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A Dynamic Discretization Discovery Algorithm for the Routing of Multiple and Highly Perishable Commodities: An Application to the Transportation of Biomedical Samples

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Abstract. In this article we propose a two-step solution algorithm to solve a vehicle routing problem for the distribution of multiple highly perishable commodities. Inspired by an application in healthcare services, the biomedical sample transportation problem, numerous commodities with short lifespan presume multiple transportation requests at the same facility in a day and restrict the maximum time to reach destination. These two characteristics create an interdependency between the routing and the pickup decisions in time that is highly complex. To address these timing issues, we model this problem as a service network-design problem over a time-expanded network. Our solution method aggregates the network at two levels. First, the commodities are aggregated and artificially consolidated, reducing the symmetry arising when multiple transportation requests are solicited within a short period of time. Second, the space-time nodes in the network are constructed dynamically, thus reducing the size of the mathematical model to be solved at each iteration. Our algorithm proves to be efficient to solve a set of real-life instances from the Quebec laboratory network under the management of the Ministère de la Santé et des Services sociaux (Ministry of Health and Social Services).

Keywords. Time-expanded network, vehicle routing problem, biomedical samples transportation problem, health care logistics, highly perishable products, blood transportation, interdepency, dynamic discretization algorithm

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1 Introduction

In logistics operations, transportation is a main component of the total cost of products and services and it plays a significant role in the efficiency of the supply chain. The planing and optimization of distribution systems have been subject of study for over 60 years including many features relevant in practice to account for the multiple challenges faced by various industries (see Lahyani et al. (2015) and Coelho et al. (2016) for recent reviews). Either limits on the trucks' capacities, loading constraints, product compatibility, time restrictions, time windows, service or frequency requirements, are all features that entail different challenges in the mathematical modeling and decision making to optimize operations on real settings (Vidal et al., 2020). Moreover, transportation models are only useful if they admit efficient optimization algorithms to cope with the complexity of large-size problems arising in practice. In the specific case of products of high perishability, an important challenge is time limits (Liang et al., 2020). Planning a centralized distribution of the different products while respecting their respective (individual) life span becomes a critical aspect for the efficiency of the entire network.

We study an optimization problem motivated by the challenge of transporting biomedical samples –highly perishable products according to the classification provided by Amorim et al. (2013)– in a healthcare network. The biomedical samples transportation problem (BSTP) introduced by Anaya-Arenas et al. (2016) and extended later in Anaya-Arenas et al. (2021) deals with the problem of collecting multiple biomedical samples at health care centers (i.e. local clinics, retirement homes or long-term care centers) of short life span in a centralized manner, and to deliver them to a regional laboratory for analysis. The *rapid physical deterioration* of the product (samples) is controlled by a tight and *fixed* life span set by authorities and managers. There is hence a short life span for each sample, between its collection from the patient and its analysis at the laboratory, that needs to be respected. After the life span is passed the product is considered as lost. However, there is a *constant* customer value inside the life span, giving managers a small flexibility to batch samples and plan coordinated pickups allowing economies of scale. The entire planning process is done for a short time horizon (one day), with multiple transportation requests from each collection center, which links the samples' life span to the routes' length. Besides biomedical samples, some food or prepared meals can enter in this category of products and we believe our algorithm can be applied to other related transportation problems.

This article's contribution is twofold. First, it proposes a novel mathematical formulation for the BSTP that includes, in a detailed matter, many of the relevant features encountered in practice. Second, it derives an efficient algorithm to handle real-life instances from a healthcare service network. Although many of the studies in the literature of perishable products focus on the management of production and inventory (e.g. Alvarez et al., 2020), perishable products have an important influence in the distribution decisions. It has been shown that including quality, freshness or life span of the products in the routing decisions explicitly, leads to transportation plans that differ substantially from those that are purely cost-driven (Amorim et al. (2013); Amorim & Almada-Lobo (2014); Anaya-Arenas et al. (2021)). The need of imposing restrictions on travel or service times, makes the delivery problem harder and entails an increase in the transportation costs. This may be necessary to avoid the cost of lost inventory or bad service quality .

The remainder of this article is organized as follows. In Section 2 we describe the BSTP considered in our study, and provide details of all the relevant features required for a proper modeling of the system. In Section 3 we present a detailed literature review focused on distribution problems that include one or more of the relevant features of the BSTP. In Section 4 we present a mathematical model for the problem. In Section 5 we introduce a dynamic discretization discovery algorithm for the BSTP. In Section 6 we present a detailed computational campaign aiming at assessing: 1) the quality of the new formulation; 2) the computational capabilities and limits of the proposed algorithm; and 3) the problem sensitivity to some important attributes, namely to the life span of products, and to the number and frequency at which commodities are generated. Finally, Section 7 concludes this manuscript and provides several avenues for future research.

2 Problem statement

We now present more details of the BSTP to highlight the challenges it raises in logistics and distribution planing. Inspired by a case study of the laboratory network in the Province of Quebec (Canada), we analyze a regional health care cluster, where the *Ministère de la Santé et des Services sociaux* (Ministry of Health and Social Services - MSSS) appoints one regional hospital as central laboratory (Lab) to perform the analysis of all the samples collected in the assigned Specimen Collection Centers (SCCs). Each SCC has a collection period, during which patients are serviced and the samples are collected. Although the samples are generated in an almost continuous way during the collection period, and each sample has a fixed life span, a SCC can generate a given number of transportation requests discretely. A transportation request is a group of samples that are ready to be transported to the Lab. According to the desired level of service, a SCC generates one or more transportation requests during its workday. The level of service is defined in agreement between the Ministry and the SCC, in proportion to its size, the number and the type of samples collected. A transportation request, made by a SCC, is associated with a specific moment in time where it is generated and, due to the life span of the samples, is also associated with a due time to indicate the latest time at which it can arrive to the Lab without compromising its integrity. The greater the level of service and the detail of the samples' information are, the larger is the number of transportation requests stated by the SCC. Fixing the time limit at the arrival at the Lab is a simplification made by the Ministry, where the operation of pre-analysis inside the Lab is ignored. Finally, note that the samples are grouped and transported in small coolers and a standard vehicle has the capacity for a very large number of them, therefore, no vehicle's capacity constraints are required.

This vehicle routing problem (VRP) aims at deciding which vehicle handles which transportation request and in which order, so that no sample perishes, while minimizing the transportation cost. In this article, we consider a pure routing cost, incurred every time that a vehicle decides to travel from one physical location to a different one. The action of waiting at any SCC may be convenient if that allows for a vehicle to collect more samples, and hence it is permitted in our problem definition. This waiting is not penalized under the cost structure, but is only considered to assure that the time restrictions are respected. The transportation of perishable commodities with a short life span, like biomedical samples, has three characteristics that make this transportation problem quite difficult to model and to solve. First, as the samples' life span is usually shorter than a SCC's collection period, it is necessary to visit each SCC more than once in a day. Second, the samples' life span are with respect to the time of generation, which affects the maximum ride-time depending on the time of pickup. Hence, the pickup decision restricts both the time to go back to the Lab (route's length) and the maximum time at which a next transportation request needs to be done. This creates a strong interdependency between the routing and the pickup timing decisions, and needs to be optimized. Third, the length of a vehicle route is restricted by the most urgent sample (he one that perishes first) in the vehicle and is hence solution dependent.

