Improving routing for medical test sample transportation to a clinical analysis laboratory using optimization approaches

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Abstract
Biomedical tests take an important role assisting physicians providing accurate diagnostics to patients. These samples are collected in specimen collection centres and are transported in cool boxes to the laboratory where they are analysed. In this work, the case of a diagnostic provider group is considered. Since this entity deals daily with a great number of samples, the flow of their arrivals must be considered to ensure for a smooth workload in the laboratory. For this reason, a Biomedical Sample Transportation Problem (BSTP) mathematical model is developed to assist this entity in the creation of their routes. These routes have the particularity that they can depart from different locations other than the laboratory. Further, a multi-start algorithm based on the developed model is introduced with the purpose of handling large instances in a reasonable amount of time. The objective is to both minimize the routes' total travel time and the number of sample boxes' arriving to the laboratory in the busiest time period. To the best of ones' knowledge, none of the previous works on the BSTP has considered the possibility of open routes as the current work presents. Application of the model in two regions with different objectives suggests that improvements can be achieved.

Keywords: Vehicle Routing Problem; Biomedical Sample Transportation Problem; Desynchronized arrivals; Open routes; Time-windows; Optimization; Metaheuristic; Multi-start algorithm

1. INTRODUCTION

One of the main challenges addressed by healthcare systems is to guarantee high-quality services having limited resources. Diagnostic laboratories are constantly seeking for ways to improve their capabilities by strengthening diagnostic accuracy, managing higher workloads faster and extend test menus. Simultaneously, they are required to become more efficient by reducing costs [1].

A significant part of a successful laboratory operation is biomedical sample transportation. In fact, a well preserved and timely biomedical sample is vital to lead to an accurate diagnosis. Daily, thousands of biomedical samples are being transported from various healthcare facilities (e.g., hospitals, private clinics and retirement homes) to laboratories to be examined. Even if large hospitals can often locally analyse samples, most centres are not sufficiently equipped to perform such tests; thus, it must be ensured that samples are safely transported to clinical analysis laboratories. Accordingly, many Specimen Collection Centres (SCCs) are assigned to the same laboratory making essential managing the flow of the samples arriving to the lab in order to avoid congestion.

Biomedical samples are perishable items; therefore, it must be ensured that once these samples are collected in the SCCs that they arrive in the laboratory in a short amount of time to guarantee that they lead to an accurate diagnosis. This short life span of biomedical samples usually makes necessary to perform more than one visit per day in each SCC in order to avoid sample perishing.

The current study is integrated in a project from SIEMENS Healthineers (SH) Enterprise Services (ES) team and addresses the aim of a clinical analysis group, which pursues its activity in the area of public health. This group deals with a great number of biomedical samples each day. Hence, the present research has the objective of improving the routing of biomedical test sample transportation to their central clinical analysis laboratory using optimization approaches. This improvement should ensure for a smoother workload at the laboratory by desynchronizing the biomedical samples arrivals while at the same time reduce the operational costs and increase the resources usage by minimizing the routes total duration. To achieve this goal, a Biomedical Sample Transportation Model (BSTP) with desynchronized arrivals and open routes is developed.

The remainder of this paper is organized as follows. In Section 2 the case-study is presented, and a literature review is performed on Section 3. Section 4 details the proposed optimization model and Section 5 describes the multi-start heuristic used. Section 6 presents performance results of the solution approaches and Section 7 outlines key results. Finally, Section 8 concludes the paper.

2. CASE-STUDY

Entity's background

The entity under study is a group of clinical pathology and aims at continuously following up both with the medical evolution and challenges in the area of clinical pathology, while providing this knowledge to medical staff and patients. To be able to provide clinical diagnoses, the group has distributed throughout Portugal several collection points and laboratories, including hospital laboratories.

An important aspect that lies behind the entity's process of providing medical diagnosis is the associated sample transportation operations and logistics. To be able to provide an accurate medical diagnosis, it is fundamental that the biomedical sample is transferred with appropriate handling from the site where it was taken to the laboratory.

The focus of the present research lies on optimizing the entity's routes in two different regions, Region A and Region B, that transport biomedical samples to the entity's central laboratory.

Associated with the way the routes in Region A are defined, arises the issue of having periods of the day where too many samples arrive in the laboratory contrary to others where very few samples arrive. This leads to significant differences in the laboratory throughput throughout the day, that needs to be softened. This is, in fact, a bottleneck problem in the samples' supply chain of the central laboratory.

Regarding Region B routes, the problem of having too many samples arriving in the lab in certain periods of the day is not a concern, since these samples usually arrive to the laboratory in the evening. Nevertheless, they still have the issue of taking a long time to be completed, which is a challenge, given the perishable nature of the biomedical samples transferred.

As a consequence of the challenges described for both these regions, the focus of the present thesis is to address them by constructing and proposing routes that, on one hand, allow for a smoother workload at the laboratory, and on the other hand, reduce the operational costs and increase the resources usage by minimizing the routes total duration.

Problem scope definition

To construct the entity's routes, not only it is necessary to attend their restrictions and limitations, but also it is important to take their objectives into consideration. In fact, the biggest challenge is to face the bottleneck in the samples supply chain related with the samples' arrival time while, at the same time, make the routes efficient by trying to reduce transportation costs by minimizing the routes' duration.

It is, therefore, the aim of this work to address this challenge by redesigning and rescheduling the collection routes in the two regions under study, considering the specific needs and challenges of each of them. More specifically, for Region A it is important to tackle the challenge of desynchronizing the samples' arrivals in the laboratory, while at the same time take into concern the reduction of transportation costs; for Region B the main concern is to minimize the routes' total duration.

