Value	Best estimate	Absolute Gap	Relative Gap
IG8	IG8-1	10800.000	4036634.739	2765279.444	1271355.295	0.315
IG8	**IG8-1***	432000.000	3981884.739	3977906.832	3977.907	0.001
IG8	IG8-2	10800.000	3878734.194	2581735.000	1296999.194	0.334
IG8	IG8-3	10800.000	3676517.822	2597240.000	1079277.822	0.294
IG8	IG8-4	10800.000	4604958.523	2882060.000	1722898.523	0.374
IG8	IG8-5	10800.010	3815298.724	2612612.222	1202686.502	0.315
IG9	IG9-1	10800.000	4338402.080	2807197.500	1531204.580	0.353
IG9	**IG9-1***	432000.000	4325627.080	2807623.333	1518003.746	0.351
IG9	IG9-2	10800.000	4613261.783	2671412.500	1941849.283	0.421
IG9	IG9-3	10800.000	5052868.649	2904910.000	2147958.649	0.425
IG9	IG9-4	10800.000	3850464.756	2520757.500	1329707.256	0.345
IG9	IG9-5	10800.010	3975344.299	2640753.750	1334590.549	0.336
IG10	IG10-1	10800.000	3947470.553	2514459.167	1433011.387	0.363
IG10	**IG10-1***	432000.000	3947470.553	2514459.167	1433011.387	0.363
IG10	IG10-2	10800.010	3885663.772	2557997.917	1327665.855	0.342
IG10	IG10-3	10800.000	4843755.880	2817906.250	2025849.630	0.418
IG10	IG10-4	10800.000	4485460.850	2562350.000	1923110.850	0.429
IG10	IG10-5	10800.000	4526793.436	2744035.000	1782758.436	0.394
IG11	IG11-1	10800.000	5306704.382	2680542.143	2626162.239	0.495
IG11	**IG11-1***	432000.000	4363794.002	2680542.143	1683251.860	0.386
IG11	IG11-2	10800.000	3964146.951	2568285.000	1395861.951	0.352
IG11	IG11-3	10800.010	4210993.851	2708141.786	1502852.065	0.357
IG11	IG11-4	10800.000	4913315.121	2651570.179	2261744.942	0.460
IG11	IG11-5	10800.010	4182513.169	2577340.000	1605173.169	0.384
IG12	IG12-1	10800.000	4627396.626	2944277.266	1683119.360	0.364
IG12	**IG12-1***	432000.000	4587246.626	2944280.955	1642965.671	0.358
IG12	IG12-2	10800.000	4189622.426	2601168.750	1588453.676	0.379
IG12	IG12-3	10800.010	5078301.390	2524639.375	2553662.015	0.503
IG12	IG12-4	10800.000	4807413.670	2671080.625	2136333.045	0.444
IG12	IG12-5	10800.000	5355350.460	2600524.063	2754826.398	0.514
IG13	IG13-1	10800.000	5945329.706	3065682.639	2879647.067	0.484
IG13	**IG13-1***	432000.000	5910654.706	3065682.639	2844972.067	0.481
IG13	IG13-2	10800.000	4248579.824	2599988.333	1648591.491	0.388
IG13	IG13-3	10800.000	4483565.358	2521253.611	1962311.747	0.438
IG13	IG13-4	10800.000	4277078.647	2545819.028	1731259.620	0.405
IG13	IG13-5	10800.010	6514623.938	2674791.111	3839832.826	0.589
IG14	IG14-1	10800.000	5363083.366	2546927.500	2816155.866	0.525
IG14	**IG14-1***	432000.000	4473019.254	2546927.500	1926091.754	0.431
IG14	IG14-2	10800.000	6380985.889	2530912.500	3850073.389	0.603
IG14	IG14-3	10800.000	7282661.424	2562895.000	4719766.424	0.648
IG14	IG14-4	10800.000	4230292.874	2638555.000	1591737.874	0.376
IG14	IG14-5	10800.000	7405965.261	2577647.083	4828318.178	0.652