Let us present this interdependency in the timing decisions via an example. We present in Figure 1 the timeline of several transportation requests for a given SCC v that starts its collection period at 6:00 and ends at 14:00. During this time frame, we assume that the SCC v take samples from many patients in a continuous matter and states a transportation request every 15 minutes (the approximated time of collecting one single biomedical sample). SCC v makes a first transportation request at 6:15. We consider here the same life span for every sample, so each transportation request has a maximum of five hours to be picked up from the SCC and to arrive to the Lab. As all the samples have the same life span, the most urgent transportation request is the first request generated after the opening of the SCC or right after a pickup has been performed. In the upper part of Figure 1, part (a), there is a feasible solution for the SCC v with three pickpus. As the most urgent request is generated at 6:15, these samples need to be picked up and taken to the lab before 11:15 (life span of 5 hours). As there is no capacity limits in the vehicles, when a pickup is performed at SCC v, all the requests accumulated up to that point are taken. Let us say that in solution (a), route $R1$ starts by performing a pickup p_1 at v at 8:20, then $R1$ can continue to visit other SCCs, but has a maximal route length of 2:55 hours. After this pickup, the next request is generated at 8:30 and it needs to arrive to the lab by 13:30. Then, route $R2$ performs a second pickup p_2 at 11:40 and has a maximum length of 1:50 hours (arriving to the lab by 13:30). Therefore, a third pickup has to be performed to get the requests from 11:45 to the closing of the center at 14:00. This pickup p_3 is performed by $R3$ at 14:15 and has a maximum of 2:30 hours to arrive at the lab. The lower part of Figure 1, part (b), presents another solution where modifying the pickup decisions allows managers to have only two pickups at SCC v but with more restricted routes. In this case the pickup p_1 is performed at 10:05, grouping more transportation requests and forcing $R1$ to arrive at the lab in 1:10 hours at the latest. Then, the most urgent request is generated at 10:15 and will have to arrive by 15:15 to the lab. A second pickup p_2 performed after closing (at 14:15) allow $R2$ to take all the request generated between 10:15 and 14:00 and still have 1:00 to visit other centers and respect samples life span.

Figure 1 illustrates how the highly perishable aspect of the transportation requests and the decision on the moment at which to perform a pickup influence directly the number of total pickups and the time restrictions for the route planning. This complexity is illustrated for a single SCC and the real-size instances on our case study can have over 15 SCCs with these characteristics. Therefore, it is crucial for managers to select the right moment to visit the SCCs (pickup decision) considering the transportation problem as a whole. Considering the number of pickups to perform as a decision of the model is an interesting feature that is rarely covered in the literature. It certainly makes the problem more complex, but can also help managers make well informed and better decisions.

3 Literature review

From a vehicle routing perspective, the BSTP is related to several classes of routing problems. We will then present in this section contributions that tackle at least one of our two key features: either the perishability of commodities or the interdependency of visits. Finally, we will present contributions specifically in the health care sector with two main applications: blood transportation or home health care planning.

There has been an important number of contributions dealing with the perishability of products in the last decade. Initially focused on the inventory management aspect of the problem (see Janssen et al., 2016, for a recent review), the contributions now extent to production and distribution planning. Amorim et al. (2013) defined in their literature review an unified framework in the definition of perishability, and they were one of the first to review contributions that embedded this complexity in a supply chain perspective. At that moment, among the more of 30 contributions analyzing perishable goods in production and/or in distribution planning, there were only two papers that considered explicitly the impact of perishability in the route planning. Moreover, the perishability of the products is usually modeled via the imposition of time windows in a single commodity

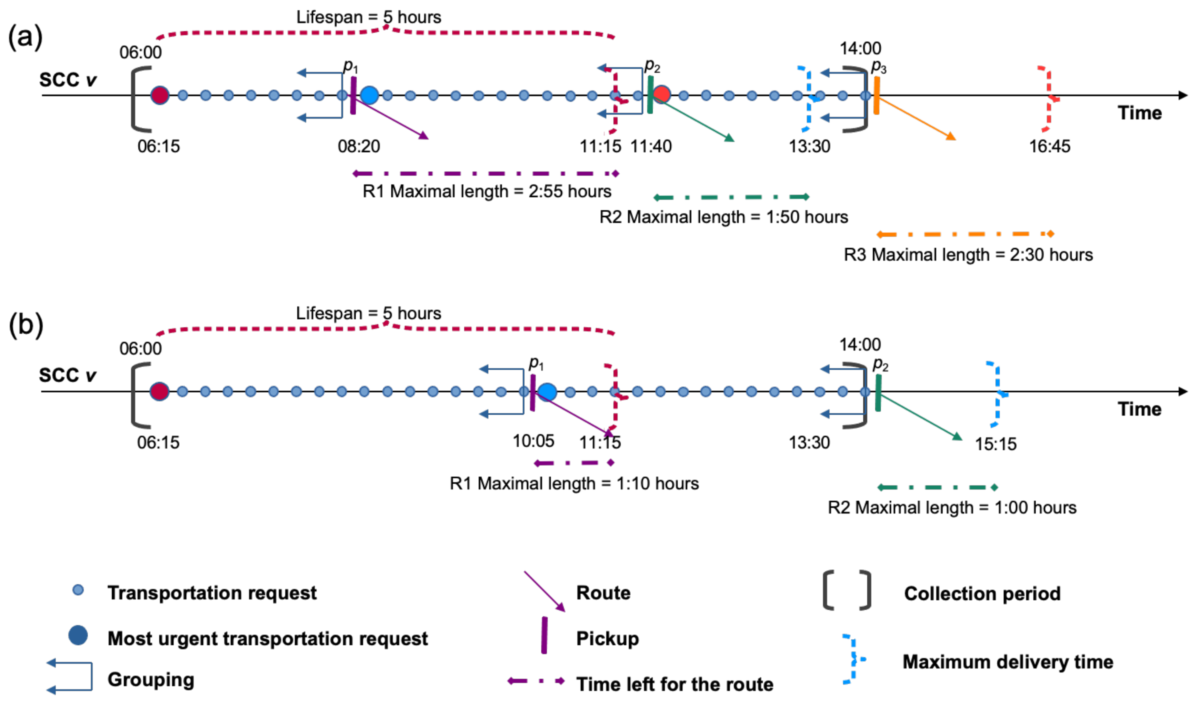

Figure 1: Feasible solution with three pickups (a) and two pickups (b).

setting. For instance, Hsu et al. (2007) and Osvald & Stirn (2008) solved routing problems heuristically, for a product with decreasing customer value, achieving a significant reduction in the percentage of perished goods. Later, Amorim et al. (2014) presented a contribution for a food company in Portugal modeling the problem as a VRP with multiple and fixed time windows, and proposed an adaptive large neighbourhood search to tackle it. Their context allows for split deliveries, so customers can be visited more than once in a day, but only in one of the time windows. These are treated as two separate decisions with no linking between the pickup decisions. On their side, Amorim & Almada-Lobo (2014) proposed a VRP with single time windows, but including freshness in the objective function. A similar modeling is adopted by Rabbani et al. (2015) who formulate it as a nonlinear optiization problem. Song & Ko (2016) considers a multi-commodity vehicle routing problem with perishable products and a nonlinear objective, which they tackle by means of a heuristic. A recent contribution by Liang et al. (2020) includes temperature and humidity attributes, for up to 30 groups of commodities. Although all these contributions include explicitly the perishable aspect of products in the route planning, the life span of the products is longer than a single period and there is no interdependency between the routing and the pickup decisions at the customers. Moreover, the time of the visits is fixed in time windows with typically a single commodity.