3. LITERATURE REVIEW

Vehicle Routing Problem

The Vehicle Routing Problem (VRP) constitutes a well-known class of optimization problems found in logistics, originated from real-life needs [2]. The problem was first introduced in 1959 by Dantzig and Ramser [3] as a generalization of the Traveling Salesman Problem (TSP) presented by Flood, in 1956 [4]. The TSP arises from the situation of a salesman who wants to visit his clients in a given set of cities and then return to his own city, in the shortest possible route.

In the classical VRP, a fleet of vehicles is based at a single depot to collect or deliver products for a set of geographically scattered nodes [5]. Each of these vehicles, whose capacity cannot be exceeded, leaves the depot, visits the nodes and returns to the depot. The aim is to find the optimal set of routes so that all the nodes are served exactly once. Thereafter, fundamental elements of a typical VRP include the road network, the vehicles, the nodes and the depot [6]. Moreover, depending on the problem, the optimization objective can vary.

VRP variants

Depending on the operational context, the problem can have different constraints, designed to represent the problems characteristics, introduced in each of the fundamental elements that leads to the generation of several VRP variants. Typical constraints include time windows, multiple depots, multiple periods, and heterogeneous fleets [7], [8].

A general assumption of the classical VRP is that each individual vehicle only performs one route over the planning horizon [9]. This assumption can be impractical, for instance, in scenarios where the fleet of vehicles is constituted by small vehicles with low capacity, since they do not have the capability of visiting a large number of nodes in each route [10], a common situation faced in metropolitan cities. The Multi-trip Vehicle Routing

Problem (MTVRP) emerges as an extension of the classical VRP that allows each vehicle to perform more than one route within a given time period. This problem considers dependency between routes, since it requires that the temporal aspects of the vehicle movements are considered. In fact, it is explicitly needed to guarantee that overlapping routes for the same vehicle do not occur and that the vehicles' total duration is less than or equal to the maximum driving time [11].

Finally, another important variant of the VRP consists in the introduction of time windows, Vehicle Routing Problem with Time Windows (VRPTW). This variant arises when the service of each node *i* is limited to a specific time window, [a_i, b_i], requiring the determination of a schedule for the vehicle routes', so that the nodes are served in their corresponding time windows [12].

VRP solution methods

With the purpose of deciding the best solution method or algorithm to solve a VRP, one must consider both the solution quality and the time taken to obtain it [13]. Since the 1980s, many approaches including exact methods and heuristics have been designed to solve the VRP. Even though exact methods can solve optimally small instances, up to around 100 nodes [14], when facing larger and real-life scenarios, these methods become unfeasible given the time required to obtain the solution. Hence, the use of heuristic procedures in these environments is more appropriate. Although heuristic methods may not ensure an optimal solution, they allow reasonable time solving [14].

Biomedical Sample Transportation Problem

Having all the relevant VRP classes and solution methodologies reviewed, the Biomedical Sample Transportation Problem (BSTP) can be introduced. The BSTP is a challenging VRP arising in the context of healthcare logistics and that can be applied specifically to the case study of the present work. This problem aims at creating a transportation plan to pick up perishable items, biomedical samples, at given locations, referred to as SCCs and to take them to facilities that have adequate treatment equipment, usually central laboratories. Thus, the transportation network consists of a group of SCCs (nodes) affected to a laboratory (depot).

There are some concerns that arise with the biomedical sample transportation, following described. After collection, the samples are consolidated in cool boxes that need to arrive at the laboratory within a given time frame to be treated otherwise, the samples deteriorate and become unusable, increasing the laboratory's costs and decreasing the quality of the service. In order to respect the sample lifespans, SCCs cannot maintain the collected biomedical samples for a long time; thereby, each SCC can have different number of sample transportation requests according to the SCC open hours, causing an interdependence of pickup times and routes. It is also important to impose a time constraint on the duration of each route to guarantee the samples' quality. Thus, the BSTP is typically characterized by multiple visits to each node, a time-window on each visit time and multiple routes for each vehicle [15], being closely related to the MTVRP and the VRPTW, previously presented.

All the aforementioned constraints fit the scope of the case study presented in this work though, there is also the need of considering desynchronization of the samples' arrival to the lab and the fact that the first route of each vehicle can start in a different location than the lab.

Anaya-Arenas *et al.* (2016) presented a version of the BSTP applied to a real-world case study in the Province of Québec in Canada. In this work, each SCC required several collection visits and each one of them needed to happen inside a given and independent time windows that satisfied the samples' lifespan. Therefore, with the aim of minimizing the route duration time a multi-start heuristic was proposed [15].

Using the same context, years later, in 2018, Toschi *et al.*, developed a metaheuristic to solve the BSTP that considered the SCC opening and closing hours as decision variables and, also the interdependency between routes. The objective focused on minimizing the routes' total duration [16].

Last year, in 2019, Anaya-Arenas proposed another metaheuristic to solve the BSTP considering the opening and closing hours of the SCCs and the moment they are visited as decision variables, while taking into consideration the interdependency between routes [17]. Nevertheless, none of the presented works considered the need for the desynchronization of the samples' arrival to the laboratory.

Closer to the context of the case study presented in this thesis, Naji-Azimi *et al.* (2016) studied the BSTP with the desynchronization of the vehicles' arrivals to the depot. To the best of ones' knowledge, they were the first and the only ones yet to consider the desynchronization of the vehicles in this context as an objective. This consideration is extremely important, due to the fact that if too many boxes of samples arrive in a short period of time to the central laboratory, samples are queued and may have to wait a long time before they are analysed, creating a bottleneck in the samples' supply chain [18]. Thus, by minimizing the maximum amount of sample boxes arriving within a given time period it normalizes both the laboratory workload and reduces sample losses. Nevertheless, in Naji-Azimi *et al.* (2016) work the possibility of open routes, routes that can depart from different places other than the lab, was not considered.