Table 29. (Continued)

Instance Group	Test Instance	Optimal Solution Method				
		CPU Time(seconds)	Objective Function Value	Best estimate	Absolute Gap	Relative Gap
IG15	IG15-1	14400.060	5371104.191	2675017.000	2696087.191	0.502
IG15	**IG15-1***	432000.000	5261604.191	2675017.000	2586587.191	0.492
IG15	IG15-2	14400.060	8188567.868	2644957.000	5543610.868	0.677
IG15	IG15-3	14400.000	8304351.723	2533148.000	5771203.723	0.695
IG15	IG15-4	14400.000	5710739.970	2436767.000	3273972.970	0.573
IG15	IG15-5	14400.000	6367656.415	2739601.250	3628055.165	0.570
IG16	IG16-1	28800.000	6124477.752	2751404.537	3373073.215	0.551
IG16	**IG16-1***	432000.000	6124477.752	2751404.537	3373073.215	0.551
IG16	IG16-2	28800.000	7130902.477	2958566.667	4172335.810	0.585
IG16	IG16-3	28800.000	8852789.943	2714048.333	6138741.610	0.693
IG16	IG16-4	28800.000	5326207.184	2544112.500	2782094.684	0.522
IG16	IG16-5	28800.000	5307215.375	2553476.111	2753739.264	0.519
IG17	IG17-1	28800.000	5061508.501	2578535.714	2482972.787	0.491
IG17	**IG17-1***	432000.000	5061508.501	2578535.714	2482972.787	0.491
IG17	IG17-2	28800.000	7237483.765	2625832.857	4611650.908	0.637
IG17	IG17-3	28800.090	10467167.707	2528061.429	7939106.279	0.758
IG17	IG17-4	28800.000	6129911.976	2575948.214	3553963.761	0.580
IG17	IG17-5	28800.000	12943272.932	2607610.000	10335662.932	0.799
IG18	IG18-1	36000.020	6574942.851	2731825.000	3843117.851	0.585
IG18	**IG18-1***	432000.000	6574942.851	2731825.000	3843117.851	0.585
IG18	IG18-2	36000.020	7067675.377	2718030.000	4349645.377	0.615
IG18	IG18-3	36000.000	7399047.535	2813855.000	4585192.535	0.620
IG18	IG18-4	36000.080	8741717.625	2515720.000	6225997.625	0.712
IG18	IG18-5	36000.040	12096555.255	2723940.000	9372615.255	0.775
IG19	IG19-1	43200.020	7686995.550	2592790.000	5094205.550	0.663
IG19	**IG19-1***	432000.000	7686995.550	2592790.000	5094205.550	0.663
IG19	IG19-2	43200.020	7718162.666	2545910.000	5172252.666	0.670
IG19	IG19-3	43200.140	6825821.627	2490840.000	4334981.627	0.635
IG19	IG19-4	43200.020	7587276.869	2515800.000	5071476.869	0.668
IG19	IG19-5	43200.000	9945633.742	2615110.000	7330523.742	0.737
IG20	IG20-1	86400.020	11936761.011	2663170.000	9273591.011	0.777
IG20	**IG20-1***	432000.000	11936761.011	2663170.000	9273591.011	0.777
IG20	IG20-2	86400.050	10189182.051	2592925.000	7596257.051	0.746
IG20	IG20-3	86400.130	9295995.429	2496845.000	6799150.429	0.731
IG20	IG20-4	86400.020	8394729.801	2649915.000	5744814.801	0.684
IG20	IG20-5	86400.000	13761874.499	2565570.000	11196304.499	0.814

- Objective Function Value: Objective function value of the best integer solution found by the solver at the end of the execution process.
- Best Estimate: Best theoretical objective function value (bound for the optimal solution).
- Absolute Gap: Difference between the “best estimate” and the “best integer solution”.
- Relative Gap: (“best estimate”-“best integer solution”)/ “best estimate”.

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