On the other hand, some researchers have tackled the perishable conditions of the products through an integrated planning of inventory and routing (inventory-routing problem - IRP). In this case, one seeks to minimize a combination of transportation and inventory costs, deciding on when and how much of each product deliver to customers in (generally) a multiperiod setting (see for instance Le et al., 2013; Diabat et al., 2016; Alvarez et al., 2020; Coelho & Laporte, 2014; Crama et al., 2018). The IRP is similar to our problem in the sense that the BSTP also requires the management of the inventory at the SCC, but in an indirect way. In the IRP the planning horizon is usually several days and customers can be visited more than once in the horizon, but only once every period. Meanwhile, all the BSTP decisions are purely operational. In all the IRP contributions, the perishability aspect of the problem influences the frequency of visits in the time horizon, but do not create interdependencies in the detailed scheduled of the routes nor in their length.

The time interdependency of the BSTP is also related to the pickup and delivery problem with time windows (PDPTW, see for instance Parragh et al., 2008; Berbeglia et al., 2007, 2010). In the PDPTW, precedence constraints bind customer nodes in pairs `(pickup, delivery)` to be serviced by the same route, in a way that the goods that are collected at the `pickup` node are then delivered to the `delivery` node, by typically respecting an additional ride-time constraint. In the BSTP, all SCC can be seen as `pickup` nodes, while the Lab plays the role of the `delivery` node. This type of distribution system is also known as *many-to-one* in the scientific literature, in particular with respect to the classification of Berbeglia et al. (2007). The visit to a SCC sets up a hard constraint on when the next visit to the same node must occur (i.e. strong time dependency as presented by Dohn et al., 2011) and also imposes a maximum ride time constraint on the route that picks up samples at a SCC, as they must be delivered to the Lab before they perish. Precedence constraints are also related to synchronization constraints. The word *synchronization*, in a broad sense, can have multiple meanings. One may require vehicles to meet at certain points, or to be bind by a form of precedence constraint, or the synchronization may make reference not to vehicles but to the products themselves. Drexl (2012) reviews the literature in vehicle routing problems with synchronization constraints. In the recent years, there have been attempts at incorporating synchronization features in urban freight transportation. In these problems, freight must typically be consolidated at intermediate facilities. Synchronizing freight at those facilities may help reduce the handling operations, and therefore make the whole operation more efficient (Grangier et al., 2016; Anderluh et al., 2021; Mirhedayatian et al., 2021). The synchronization features, always entail complex timing considerations and make the algorithmic of handling these problems far more complex than in the absence of synchronization (e.g. Hojabri et al., 2018; Tilk et al., 2019).

In the specific context of optimizing health care services, the BSTP is related and relevant to different applications, mainly the blood transportation and the Home Health Care services (HCC). Route planning problems in the presence of multiple attributes, synchronization and time dependencies are common in the context of Home Health Care (HCC) operations. Here, nurses and other medical or support staff are scheduled and routed to perform various services at patients' homes (see Fikar & Hirsch, 2017, for a review in this topic). This application generally considers the construction of routes with multiple time windows, skills of nurses and synchronization of activities (like the PDPTW and VRP with time dependency). However, the tasks related to the HHC can easily lead to a routing problem with high perishability and it is worth to investigate more on this topic. For instance, Liu et al. (2013) presented a PDPTW but forcing a single visit per patient and, even if samples could be collected at a patient's home, the time limit was extended to last more than the shift length. Moreover, Fikar & Hirsch (2015) and Mankowska et al. (2014) included resource synchronization and maximum shift times and maximum ride times for the nurses, but no high perishability is included. Kergosien et al. (2014) is, to the best of our knowledge, the only HHC problem that considers perishability to (implicitly) influence the routing decisions. They proposed a travelling salesman problem for nurses and included drop off nodes in the routes to respect the time limit of the samples. All these complex problems are solved with heuristics.

The reality of the short life span of the samples is usually included in several studies of blood samples transportation. Recently, Osorio et al. (2015), Baş et al. (2016) and Pirabán et al. (2019) present comprehensive reviews on blood supply chain management. The main echelons of the blood supply chain are: collection, production, inventory and distribution. The biomedical sample transportation is an essential part of the collection and distribution echelons. However, many contributions can consider the transportation of samples after a pre-treatement is performed or after blood products are collected, which provides maximum transportation times of more than a day (e.g. Zahiri et al., 2015; Hemmelmayr et al., 2009). There are a few contributions that include the life span of samples in the objective function by either maximizing processed samples (e.g. Şahinyazan et al., 2015; Yücel et al., 2013) or by minimizing perished samples (Elalouf et al., 2018). Closer to our problem, we can find Anaya-Arenas et al. (2016), who introduced the BSTP, by setting several fixed and independent time windows for each sample collection center and a ride time constraint. Later, Naji-Azimi et al. (2016) presented a variant of the BSTP, seaking to desynchronize truck's arrival to the Lab. However, those versions of the BSTP assumed that samples' deterioration begins when the samples leave the SCC, therefore, the available transportation time is fixed and not dependent of the times at which pickups are scheduled.

To the best of our knowledge, only Doerner et al. (2008), Doerner & Hartl (2008) and Anaya-Arenas et al. (2021) consider that the samples' deterioration begins once it is collected from the patients and include explicitly any perishability constraints. Therefore the available transportation time (or ride time) depends on the moment in which the visits are performed linking pickup and routing decisions. Doerner et al. (2008); Doerner & Hartl (2008) defined a blood collection problem as VRP with multiple and interdependent time windows. Assuming a continues production and fixed deterioration times, the authors defined a minimum number of pickups, where the time of a pickup at a given customer determines the maximum time available for the subsequent pickup at the same customer. Anaya-Arenas et al. (2021) in addition to the interdependence between pickups defines the collection centers' opening hours. Even if their context is similar to ours, in their cases, the minimum number of pickups of each SCC is previously defined. Contrarily, in our case, we seek to define the number of pickups for each SCCs according to the desired level of service in a way that minimizes the transportation costs, by considering each sample as an unique, distinguishable commodity. Therefore, we can conclude that none of the previous works attempt to simultaneously (1) define the optimum number of pickups; (2) set the pickup and routing decisions according to the high perishability of the samples while admitting its interdependency; and (3) do all this by considering each sample as an unique commodity.

4 Mathematical formulation

This section formalizes the problem described in Section 2 as a mathematical program over a time-expanded network. Each instance in the BSTP has m vehicles available to transport the biomedical samples between n SCCs (indexed from 1 to n) and one Lab (indexed as node 0). We denote $V = \{v_0, \ldots, v_n\}$ the set of physical nodes in the network. Sometimes we will refer to the Lab as the node l, which we assume corresponds to node v_0. Let $\tau(u, v)$ be the traveling distance from node $u \in V$ to $v \in V$, with $\tau(u, u) = 0$ for every $u \in V$. These travel times include the time of loading and unloading at the tail node of the arc. We define a time-expanded network $G^E = (V^E, A^H \cup A^D)$ constructed as follows. Le us assume that the planning horizon is divided in θ time periods, where $T = \{t_0, t_1, t_2, \cdots, t_\theta\}$, with $t_0 = 0$. We define Δt as the common length of the periods (i.e. $\Delta t = t_i - t_{i-1}$). We define the set of expanded nodes as $V^E = V \times T$, where each node $(v, t) \in V^E$ represents the physical node $v \in V$ at time $t \in T$. For a given node $i = (v, t) \in V^E$, we define $v(i), t(i)$ the physical and temporal components associated with node i. The arc set A^H contains arcs of the form (i, j) for all $i \in V^E$, $j \in V^E$, where $v(i) = v(j)$ and $t(j) = t(i) + \Delta t$. That is, the *horizontal* arcs of the time-expanded network, i.e. arcs that only represent waiting times at a given location. The arc set A^D contains arcs of the form (i, j) for all $i \in V^E$, $j \in V^E$, where $v(i) \neq v(j)$ and $t(j) - t(i) = \tau(v(i), v(j))$. In other words, the arc set A^D contains the *diagonal* arcs of the expanded network. To expand the network, the travel times have to be rounded up to multiples of Δt, so that any feasible solution on the time-expanded network can be converted to a feasible solution on the flat network. Let $A^E = A^H \cup A^D$ be the set of expanded arcs of the form (i, j) with $i, j \in V^E$. Let K be the set of transportation requests, where each $k \in K$ is associated with an origin node $o_k \in V^E$ where it is generated, and a destination node $d_k \in V^E$ with $v(d_k) = v_0, t(d_k) > t(o_k)$ representing the moment at which it must have arrived to the lab before it perished (i.e. the life span of the sample)