From above it can be said that there is the need of developing a more detailed model that not only is able to desynchronize the arrivals in the lab and minimize the routes' total time, as the one developed by Naji-Azimi *et al.* (2016) does, but also that allows for the possibility of having the routes start in a different places other than the lab. It is in this form that the current research will contribute to assist in the resolution of a real-world case study, the one previously described and encountered in the entity under study.

4. THE BIOMEDICAL SAMPLE TRANSPORTATION MODEL

Problem Statement

In order to formulate the BSTP with desynchronized arrivals and open routes, it is firstly important to distinguish both the SCCs locations and the collection requests, since each SCC can have more than one collection request. The n SCCs are defined as:

$$V' = \{v_1', \ldots, v_n'\} \quad (1)$$

, where each SCC l requires Q_l collection requests leading to a total of $p = \sum_{l=1}^{n} Q_l$ requests. Each one of these requests is composed of one box that contains several biomedical samples.

The BSTP can be modelled as a complete graph $G = \{V, A\}$, where:

$$V = \{v_0, v_1, \ldots, v_p, v_{p+1}, v_{p+2}, \ldots, v_{p+d+1}\} \quad (2)$$

is the set of nodes in the network. p represents the number of transportation requests and d the number of drivers. More specifically, the subset $P = \{v_1, v_2, \ldots, v_p\}$ corresponds to the transportation request nodes. Additionally, P_l is denoted as the set of request nodes found in V which matches the same SCC location. Since the first route of each day of each vehicle may depart from a different location rather than the central lab, the departing places must also be presented in the set of nodes in the network, therefore they are represented by the nodes $\{v_{p+2}, \ldots, v_{p+d+1}\}$. Finally, the laboratory is represented by the nodes $\{v_0, v_{p+1}\}$. With the exception of the first route of each day, which may start in a different location and finish in the lab, all of the other routes start and finish in the laboratory.

The arc set of the graph can then be defined as:

$$A = \{(v_i, v_j) : v_i, v_j \in V, \quad i \neq j, \\ i = 0, \ldots, p+d+1 \; and \; not \\ (i = 0 \; V \; i = p+1; \; j = p+2, \ldots, p+d+1\} \quad (3)$$

, where a travel time between nodes, t_{ij}, is assigned to each arc (v_i,v_j). Moreover:

$$t_{ij} = 0 \quad if \quad \exists \; l \text{ such that } i, \; j \in P_l \quad (4)$$

, in other words, if i and j correspond to two requests from the same SCC the travel time to go from one to the other is zero. It is important to note that in general $t_{ij} \neq t_{ji}$, being one of the reasons why a directed graph is used to model the problem. Furthermore, each request j has to be carried out within a given time window $[a_j, b_j]$. Finally, two requests of the same SCC cannot be served in the same route.

Further, to carry out the transportation requests there are available K uncapacitated vehicles. Each one of these can execute multiple routes ($r = 1, \ldots, R$). Each vehicle has a limitation on the length on the working day, T_k. Additionally, both the average loading time for each transportation request in the SCCs, τ_i, and the unloading time at the lab before a new route starts, τ_0, have to be considered. Moreover, as mentioned in previous sections, the perishable nature of the biomedical samples requires having a maximal transportation time associated with the requests. Thereafter, there is also a maximal transportation time for the samples of request i, T_{max}^i.

The objective of this problem is then to minimize both the routes' total duration (including the waiting times at the SCCs) and a weighted penalty θ related with the maximum number of boxes that arrive in the laboratory in the busiest time period.

Mathematical formulation

In this section the details of the mathematical model used to define the biomedical sample transportation problem with desynchronized arrivals and open routes of the entity under study are presented. Thus, the sets, the parameters, the decision variables, the objective function and the constraint equations are presented below.

Table 1 – Model notation: Sets.

Notation	Description
Sets	
i	index of the nodes: $i = 0, \ldots, p+d+1$
j	index of the nodes: $j = 0, \ldots, p+d+1$
k	vehicles: $k = 0, \ldots, K$
r	routes per vehicle: $r = 0, \ldots, R$
t	time periods: $t = 0, \ldots, T$

Table 2 – Model notation: Parameters and Decision Variables.

Notation	Description
Parameters	
T_k	Limit on the working day of vehicle k
τ_i	Loading time of request i
τ_0	Unloading time at the laboratory
T_{max}^i	Maximal transportation time for the samples associated with request i
θ	Weighted penalty linked to the maximum number of boxes that arrive at the laboratory during the busiest time period
M	Large constant
d	Number of drivers
a_i	Start of time windows of request i
b_i	End of time windows of request i
t_{ij}	Travel time from node i to node j
ω	Units to discretize time
Decision Variables	
$x_{ijkr} \in \{0,1\}$	Takes the value of 1 if vehicle k in its route r travels from request i to request j; 0 otherwise
y_{itkr}	takes the value of 1 if request i carried out by vehicle k in its route r arrives at the laboratory during the t^{th} time period; 0 otherwise
$u_{ikr} \in R_0^+$:	represents the visit time (start of loading) of the r^{th} route of vehicle k of the transportation request i.
$w \in N^+$	represents the highest number of boxes arriving to the Lab during the most visited time period.

The mathematical model reads as follows:

$$Min \quad \sum_{k=1}^{K}\sum_{r=1}^{R}\left(u_{p+1kr}-u_{0kr}\right)+\theta\cdot w \tag{5}$$

Subject to:

$$\sum_{k=1}^{K}\sum_{r=1}^{R}\sum_{i=0\,\&\,i\neq p+1}^{p+d+1} x_{ijkr}=1, \quad j=1,\dots,p \tag{6}$$

$$\sum_{k=1}^{K}\sum_{j=1}^{p} x_{ijkr}=1,\ i=p+2,\dots,p+d+1;\ r=1 \tag{7}$$

$$\sum_{j\in P_l}\sum_{i=0\,\&\,i\neq p+1}^{p+d+1} x_{ijkr}\le 1,\ l=1,\dots,n;\ k=1,\dots,K;\ r=1,\dots,R \tag{8}$$

$$\sum_{i=0}^{p} x_{ijkr}-\sum_{l=1}^{p+1} x_{jlkr}=0, \quad r=2,\dots,R;\ j=1,\dots,p;k=1,\dots,K \tag{9}$$

$$\sum_{i=1\&\,i\neq p+1}^{p+d+1} x_{ijkr}-\sum_{l=1}^{p+1} x_{jlkr}=0, \quad r=1;\ j=1,\dots,p;\ k=1,\dots,K \tag{10}$$

$$\sum_{j=1}^{p} x_{0jkr}\le 1, \quad r=2,\dots,R;\ k=1,\dots,K \tag{11}$$

$$\sum_{j=1}^{p} x_{ijkr}\le 1, \quad r=1;\ k=1,\dots,K;\ i=p+2,\dots,p+d+1 \tag{12}$$

$$\sum_{j=1}^{p} x_{0jkr}-\sum_{j=1}^{p} x_{j,p+1kr}=0,\ r=2,\dots,R;\ k=1,\dots,K \tag{13}$$

$$\sum_{i=p+2}^{p+d+1}\sum_{j=1}^{p} x_{ijkr}-\sum_{j=1}^{p} x_{j,p+1kr}=0,\ r=1;k=1,\dots,K;\ i=p+2,\dots,p+d+1 \tag{14}$$

$$a_j-T_k\cdot\left(1-\sum_{i=0\&i\neq p+1}^{p+d+1} x_{ijkr}\right)\le u_{jkr}\le b_j+T_k\cdot\left(1-\sum_{i=0\&i\neq p+1}^{p+d+1} x_{ijkr}\right), \quad j=0,\dots,p+d+1;\ k=1,\dots,K;r=1,\dots,R \tag{15}$$

$$u_{ikr}-u_{jkr}+\left(b_i+\tau_i+t_{ij}-a_j\right)\cdot x_{ijkr}\le b_i-a_j, \quad r=2,\dots,R;\ k=1,\dots,K;j=1,\dots,p+1;\ i=0,\dots,p \tag{16}$$

$$u_{ikr}-u_{jkr}+\left(b_i+\tau_i+t_{ij}-a_j\right)\cdot x_{ijkr}\le b_i-a_j, \quad r=1;\ k=1,\dots,K\ j=1,\dots,p+1;i=1,\dots,p,p+2,\dots,p+d+1 \tag{17}$$

$$u_{0kr}\ge u_{p+1,k,r-1}+\tau_0,\ k=1,\dots,K;\ r=2,\dots,R \tag{18}$$

$$u_{p+1,k,r}-u_{jkr}\le T_{max}^j+T_k\cdot\left(1-\sum_{i=0}^{p} x_{ijkr}\right), \quad r=2,\dots,R;\ k=1,\dots,K;\ j=1,\dots,p \tag{19}$$

$$u_{p+1,k,r}-u_{jkr}\le T_{max}^j+T_k\cdot\left(1-\sum_{i=1\&\,i\neq p+1}^{p+d+1} x_{ijkr}\right), \quad r=1;\ k=1,\dots,K;\ j=1,\dots,p \tag{20}$$

$$u_{p+1,kr}-u_{ik1}\le T_k, \quad r>1;\ k=1,\dots,K;\ i=p+2,\dots,p+d+1 \tag{21}$$

$$\sum_{k=1}^{K}\sum_{r=1}^{R}\sum_{t=0}^{T} y_{itkr}=1, \quad i=1,\dots,p \tag{22}$$

$$y_{itkr}\le\sum_{j=1}^{p+1} x_{ijkr}, \quad i=1,\dots,p;\ t=0,\dots,T;k=1,\dots,K;\ r=1,\dots,R \tag{23}$$

$$u_{p+1,kr}<\omega\cdot(t+1)+M\cdot(1-y_{itkr}),\ i=1,\dots,p;\ t=0,\dots,T;k=1,\dots,K;\ r=1,\dots,R \tag{24}$$

$$u_{p+1,kr}\ge\omega\cdot t-M\cdot(1-y_{itkr}), \quad i=1,\dots,p;\ t=0,\dots,T;k=1,\dots,K;\ r=1,\dots,R \tag{25}$$

$$w\ge\sum_{k=1}^{K}\sum_{r=1}^{R}\sum_{i=1}^{p} y_{itkr}, \quad t=0,\dots,T \tag{26}$$

$$u_{0kr}=u_{ikr}, \quad r=1;\ i=p+2,\dots,p+d+1;k=1,\dots,K \tag{27}$$

$$u_{0kr}\le u_{p+1kr}, \quad r=2,\dots,R;\ k=1,\dots,K \tag{28}$$

$$u_{ikr}-\sum_{j=0\&i\neq j}^{p}\left(a_j+\tau_j-a_i+t_{ji}\right)x_{jikr}\ge a_i, \quad i=1,\dots,p;\ r=1,\dots,R;k=1,\dots,K \tag{29}$$

$$\sum_{j=1}^{p}\sum_{i=p+2}^{p+d+1} x_{ijk1}-\sum_{j=1}^{p}\sum_{i=p+2}^{p+d+1} x_{ijk-1,1}\le 0, \quad k=2,\dots,K \tag{30}$$

$$\sum_{r=1}^{R}\sum_{i=1}^{p} x_{ijkr}-\sum_{l=1}^{j-1}\sum_{r=1}^{R}\sum_{i=1}^{p} x_{ilk-1r}\le 0, \quad j=1,\dots,p;\ k=2,\dots,K \tag{31}$$