We model the BSTP using two types of decision variables, namely design variables y, and flow variables x. The decision variable y_{ij}, represents the number of vehicles that travel from node $i \in V^E$ to node $j \in V^E$. A routing cost c_{ij} equal to $\tau(v(i), v(j))$ is incurred each time that a vehicle travels using an arc $(i, j) \in A^D$. The flow variable x^k_{ij} represents whether a transportation request $k \in K$ travels from $i \in V^E$ to $j \in V^E$. The following additional conventions are used to present the model compactly. Let $l_0 \in V^E$ represent the Lab ($v(l_0) = v_0$) at time 0 ($t(l_0) = 0$), and let $l_\theta \in V^E$ represent the Lab ($v(l_\theta) = v_0$) at time $t(l_\theta) = t_\theta$. Let $\delta^+(i)$ be the set of arcs $(j, i) \in A^E$ that arrive to node $i \in V^E$, and $\delta^-(i)$ the set of arcs $(i, j) \in A^E$ that leave the node $i \in V^E$. For a set of arcs $B \subseteq A^E$ we denote $y(B) = \sum\{y_{ij} : (i, j) \in B\}$, and for an additional commodity index k we let $x^k(B) = \sum\{x^k_{ij} : (i, j) \in B\}$. The following mathematical model provides an optimal solution for the BSTP:

$$Minimize \qquad \sum_{(i,j)\in A^D} c_{ij} \cdot y_{ij} \tag{1}$$

Subject to:

$$y(\delta^-(l_0)) \leq m \tag{2}$$
$$y(\delta^+(i)) - y(\delta^-(i)) = 0 \qquad \forall i \in V^E \backslash \{l_0, l_\theta\} \tag{3}$$
$$x^k(\delta^-(o_k)) = 1 \qquad \forall k \in K \tag{4}$$
$$x^k(\delta^+(d_k)) = 1 \qquad \forall k \in K \tag{5}$$
$$x^k(\delta^+(i)) - x^k(\delta^-(i)) = 0 \qquad \forall k \in K, i \in V^E \backslash \{o_k, d_k\} \tag{6}$$
$$x^k_{ij} \leq y_{ij} \qquad \forall (i, j) \in A^D \tag{7}$$
$$y_{ij} \in \mathbb{N} \qquad \forall (i, j) \in A^E \tag{8}$$
$$0 \leq x^k_{ij} \leq 1 \qquad \forall (i, j) \in A^E, \forall k \in K \tag{9}$$

The objective function (1) minimizes the total routing cost. Constraint (2) ensures that at most m vehicles are used. Constraints (3) ensure that the vehicles' flow conservation is satisfied at all nodes, so all vehicles that leave l_0 ultimately arrive to l_θ. Constraints (4) state that the transportation request k becomes available at node o_k. Constraints (5) ensure that the transportation request k arrives at node d_k, before it perishes. Constraints (6) are the transportation requests' flow conservation constraint, so the transportation request k does not stay in a node different to d_k. These constraints avoid that a transportation request stays in another place different to the Lab at time d_k. Constraints (7) ensure that a transportation request can only leave a physical node $v \in V$ in a vehicle. These link the design and the flow variables. Constraints (8) and (9) define the nature of the decision variables. Variables x^k_{ij} are not required to be defined as binary even if splits are not allowed, given the total unimodularity of the set of constraints (4)-(7) for an integer vector y.

This problem formulation simplifies the time constraints and the pickups interdependency by making them explicit in the model, i.e. the commodity flows may only exist between the time of generation at a SCC and its due time of arrival at the Lab. Furthermore, the model indirectly optimizes the number of pickups at each SCC according to the level of service desired. This is a modeling improvement over the model introduced in Anaya-Arenas et al. (2021) in which the number of pickups at every SCC must be provided as an input. Nonetheless, the size of the model (number of variables and constraints) depends linearly on the granularity of the time expansion and on the number of commodities and, consequently, may become intractable for too fine time granularity and/or too many commodities.

5 Solution methods

The time-expanded model introduced in this article has the great disadvantage of having its size depend linearly on the granularity of the time expansion (i.e. Δt) and on the number of commodities that are generated. This issue becomes apparent for large time horizons with very fine time granularity and for commodities that are generated at very short time intervals. To reduce the impact of the time expansion and of the number of commodities, we propose two different approaches. The first approach is a *smart* network expansion. In this case, we exploit some characteristics of the problem to reduce the number of expanded nodes, expanded arcs and variables associated with them without compromising the optimality of the solution. We refer to this as a preprocessing for the full time-expanded network. The second approach is a dynamic network construction and transportation request grouping. In this approach, we iteratively construct smaller networks, each of which has a reduced number of time periods and commodities, and that provide dual bounds for the problem. Each network is a tightening of the previous one, and the method is assured to converge to an optimal solution. Our approach can be seen as an extension of Boland et al. (2017) in which, in addition to the aggregation of time periods, we allow for the aggregation of transportation requests to reduce the problem size even further.

5.1 Full time-expanded network preprocessing

The proposed preprocessing is a two step procedure, where the first step reduces the number of nodes in the expanded network, and the second step limits the number of x^k_{ij} model variables.

The first part of the preprocessing exploits the fact that all the routes must start and end in the Lab (whose physical location is denoted as $l = v_0$). Therefore in the time-expanded network, the earliest arrival of a vehicle to a node $v \in V$ is at time $t = \tau(l, v)$. Then a node $i = (v, t) \in V^E$ with $t < \tau(l, v)$ will not be part of a feasible solution. On the other hand, if all the routes end in the Lab, all the vehicles must be in the Lab at the end of the time horizon, and the latest moment that a vehicle can be in node $v \in V$ is at time $t = t_\theta - \tau(v, l)$. Thus a node $i = (v, t) \in V^E$ with $t > t_\theta - \tau(v, l)$ will not be part of a feasible solution, because no vehicle is allowed to reach the Lab after t_θ. All nodes that are found to be unreachable using this procedure are thus ignored and do not make part of the expanded network.

The second step reduces the number of variables x^k_{ij}, as follows. The flow of a commodity k can only exist between its origin $o(k)$ and its destination $d(k)$. One can therefore execute an enumeration procedure starting at $o(k)$, to find all nodes $V^{fk} \subseteq V^E$ and arcs $A^{fk} \subseteq A^E$ that are reachable from $o(k)$. The same argument can be used to find all nodes $V^{bk} \subseteq V^E$ and arcs $A^{bk} \subseteq A^E$ from which one can reach $d(k)$. For that commodity, one can hence restrict the network to the nodes $V'^k = V^{fk} \cap V^{bk}$ and to the arcs $A'^k = A^{fk} \cap A^{bk}$, thus ignoring the flow variables x^k_{ij} for all nodes and arcs in the network that cannot make part of a feasible $o(k)$-$d(k)$-path.

5.2 Dynamic network construction and transportation request grouping

We propose a solution approach that solves auxiliary problems in an iterative fashion by reducing the problem size at two levels: (1) by considering a reduced subset of time periods; and (2) by grouping some commodities. These two procedures are performed in such a way that the resulting problem provides a valid dual bound of the original problem, although perhaps not a feasible solution. This is complemented by an ad-hoc heuristic that aims at finding a feasible solution (therefore a primal bound) that lies not too far from the dual bound in terms of cost. Finally, we propose a recovery procedure that tightens the relaxed problem from one iteration to the next, in an incremental fashion.

5.2.1 Initial commodity grouping and expanded network

We first initialize the commodity groupings. A grouping is always restricted to commodities generated consecutively at the same SCC. We perform an iterative procedure to generate these initial groupings, as follows. First, all the commodities generated at the same SCC are grouped together. For each such grouping, that we denote S, we let $w_0(S)$ be the latest generation time among all commodities in S. We also let $w_f(S)$ be the earliest due time or all those commodities. If $w_0(S) + \tau(s, l) > w_f(S)$ (with s denoting the SCC and l the lab), we declare this grouping as being infeasible, since serving all the commodities in S simultaneously is not possible. We then split S into two balanced groupings S_1, S_2, by leaving the first (in terms of time generation) $\lfloor |S|/2 \rfloor$ commodities to form S_1, and the rest to form S_2. This verification and splitting procedure is repeated until all groupings become feasible. For each grouping S at the end of this procedure, we assume that its generation time $t_0(S)$ coincides with the earliest generation time among all commodities in S, and its due time $t_f(S)$ coincides with the latest due time. This assures that a feasible path in the full expanded network that serves at least one customer in S can be mapped to a feasible path in the reduced network where all commodities in S are grouped together.

Each grouping S constructed using the procedure above can be seen as an unique and unsplittable commodity generated at time $t_0(S)$ that needs to be delivered at the lab by time $t_f(S)$. For each SCC v, we consider one node $(v, 0)$ at the beginning of the time horizon, and one pair of nodes $(v, t_0(S)), (v, t_f(S))$ at the generation and due times for each grouping S generated at the SCC. For every node $i = (v, t)$ constructed in this way, we let $next(i)$ be the next instant in time for which there exists an expanded node at $u \in V$. For the creation of the expanded nodes at the lab we proceed as follows. We first create two nodes $(l, 0), (l, t_\theta)$ at the beginning and the end of the time horizon, and for every expanded node i associated with a SCC $v \in V$, we create two nodes $(l, t(i) - \tau(l, v(i)))$ and $(l, t(i) + \tau(v(i), l))$.

To construct the arc set A^{Er} in the reduced network, we proceed as follows. Let V^{Er} be the set of nodes in the reduced network. For every node $u \in V$ and for every time $0 \leq t \leq t_\theta$ we let $\beta(u,t) = \max\{s : (u,s) \in V^{Er}, s \leq t\}$ be the largest time $s \leq t$ for which there exists a node in V^{Er}. First, we create horizontal arcs from every node in the reduced network, to the next node in time. These arcs are used to represent waits at the SCCs and the lab. For a node $i = (u,t) \in V^{Er}$, we also consider arcs to other physical nodes, as follows. For every other node $w \in V \setminus \{u\}$, we let $s = \beta(u, t + \tau(u,w))$ and create an arc with tail in i and head in (w,s). The routing cost between two nodes $i,j \in V^{Er}$ such that $v(i) \neq v(j)$ is set to $\tau(v(i), v(j))$, as it was defined in the original full expanded network.

The following proposition assures that the model represented by the reduced expanded network (V^{Er}, A^{Er}) provides a valid lower bound of the problem.

Proposition 1. *The optimal value z_r^* of a solution to the model induced by the reduced expanded network (V^{Er}, A^{Er}) is such that $z_r^* \leq z^*$, where z^* is the optimal value of the full expanded model.*

Proof. The proof works by showing that, for any feasible vehicle route $\mathcal{R}$ in the full expanded model of cost $c(\mathcal{R})$, it exists a vehicle route $\mathcal{R}^r$ that is feasible w.r.t. the reduced expanded model that delivers the same commodities (or more) of cost $c^r(\mathcal{R}^r)$, such that $c^r(\mathcal{R}^r) \leq c(\mathcal{R})$, where c, c^r represent the cost structures of the full and of the reduced expanded model, respectively.

Let $\mathcal{R} = (v_i = (u_i, q_i))_{i=0}^{p+1}$ be such a route in the full expanded network. Without loss of generality we can assume that $u_i \neq l$ for every $1 \leq i \leq p$, since a full route can be composed as a concatenation of these simpler pieces. On each visit to a SCC u_i, one can assume that the vehicle collects all the commodities that are generated by (or before) q_i and that are due at the lab at time q_n or later. We denote by κ_i the total set of commodities that are collected upon a visit to u_i. This can be defined recursively as $\kappa_0 = \emptyset, \kappa_i = \kappa_{i-1} \cup \{k \in \{1 \dots K\} : o(k) = u_i, t(o_k) \leq q_i, t(d_k) \geq q_n\}$ for every $i \in \{1 \dots p\}$. We construct a route $\mathcal{R}^r$ in an iterative process that goes according to the pseudocode depicted in Algorithm 1.

Algorithm 1 Construction of a feasible route $\mathcal{R}^r$ for the relaxed expanded network from a route $\mathcal{R}$ feasible for the full expanded network

Require: Route $\mathcal{R} = (v_i = (u_i, q_i))_{i=0}^{p+1}$
Ensure: Route $\mathcal{R}^r = (v_i^r = (u_i^r, q_i^r))_{i=0}^{p'+1}$
1: Let $i, j \leftarrow 0, \gamma \leftarrow \emptyset$
2: Let $v_0^r \leftarrow (u_0^r, q_0^r) = (u_0, \beta(u_0, q_0))$
3: **repeat**
4: $\quad j \leftarrow j + 1$
5: $\quad$ **if** $\gamma \subset \kappa_i$ **then** ▷ Need to wait to collect more commodities
6: $\qquad v_j^r \leftarrow (u_{j-1}^r, next(v_{j-1}^r))$
7: $\quad$ **else** ▷ The route can leave to the next node
8: $\qquad i \leftarrow i + 1$
9: $\qquad v_j^r \leftarrow (u_i, \beta(u_i, q_{j-1}^r + \tau(u_{i-1}, u_i)))$
10: $\quad$ **end if**
11: $\quad \mathcal{T} \leftarrow \{S \in \text{all groupings} : v(S) = u_j^r, t(o_S) \leq q_j^r, t(d_S) \geq \beta(l, q_n)\}$
12: $\quad \gamma \leftarrow \gamma \cup \{k : k \in S, S \in \mathcal{T}\}$ ▷ Update the commodities collected
13: **until** $u_j^r = l$

The logic behind this algorithm is the following. We build the route $\mathcal{R}^r$ by trying to replicate the same vehicle movements as those of $\mathcal{R}$. In that way, the routing costs of both routes must necessarily coincide. The problem is, because the arrivals may not occur at the same time, it may happen that the vehicle in the reduced expanded network cannot collect all the same commodities because its arrival happened too early. In this case, we add waiting times at the node, so as to make sure that the commodities collected by $\mathcal{R}$ up to that point are also collected by $\mathcal{R}^r$. Only then, the vehicle is allowed to leave the node. It is clear from the construction of the route $\mathcal{R}^r$, that its routing cost is equal to that of $\mathcal{R}$. We will now prove that this route is feasible in the reduced expanded network.