$$\sum_{i=1}^{p}\sum_{r=1}^{R}\sum_{t=0}^{T} y_{itkr}\le M\cdot\sum_{i=1}^{p}\sum_{t=1}^{T} y_{itk-1,1}, \quad k=2,\dots,K; \tag{32}$$

$$\sum_{i=1}^{p}\sum_{t=0}^{T} y_{itkr}\le M\cdot\sum_{i=1}^{p}\sum_{t=1}^{T} y_{itk,r-1}, \quad k=1,\dots,K;\ r=2,\dots,R \tag{33}$$

$$\sum_{k=1}^{K}\sum_{r=1}^{R} x_{ijkr}=0, \quad \forall\, i,j\in V\setminus\{0,p+1\}\mid\left(a_i+\tau_i+t_{ij}>b_j\right) \tag{34}$$

$$\sum_{k=1}^{K}\sum_{r=1}^{R} x_{ijkr}=0, \quad \forall i,j\in V\setminus\{0,p+1\}\mid\left(a_i-b_j+\tau_j+t_{j,p+1}>T_{max}^i\right) \tag{35}$$

$$\sum_{k=1}^{K}\sum_{r=1}^{R}\sum_{l=1}^{t-1} y_{ilkr}=0,\ \forall\, i\in V\,\{0,p+1\}\mid\left(a_i+\tau_i+t_{i,p+1}\ge\omega t\right);\ t=1,\dots,T-1 \tag{36}$$

The first part of the objective function (5) minimizes the routes' total duration (i.e., the sum of the end time minus starting time of each route of each vehicle) which includes the necessary waiting time at each SCC. The second part of the equation implements a penalty factor θ to the maximum number of boxes arriving during the busiest time period, w. Constraints (6) assures that each request is serviced by exactly one route. Constraints (7), ensure that the first route of each day (i.e., when r equals 1) departs from one of the possible departing places that is not the central lab. Constraints (8) ensure that each route should only visit one original point at a time. Flow conservation is certified by constraints (9) and (10). Constraints (9) guarantee flow conservation for the routes that start in the lab (i.e., for $r > 1$) and constraints (10) for the first route of each vehicle (i.e., for $r = 1$). Constraints (11) and (12) state that the vehicle k can start a route r or not. Constraints (11) refer to routes that start in the lab and constraints (12) to the ones that start in a different location. If a given route has started it has to finish in the lab to deliver the samples. Thereafter, constraints (13) and (14) guarantee it for both routes that start in the laboratory and the ones that start in a different location, respectively. Constraints (15) states that the time windows for each request must be respected. The sub-tour elimination constraints are represented by the constraints (16) and (17). Constraints (16) characterizes the routes that start in the laboratory and constraints (17) the ones that do not. Constraints (18) ensure that route r of vehicle k must start at least later than the arrival of its route $k-1$ plus the waiting time in the laboratory between routes τ_0. Constraints (19) and (20) ensure that the time that takes to return to the depot after visiting a given node is restricted so that the samples' lifetime is satisfied. Constraints (19) refers to the routes that start in the lab and constraints (20) to the ones that do not. Since each vehicle has a limitation on the length on the working day, constraints (21) set the maximum duration of vehicle k which has to be less than T_k. Constraints (22) state that the request i will arrive in the laboratory within a given time period t. Constraints (23) ensure that if request i has been visited by the r^{th} route of vehicle k the variable y_{itkr} can take the value of 1. Constraints (24) and (25) strengthen the connection within flow and y variables and divide time into periods of ω units of time. When using these constraints in the case where $y_{itkr} = 1$ we have $\omega \cdot t \leq u_{p+1kr} \leq \omega \cdot (t + 1)$, meaning that the laboratory has to be visited within the t^{th} time period, therefore within time ωt and $\omega \cdot (t+1)$. Constraints (26) calculate the laboratory maximum workload during the available time periods. In fact, the number of sample boxes that arrive in the lab in a specific time period is the same as the number of SCCs visited by the routes that returned to the lab in that same period. Supposing that a box of samples is gathered at each SCC request the workload is the number of boxes that arrive at the laboratory within this time period. Since the objective function considers the starting time of the route of each vehicle the time of the lab, one has to guarantee that for the first route of each vehicle (the ones that do not start in the lab) that this value is equal to the time they depart from that first location guaranteed by constraints (27). Moreover, constraints (28) enforce that the arrival time in the laboratory of a given route r occurs after its departing time. Constraints (29) define a lower bound on the minimum value of variable u. In fact, when visiting the arc (i,j) by the r^{th} route of vehicle k the variable x_{ijkr} equals 1 and consequently, $u_{ikr} + \tau_i + t_{ij} \leq u_{jkr}$. In case that x_{ijkr} equals 0 we have $u_{jkr} \geq a_i$ which is always valid. Constraints (30) and (31) are based on the symmetry breaking constraints developed by Coelho and Laporte in 2014 [19]. Essentially, by ordering the use of the vehicles and the assignment of request to vehicles these constraints are able to remove symmetric solutions. Constraints (32) and (33) are symmetry defeating constraints which break the symmetry caused by variables y enhancing the model. In particular, constraints (32) state that if the first route of vehicle $k-1$ has not been used, then the requests cannot be carried out by routes of the vehicle k. In addition, constraints (33) states that route r of vehicle k can only be used if to route $r-1$ of this same vehicle is already associated at least one request. Constraint sets (34) and (35) state that one cannot travel from request i to request j when $a_i + \tau_i + t_{ij} > b_j$ and $a_i + \tau_j + t_{j,p+1} - b_j > T^i_{max}$. Constraints (36) exhibits the connection concerning the earliest visit time of a given request and the possible time periods where the corresponding samples can arrive in the laboratory. Essentially, when $a_i + \tau_i + t_{i,p+1} \geq \omega t$, request i cannot arrive to the laboratory earlier than the t^{th} time period.

5. HEURISTIC METHOD

Multi-Start Heuristic Algorithm

Multi-start algorithms hold two phases: the first one where an initial solution is generated and a second one where the generated solution is commonly, but not always, improved [20]. In the specific case of this algorithm, the first phase comprises the *Construction* procedure while the second phase is constituted by the *Extraction-Reinsertion* and *Swap* procedures.

To guarantee that diverse iterations lead to different solutions, a level of randomization is applied in two parameters: in the maximal sample transportation time (T_{max}) and in the maximum length of a vehicle working day (T_K). Both parameters influence the *Construction* procedure, which creates different feasible or unfeasible solutions. Moreover, these two parameters are adapted in conformity with the feasibility of the solution and only solutions that are feasible can pass to the improvement steps. Algorithm 1 provides an insight on the general steps of the multi-start algorithm used.

Algorithm 1: Multi-start algorithm

$BestSolution = \emptyset$
$Temp_{T_k} = T_k$
$Temp_{T_{max}} = T_{max}$
For $Iter = 1\ to\ Max_{iter}$ **do**
  Repeat
    $\overline{T_k} = random\ (0,\ T_k - Temp_{T_k}) + Temp_{T_k}$
    $\overline{T_{max}} = random\ (0, T_{max} - Temp_{T_{max}}) + Temp_{T_{max}}$
    $CurrentSolution$ = **Construction** ($\overline{T_k}$, $\overline{T_{max}}$)
    If $CurrentSolution$ is feasible **then**
      $Temp_{T_{max}} = Temp_{T_{max}} - \alpha \cdot T_{max}$
      $Temp_{T_k} = Temp_{T_k} - \alpha \cdot T_k$
    Else
      $Temp_{T_{max}} = Min\{Temp_{T_{max}} + \alpha \cdot T_{max}, T_{max}\}$
      $Temp_{T_k} = Min\{Temp_{T_k} + \alpha \cdot T_k, T_k\}$
    End If
  Until $CurrentSolution$ is feasible
  $CurrentSolution$ = **Extraction-Reinsertion** ($CurrentSolution$)
  $CurrentSolution$ = **Swap** ($CurrentSolution$)
  If $CurrentSolution$ improves the cost of the best-known solution **then**
    $BestSolution = CurrentSolution$
End for

After obtaining an initial feasible solution, the improvement procedures are now applied. Thus, the *Extraction-Reinsertion* and the *Swap* procedures attempt to improve the quality of the solution coming from the *Construction* procedure. To do so, the original values of the sample travel time and the vehicle travel time are used. After the maximum number of iterations has been achieved the algorithm stops and the best solution found is returned.

Construction procedure

As stated, the construction procedure forms an initial solution, where the nodes are sequentially added to the routes. Routes are initialized by adding their respective starting and finishing points. To select the first node to be visited, n_1, the following set of rules are used:

- $N_1 = argmax_{i \in P}\{t_{i,p+1}\}$, i.e., the set of request nodes $i \in P = \{v_1, v_2, \dots, v_p\}$ whose travel time is the greatest to the laboratory;
- $N_2 = argmin_{i \in N_1}\{b_i\}$, i.e., the set of request nodes $i \in N_1$ whose time window upper bond is the lowest;
- A random node, n_1, is selected from N_2.

After inserting the first node, n_1, in the working route, to insert a new node certain rules are to be followed. Firstly, a node from the unvisited set of nodes is chosen in sequence and the possibility of adding it in every position of that route is evaluated. If there are feasible placing positions, the node will be placed in the position that conducts to the smallest increase in the route's total travel time. In case there is not a feasible position for that node in that route, the algorithm tries to place the next unvisited node in that same route. The process repeats until all unvisited nodes are tested to be placed in that route. Afterwards, the same process occurs for the other unfilled routes.

Extraction-Reinsertion procedure

The first improvement procedure, the *Extraction-Reinsertion* procedure, has the purpose of reducing the value of the objective function by repositioning some of the nodes of the solution previously obtained in the *Construction* procedure. Hence, to calculate this cost, the length of the time period, ω, has now to be considered. This procedure lies on taking every node and place it on its best feasible position. Thus, starting from first route of the first vehicle all the nodes are repositioned in all possible locations. After trying to place a node in all positions the node is placed in the feasible position that leads to the best improvement. This procedure is repeated until no further improvement can be reached.

Swap procedure

The second improvement procedure, the *Swap* procedure, also aims at minimizing the cost of the current solution, i.e., the one coming from the *Extraction-Reinsertion* procedure. To improve the solution, following the order of the nodes in the current solution, each pair of nodes is considered, and their corresponding positions are swapped. The swap is applied to all possible combination of two nodes over all the vehicles' routes. As soon as a move improves the solution's cost, it is accepted. This procedure stops whenever the swapping of all the available nodes offers no more improvement.

6. PERFORMANCE NUMERICAL RESULTS

To test the mathematical model and the algorithm, a set of 15 significant instances (small, medium and large) was designed based on the geographical locations considered by the entity in Region A to construct their routes. The aim is to find the parameters that fit best the entity's context to be used in the case study resolution chapter and to compare the results obtained with the mathematical model with the ones provided by the heuristic method previously presented. Hence, the mathematical model was developed and implemented using the optimization software GAMS and the heuristic algorithm was developed and implemented using Python 3.8.1.

The first experiment lied on finding which penalization fits best the entity's context: if $\theta = 25$, $\theta = 50$ or $\theta = 75$. The penalty that is found to fit better their purpose is the one where $\theta = 50$, since it offers a favourable balance between the number of boxes arriving in the busiest period and the routes' total time. This value does not penalize to much the arrivals in the laboratory and is able to find favourable results for the routes' total time. Furthermore, it gives better gap results when comparing with the penalization of $\theta = 25$ and was able to provide results in some instances where the penalty of $\theta = 75$ was not.