The algorithm above allows to establish a mapping of the nodes visited by $\mathcal{R}$ to some of the nodes visited by $\mathcal{R}^r$, which happens at line 7 of the algorithm when the route is allowed to leave a node carrying all the commodities also picked up by $\mathcal{R}$ (and probably more). If the mapping of the p-th node in $\mathcal{R}$ corresponds to node p' in $\mathcal{R}^r$, we will prove that $q_{p'}^r \leq q_p$. This is certainly true for the node at index 0 in $\mathcal{R}^r$, since by definition $q_0^r = \beta(u_0, q_0) \leq q_0$. Let us assume by induction that our hypothesis holds for the p-th node in $\mathcal{R}$, which is mapped to the p'-th node in $\mathcal{R}^r$. Route $\mathcal{R}$ then leaves to node v_{p+1} while route $\mathcal{R}^r$ to node $v_{p'+1}^r$. But this last node does not necessarily correspond to the mapping of node v_{p+1} since it may have arrived earlier to the next node, potentially picking up less commodities. If this is the case, one must add waiting arcs in $\mathcal{R}^r$ as specified in line 6. But remember that the groupings are defined in such a way that their availability is earlier (or at most at the same time) than that of each commodity in it. The waiting time will only then be added until seeing these commodities become available, at a time that is necessarily lower than or equal to the real time of generation of each commodity in the grouping. Also, remember that the due time of a grouping equals the latest due time among all commodities in it, meaning that the arrival of route $\mathcal{R}^r$ back to the lab must necessarily be feasible. □

5.2.2 Feasibility check

The next step in the process is to perform a feasibility check to assess whether the solution to the reduced problem can be mapped to a solution of the original problem at the same cost, and identify infeasible arcs/groupings if deemed necessary.

As for the feasibility of the network expansion, our method simply checks if that, for all the routing arcs (i, j) in the optimal solution on the reduced expanded network, the length $t(j) - t(i)$ equals $\tau(v(i), v(j))$. Every arc that does not satisfy this condition is deemed infeasible. We denote by A^I the set of arcs that are deemed infeasible according to this criterion.

With respect to the feasibility of the groupings, we check if the pickup and delivery times for the ungrouped commodities are satisfied, i.e. if the pickup time t of a group S is such that $t(o_k) \leq t$ for every $k \in S$, and if the delivery time s of the group is such that $t(d_k) \geq s$ for every $k \in S$. The groupings that are deemed as being infeasible with respect to this criterion are added to a set K^I.

If at the end of this procedure, $A^I = K^I = \emptyset$, we have indeed identified a feasible solution of the problem of the same cost as the dual bound. The method ends and returns this solution.

5.2.3 Computation of an upper bound

After the solution of a MIP to obtain a dual bound, we execute the following procedure aiming at finding a feasible solution of the exact same value. To this end, we create an auxiliary network with the smallest granularity, as follows. For each grouping S, we create a commodity having as generation time the latest possible generation time among all commodities in S, and due time the earliest due time among them (which is a real feasible grouping). For each arc $(i, j) \in A^{Er}$ that appears in the optimal solution to the reduced MIP, we consider all possible arcs linking $v(i)$ and $v(j)$ in the auxiliary network. We also consider all possible waiting arcs linking any two nodes consecutive in time. This network contains much fewer arcs than the original full expanded network, and the generation and due times for the commodities have been constructed in such a way that the auxiliary MIP model searches for a feasible way of delivering the commodities by respecting the predefined groupings. This problem, if feasible, necessarily admits an optimal solution that uses the same routing arcs as that of the MIP, but maybe in different numbers (remember that the design variables in our model are integral, and not necessarily binary).

5.2.4 Network expansion

If the feasibility check and the upper bounding procedures fail, we proceed with expanding the network at two levels, using the arcs in A^I and the groupings in K^I.

First, all arcs in A^I are used to expand the network by creating new nodes and several other arcs, and by removing all the arcs that are found to be inconsistent with the new expanded network. An arc (i, j) in the expanded network is said to be consistent if $t(j) = \beta(v(j), v(i) + \tau(v(i), v(j))))$. For each arc $(i, j) \in A^I$, we create nodes $i' = (v(i), t(j) - \tau(v(i), v(j)))$ and $j' = (v(j), t(i) + \tau(v(i), v(j)))$. We update the horizontal arcs at nodes $v(i), v(j)$ to assure that only the arcs between nodes that are consecutive in time are kept. We also add nodes at the lab at times $t(i') - \tau(l, v(i)), t(i') + \tau(l, v(i)), t(j') - \tau(l, v(j))$ and $t(j') + \tau(l, v(j))$. New arcs are added to the new expanded network following the same reasoning used to build the initial expanded network. In addition, we remove all arcs that are found to be inconsistent with the new network.

Second, for every grouping $S \in K^I$, we compute the maximum difference between the generation time of every commodity in S and the pickup time in the reduced network. We also compute the maximum difference between the delivery time of S at the lab, and the due time of every commodity in S. The infeasibility of a grouping S is computed as the maximum of these two values. From the grouping attaining the maximum infeasibility, we create two smaller groupings by halving S, thus creating S_1 containing the first $\lfloor |S|/2 \rfloor$ commodities (according to their time of generation) and the rest to form S_2. We replace S then from the set of groupings by S_1, S_2. We follow the same reasoning used for the initialization of the expanded network to add these two new commodities to it, thus creating more nodes at the associated SCC and at the lab, and new arcs. All the old arcs that are deemed inconsistent in the new expanded network are removed from it.

Please note that we have been careful to construct, using these two procedures, an enlarged expanded network that satisfies the same hypothesis necessary for the validity of Proposition 1, therefore the same arguments can be applied to assure that the new model, on the new expanded network, provides a dual bound of the the original problem. This dual bound is necessarily non-decreasing as the new network is an expansion of the previous one.

5.2.5 High-level description of the algorithm

We now present a high-level description of our iterative algorithm. Roughly speaking, our method begins with an initial network as described in Section 5.2.1. Then, it iterates between the computation of a dual bound, a feasibility check and a network expansion. Upper bounds are also used to speedup the overall computing times. The algorithm can be summarized in the pseudocode described in Algorithm 2. This pseudocode can be trivially modified to replace the stopping condition by a less restrictive one in case where optimality may become challenging.

Algorithm 2 High-level description of the iterative algorithm

```
Require: Weighted network G = (V, A, c)
Ensure: Dual bound z_D, primal bound z_P, feasible solution S
Initialize the reduced weighted network G^r = (V^r, A^r, c^r)          ▷ Section 5.2.1
Let z_D ← −∞, z_P ← ∞, S ← ∅
while z_D < z_P do
    Solve the reduced problem on G^r, and let z_D, S' be the optimal value and solution
    if S' is feasible then                                            ▷ Section 5.2.2
        Update z_P ← z_D and return z_D, z_P, S'
    else
        Use S' to compute a primal bound z_P and a solution S         ▷ Section 5.2.3
        Expand the network to update G^r                              ▷ Section 5.2.4
    end if
end while
return z_D, z_P, S
```

6 Computational experiments

This section presents and discusses the results of the experiments conducted to test the quality and the behavior of the time-expanded formulation, and the computational capabilities and limits of the proposed algorithm. These experiments are realized over a set of instances inspired from a real-life application regarding the distribution management of biomedical samples from a laboratory network under the management of the *MSSS*. In the first section, we provide the description of the instances used, in terms of the number of transportation requests, and the geographical and temporal sparsity. Next, we present and analyze the results obtained.