The second experiment was to find the best form to discretize time: if in intervals of 30 minutes or 60 minutes (i.e., $\omega = 30$ or $\omega = 60$). The parameter that is found to fit the entity's scope is $\omega = 60$ since it outperformed significantly $\omega = 30$, given that the time to obtain solutions for this parameter was remarkably lower. In terms of the objective function, the results were the same for the small and medium size instances. For the larger instances, one can encounter different performances, since that for some instances the results for $\omega = 60$ outperformed the ones for $\omega = 30$, while for others the opposite occurred.

The last experiment lied on finding what is the most suitable value of iterations that balances the computational time and the quality of the solution, if 1, 50 or 100 iterations. With the results obtained one can perceive that 1 iteration was the only value that provided remarkably worse results. The difference obtained for 50 and 100 iterations, was not significant since it only provided different results for one instance. Thus, if the aim is to work with a small amount of collection requests 100 iterations should be the value chosen, while if one is working with large instances a smaller number of iterations should be selected.

For all of the experiments performed, the optimization software was not able to find results for the large instances, providing only results for the small and medium size instances. The heuristic method, on the other hand, was able to find results for all of the considered instances and required less computational time. The results obtained for the experiments were that the values for the heuristic method were very similar to the optimization software ones. More specifically, for the small instances the differences were always bellow 2% and for the medium size instances the differences were bellow 20%.

In summary, the heuristic algorithm is a good alternative to the optimization solver. In terms of the parameters to use, for Region A a penalization of 50 and a time discretization into periods of 60 minutes proved to find more adequate results. On the other hand, for Region B since the aim is only to minimize the routes' time a penalization of 0 should be considered. Regarding the number of iterations to consider it should be 50 for when the number of collection requests is very high and 100 when one deals with a smaller number of collection requests. Thus, these will be the values considered when using the heuristic methodology in the next chapter.

7. CASE STUDY RESULTS AND DISCUSSION

Region A

Associated with the manner that routes are currently defined in this region, arises the issue of having periods of the day where too many samples arrive in the lab and others where very few arrive. This leads to significant differences in the lab throughput throughout the day. Thus, emerging the need of improving them by desynchronizing their arrivals.

The results obtained for this region using the heuristic algorithm are presented in the following table, Table 3.

Table 3 - Numerical comparison of the routes currently established with the ones provided by the heuristic method in Region A.

	Current routes		Proposed routes	
	Distance (kms)	Time (min)	Distance (kms)	Time (min)
Total	3744	7642	3958	7839
Average	117	239	124	245
Min.	25	85	37	97
Max.	522	517	536	485
w	151		118	

Analysing Table 3, it is possible to understand that with the proposed routes there is an increase of 214 kms and 197 minutes on each day. In percentage, this corresponds to an increase of 5,7% in terms of distance and of 2,6% in terms of time. The routes in average also take more 6 minutes and 7 kms to be performed. Comparing the results for the shortest and longest routes, one would have more homogeneous routes with the heuristic algorithm results since that the shortest route would take more time to be completed, and the largest less time. Moreover, having the longest route performed in less time is beneficial for the entity due to the perishable nature of biomedical samples. Regarding the highest number of boxes arriving in the busiest time period, a decrease of 33 boxes would be attained.

To comprehend the change in the arrivals, graphs regarding the number of boxes arriving in the lab in function of the arrival times were plotted for both the current and the proposed routes.

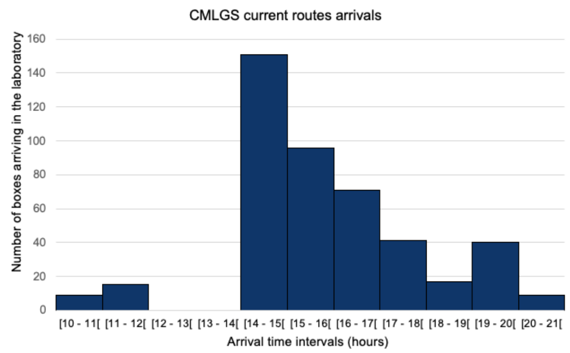

Figure 1 – Estimation of the number of boxes arriving in the central laboratory per hour by the current routes.

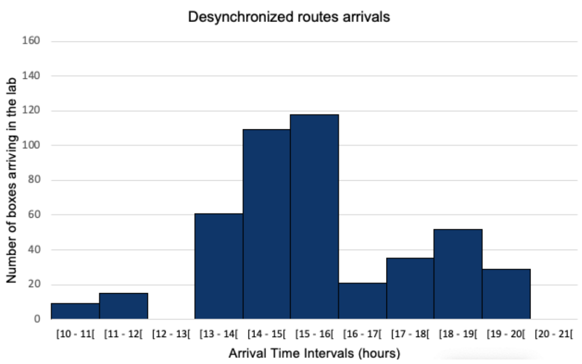

Figure 2 – Estimation of the number of boxes arriving in the central laboratory per hour by the proposed routes.

Concerning the results obtained for the arrivals of the current ones (Figure 1) and the proposed ones (Figure 2) major differences can be identified. More specifically, apart from the early morning routes where the arrivals are maintained, with the new routes it would be possible to have boxes arriving earlier in the lab. As a matter of fact, it would be possible to have samples arriving at 13h in comparison to the current routes where samples only arrive after 14h. Also, the peak of 151 boxes that occurred from 14h to 15h in the current routes would pass to occur between 15h and 16h having 118 boxes arriving in that interval, a difference of 33 boxes. Another important fact to point out lies on the afternoon peak that occurs in the current routes in the interval from 19h to 20h that would occur earlier between 18h and 19h. Finally, the proposed routes would also allow not having boxes arriving in the lab after 20h which is beneficial for the entity since it could allow the lab to close earlier. In general, the new routes would both allow having samples arriving earlier in the lab as well as providing for a smoother workflow in the lab, allowing the samples to be analysed earlier which in turn would make results to be sent to patients also earlier.