6.1 Instances

To know the transportation needs of each service area, the *MSSS* conducted a detailed survey spanning from June to August 2013 to the SCCs and Labs in each service area. In the survey, each SCC and Lab was required to provide, for each day of the week, information such as opening and closing hours, number and type of samples, and kind of tests needed. Interested readers can consult Anaya-Arenas et al. (2016) for a detailed description of the survey. The differences between the days of the week lead to a different types of instances. For instance, weekends were found to be regularly less busy than weekdays, resulting on fewer SCCs being open those days. Furthermore, days with more demand lead to instances with more transportation requests. Other factors that influence the characteristics of an instance are the geographical and demographic data of each administrative region. According to that, two types of instances could be distinguished:

- **Rural instances:** Correspond to service areas that cover a large territory, with large distances between the nodes of the network and in consequence large traveling times as well.
- **Urban instances:** Correspond to service areas close to main the main cities. They typically have a bigger demographic density, usually with a large number of SCCs and short traveling times.

The type of instance can also have an impact on the topology of the solutions each problem admits. On rural instances, the larger traveling times make it necessary to have vehicle routes servicing a small number of SCCs before they need to get back to the Lab. On the other hand, urban instances usually admit solutions with a much larger number of SCCs between two stops at the Lab, typically increasing the routing complexity.

Anaya-Arenas et al. (2021) tested a set of 38 instances for a variant of the problem in which the number of pickups and the total collection period at each SCC were given as an input by the *MSSS*. The perishability requirements were only partially captured then, as the instances included a maximum time to keep samples inside the SCC and a maximum routing time, assuming that the sum of these two time limits is less than the sample's life span. We have then modified the instances by adapting them to our problem setting. The main difference is related to the fact that a transportation request is not directly associated to a pickup in our modeling. Therefore, the number of pickups at every SCC will be decided as an output of the optimization process. Moreover, we propose a much more realistic modeling for the perishability constraints by explicitly capturing the life span of each commodity in the time-expanded network since the time of its generation. To adapt the instances to our problem, we have proceeded as follows. For each instance we need to explicitly define the moment $t(o_k)$ at which each transportation requests is generated at every SCC $v \in V$. First, we define a parameter Δk, that indicates the frequency at which the transportation requests are generated. Thus, the number of transportation requests for each center is the ratio between the collection period at the SCC and Δk. The time of generation $t(o_k)$ for every such commodity is uniformly spreaded in time. For example, if we associate a total of 3 transportation requests to a given SCC $v \in V$, they will be generated at times $1/3O_v$, $2/3O_v$ and O_v, where O_v is the collection period of the SCC $v \in V$. Figure 2 illustrates the distribution of the transportation requests for a SCC $v \in V$ with one, two, three, and up to k transportation requests. The due time $t(d_k)$ of each commodity is set according to the following criterion. For a Δk of 15 minutes, we establish the due time to be 5 hours after the generation of each sample. For a Δk of three hours, we only allow for a life span of three hours, in an attempt to capture the fact that the larger value of Δk means that samples are consolidated and grouped for up to three hours before a pickup, hence the shorter life span aims at ensuring that the sample that was generated the earliest in that group will still be able to reach the lab before it perishes. We let the maximum number of vehicles m be equal to the number of transportation requests on each instance. But because this is only given as an upper bound, our optimization model always finds solutions that use a much lower number of vehicles. In Tables 1-2 we provide aggregated data about the number of SCCs and transportation requests associated with the instances generated for the cases where $\Delta t = 5, \Delta k = 180$, and $\Delta t = 1, \Delta k = 15$. Under column *SCC* we report the number of SCC associated with the instance. Columns *total*, *min*, *max*, *avg* are used to report the total number of transportation requests of the problem (all SCC aggregated) as well as the the minimum, maximum and average number of transportation requests per SCC.

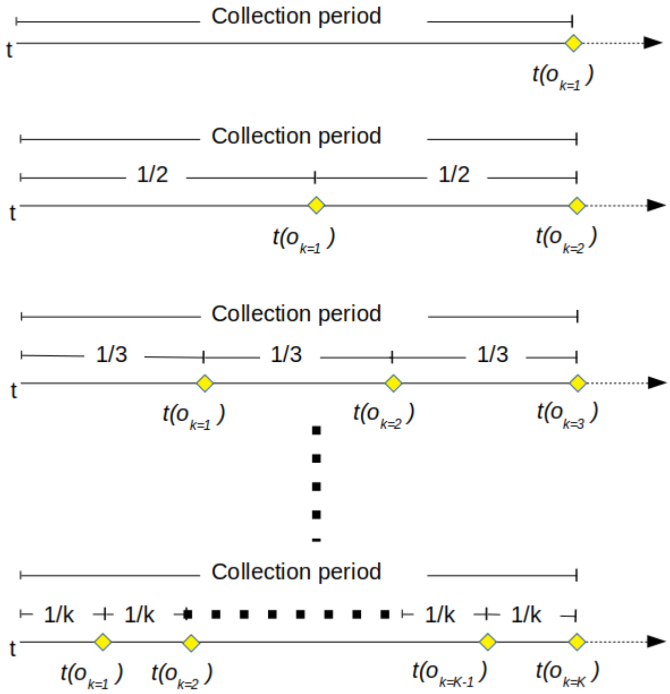

Figure 2: Time distribution of the transportation requests

6.2 Computational results

In this section we present and analyze our modeling approach and the sensitivity of our algorithm to a series of factors. To this end we consider two experiments. The first experiment aims at assessing the quality of our modeling framework and of our time-expanded formulation, by comparing it —both from a computational and from a modeling perspective— to the model of Anaya-Arenas et al. (2021). Our second experiment assesses the performance of our method by comparing it against two variants of it and to the direct solution of the full time-expanded model boosted with the acceleration strategies presented at Section 5.1.

		$\Delta t = 5, \Delta k = 180$				$\Delta t = 1, \Delta k = 15$			
Instance	SCC	total	min	max	avg	total	min	max	avg
01	2	7	1	6	3.5	69	7	62	34.5
02	2	8	3	5	4.0	80	25	55	40.0
03	2	6	1	5	3.0	57	7	50	28.5
04	3	3	1	1	1.0	21	7	7	7.0
05	3	5	1	3	1.7	42	7	28	14.0
06	3	11	3	5	3.7	113	33	55	37.7
07	4	6	1	3	1.5	57	7	36	14.3
08	4	11	1	8	2.8	110	7	89	27.5
09	4	8	1	3	2.0	66	7	25	16.5
10	4	20	6	8	5.0	277	63	88	69.3
11	4	13	3	4	3.3	114	25	39	28.5
12	4	11	2	4	2.8	107	15	44	26.8
13	4	10	1	4	2.5	101	9	44	25.3
14	5	11	1	7	2.2	108	7	80	21.6
15	5	11	1	7	2.2	108	7	80	21.6
16	5	12	1	7	2.4	125	7	80	25.0
17	5	9	1	3	1.8	73	7	25	14.6
18	5	9	1	5	1.8	80	7	52	16.0
19	6	10	1	5	1.7	90	7	55	15.0
20	6	15	1	4	2.5	143	45	7	23.8

Table 1: Small problem instances

		$\Delta t = 5, \Delta k = 180$				$\Delta t = 1, \Delta k = 15$			
Instance	SCC	total	min	max	avg	total	min	max	avg
21	9	18	1	5	2.0	167	7	53	18.5
22	8	21	1	5	2.6	200	7	53	25.0
23	7	17	1	4	2.4	173	7	47	24.7
24	9	19	1	4	2.1	187	7	47	20.7
25	9	36	1	7	4.0	373	7	74	41.4
26	12	20	1	4	1.6	182	7	47	15.1
27	11	40	1	7	3.6	416	7	74	37.8
28	17	27	1	4	1.5	227	6	46	13.3
29	10	36	1	5	3.6	373	7	53	37.3
30	11	38	1	5	3.4	388	7	53	35.2
31	12	40	1	5	3.3	396	6	52	33.0
32	17	37	1	5	2.1	356	4	50	20.9
33	13	42	1	5	3.2	417	6	52	32.0
34	18	46	1	8	2.5	467	6	88	25.9
35	19	41	1	5	2.1	406	6	50	21.3
36	19	41	1	5	2.1	407	6	50	21.4
37	19	44	1	5	2.3	445	6	50	23.4
38	17	50	1	5	2.9	502	6	52	29.5