Finally, to further analyse the impact of these arrivals in the workflow of the lab, and since the labs' capacity is not explicitly known in terms of how many boxes can be analysed per hour, three different scenarios were created to analyse different possible capacities for the lab workflow. The three scenarios lied on having a lab capacity of 60, 80 or 100 boxes per hour. For the results obtained in these scenarios it would be possible to have all the samples analysed one hour earlier comparing to the currently established routes. Also, for scenario 2 and 3 it would allow having the full capacity being utilized for less hours, providing for a smoother workload in the lab.

In summary, although the new routes require an increase in terms of the routes total distance and total travelled time, it would be possible to have all of the lab work to be completed earlier. Not only this would allow results to be sent earlier to patients, but also would allow freeing the technicians that had to work during this hour, which could in turn compensate the cost associated to the increase in the routes travel time.

Region B

The aim when calculating routes for Region B is to minimize the routes' total travel time, not considering the desynchronization of the arrivals.

The numerical results obtained for this region using the heuristic algorithm are now presented in the following table, Table 4.

Table 4 – Numerical comparison of the routes currently established in with the new routes provided by the heuristic method.

		Current	Proposed	Improve-ment
Time	R1	10h00–19h01	11h43–18h39	-
	R2	11h00–18h04	10h02–18h09	-
	R3	10h00–20h42	09h56–18h58	-
	Total	26h47	24h05	02h42
	Av.	~ 09h01/route	~ 08h07/route	54min/route
Distance	R1	502 kms	383 kms	-
	R2	355 kms	397 kms	-
	R3	590 kms	465 kms	-
	Total	1447 kms	1245 kms	202 kms
	Av.	~ 482 kms	~ 415 kms	67 kms/route

By analysing Table 4, one can observe the improvements in terms of time and distance. In fact, with the new routes, an improvement of 02h42 (i.e., less 11,2% in terms of time) would be achieved. Regarding the total distance, an improvement of 202 kilometres (i.e., less 16,2% in terms of distance) would be attained. Concerning the schedules of the routes the maximum time that a route would take would pass from 10h40 to 09h02. The shortest route would also diminish since it would pass from taking 07h04 to be around 06h56. The remaining route would also be improved since it would change to last from 09h01 to last 08h07. As a matter of fact, the results obtained with the heuristic algorithm provide more balanced routes in terms of time and distance since the difference between the longest and the shortest routes is less than from the ones currently established.

Furthermore, the routes retrieved by the algorithm were also improved with regard to the arrival times, since all of them would arrive before 19h on the contrary to the currently established ones where the longest route arrives at almost 21h. This would enable samples to arrive earlier to the lab and to be tested earlier which in turn would allow results to be sent to the patients also earlier.

In conclusion, the heuristic algorithm was very effective calculating Region B routes since it was able to provide the results desired by the entity. Not only the routes were improved in terms of distance and total travel time, but it would also enable results to be delivered earlier to patients.

8. CONCLUSIONS AND FUTURE WORK

BSTPs are highly complex problems which are designed to transport biomedical samples from SCCs to the lab to be analysed. Supported by a case study description and an extensive literature review, a BSTP model with desynchronized arrivals and open routes was proposed. Its main goal is to assist a clinical analysis group, by reconstructing their current routes. Two objectives are considered in the model: minimization of the routes' total travel time and the number of sample boxes' arriving to the lab in the busiest time period. Besides, a multi-start heuristic was introduced to handle large instances in a reasonable amount of time.

Firstly, to test the mathematical model and the heuristic, a set of 15 instances characterized by their size was created having as a basis the geographical regions that the entity considers when constructing the routes.

The heuristic proved to be efficient in minimizing both the routes total duration as well as the number of arrivals during the busiest period, since it provided similar results and in less time in relation to the optimization program. In fact, it presented a relative error always bellow 20%. In addition, it also granted results for the large instances which GAMS could not find results.

The parameters that fit best the case study context were also studied, arriving to the conclusion that the finest penalization to desynchronize arrivals would be of 50 (i.e., $\theta = 50$) and that the finest time discretization would be into periods of 60 minutes (i.e., $\omega = 60$). Finally, the most appropriate number of iterations for the algorithm was investigated. Hence, arriving to the conclusion that if the aim is to work with a relatively small amount of collection requests it is appropriate to use 100 iterations, while if one is working with a set of large instances a smaller number of iterations must be selected to obtain results requiring computational time.

The model was applied to two different regions: Region A and Region B. While the aim of the former region was to both desynchronize the arrivals in the lab and minimize the total travelled time, the aim of the latter region was only to minimize the total travelled time. When applying the algorithm for Region A the arrivals were successfully desynchronized, however implying an increase of 5,7% and of 2,6% in the routes' total distance and total time, correspondingly. For Region B, improvements of 16,2% and of 11,2% can be attained in terms of the total distance and total time, respectively.

Within the developed work, although important results were obtained also some limitations can be identified that can be taken as basis for future work in the problem. Thus, regarding the heuristic algorithm proposed and in order to obtain solutions with higher quality, changes in the algorithm could be performed. Firstly, further randomization should be introduced in the creation of the initial solution at each iteration in the algorithm. Also, in the improvement steps, diversification of the search should be achieved in order to further explore the solution space. An additional suggestion lies on allowing for soft time windows in order to obtain improved solutions.

Still on the developed metaheuristic, improvements in the performance of the algorithm should be carried out in order to reduce the computational time taken to calculate the routes.

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