Table 2: Large problem instances

6.2.1 Quality of our modeling framework and mathematical model

Our first experiment aims at assessing the quality of our modeling framework and of our mathematical model. To that end, we have executed our method on 38 problem instances, with a Δt of 5 minutes and Δk of three hours. These instances are the closest in terms of data generation to those of Anaya-Arenas et al. (2021) as they roughly consider the same amount of samples' consolidation at the SCC with a number of transportation requests that is equal to (or increases at most in two) the values provided as an input by the *MSSS*. The traveling times in this network are rounded up to the closest integer multiple of 5 (leaving 5 minutes as the shortest possible traveling time in this network). Unfortunately, the commercial solver can solve the proposed formulation for a Δt of one minute and a Δk of 15 minutes for only 14 of the first 20 instances (see 5 for details). In Table 3 we report, for the eleven most difficult problems, a comparison between the results reported in Anaya-Arenas et al. (2021) and our model. In this table, $ILS\ P$ denotes the total number of pickups provided as an input of the problem by the $MSSS$, $ILS\ gap$ the optimality gap reported after 10 hours of computational time of the solver solving the mathematical model of Anaya-Arenas et al. (2021), *Pickups* the number of pickups found as an output of our mathematical model, *gap* the optimality gap of our model after a maximum of one hour of computation, and *CPU time* the total CPU time (in seconds) spent by the solver.

The first observation that we would like to make is regarding the efficiency of the solution in terms of the number of pickups required to serve the demand. Our method is capable of identifying solutions with about 10% less pickups on average, when compared against the data provided by the *MSSS* as an input. Second, in terms of computing efficiency, we observe that our time-expanded model provides much better optimality guarantees, with solutions that lie no further than a 13% from the optimal, as compared to the poor optimality gaps reported in Anaya-Arenas et al. (2021), and this is in much shorter computing times. This is a very encouraging result from the health care management perspective. This new formulation allow managers to find the optimal number of pickups at each SCC, while reducing transportation costs and respecting the actual perishability of the samples.

Instance	ILS P	ILS gap	ILS time	Pickups	gap	CPU time
28	24	47.0	36000	20	0.0	126
29	30	100.0	36000	25	0.0	2032
30	32	100.0	36000	22	1.9	3699
31	34	100.0	36000	31	0.1	3724
32	35	76.0	36000	28	1.6	4065
33	36	100.0	36000	35	0.0	2357
34	39	86.0	36000	33	3.4	4169
35	40	76.0	36000	31	2.3	4140
36	40	79.0	36000	49	13.0	4009
37	41	81.0	36000	41	4.4	4113
38	50	100.0	36000	45	10.6	3969

Table 3: Comparison between our new mathematical model and that of Anaya-Arenas et al. (2021)

6.2.2 Performance of the proposed method

In this section we present an experiment aiming at assessing the computational capabilities of the proposed method. To this end, we consider the 20 first problems from our testbed, but with time granularities of Δt equal to one, and with commodities generated every Δk of 15 minutes. This produces problems that are far more difficult than those considered in our previous experiment. For that reason, we had to omit the results for the larger problems as all the methods struggled to provide meaningful results within a time limit of six hours. In Figure 3 we report the number of aggregated transportation requests in the last iteration of our proposed method ($|K^r|$), as the ratio against the original number of transportation requests ($|K|$). We omit this ratio for problems 10 and 20 that timed out in the maximum allowed time of six hours. For the rest, we observe that our iterative algorithm is capable of reducing in more than a 40% the number of transportation requests, with a maximum reduction of almost a 80%. Not only this reduction affects the size of the mathematical models solved, but also helps at reducing the symmetries involved when handling many transportation requests that in the end could have been seen as one.

We have performed a second experiment aimed at assessing the computational capabilities of our method, and the benefit associated with the development of two of the core ingredients, namely the commodity grouping, and our primal heuristic. In Figure 4 we report a profile curve of the computing times associated with three variants of our method, and of the solution of the full time-expanded model boosted with the addition of the reduction techniques introduced in Section 5.1. For our iterative method, we consider the following three variants: 1) the proposed method, including both the commodity grouping and the primal heuristic; 2) the proposed method without the commodity grouping; and 3) the proposed method without the primal heuristic. Figure 4 reports, for every $0 \leq y \leq 21600$, the number of problems x that are solved within that limit. The results show a clear

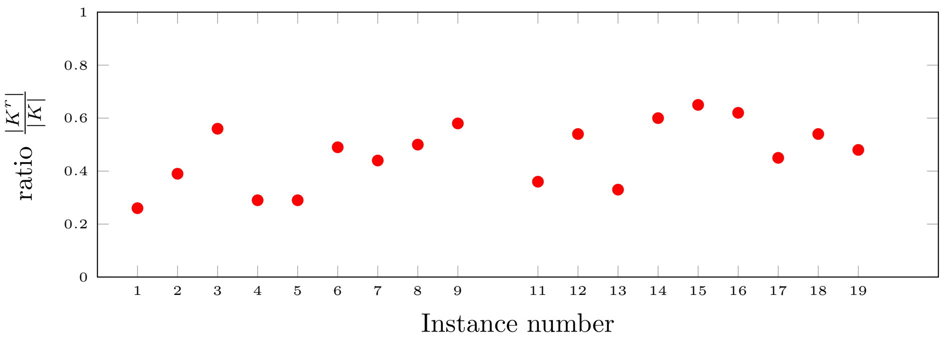

Figure 3: Ratio between $|K^r|$ at the end of the method and $|K|$

advantage for our method as compared to the direct solution of the full time-expanded model, as it allows to reduce the CPU times by a factor of 10 and solve five more problems. When comparing the three variants of our method, we observe the benefit of performing the commodity grouping and the primal heuristic, as they allow for the solution of more problems in typically shorter computing times for the more difficult problems.

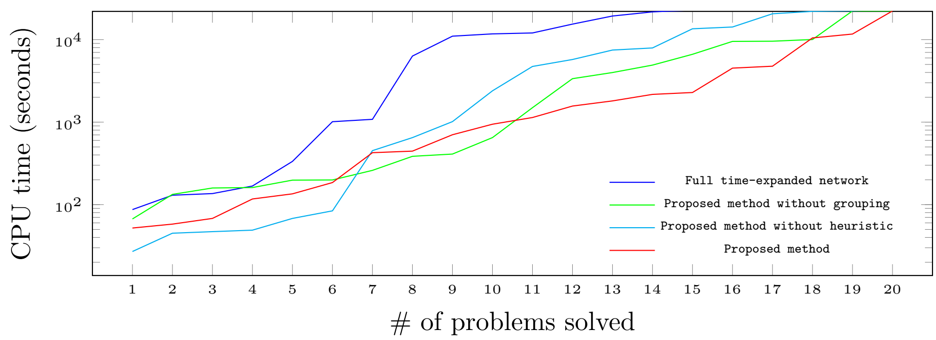

Figure 4: Number of problems solved to proven optimality by each algorithm variant

The algorithm has been proved to be efficient to solve to optimality BSTP instances with more than 200 commodities tracked individually, with high interdependency (an average of 40 transportation requests per SCC) and this in less than 1000 seconds on average. The detail of the computational results on the 20 instances tested is presented in the Appendix A.

7 Concluding remarks

We have presented a novel and efficient formulation for the biomedical samples transportation problem (BSTP) — an optimization problem aiming at deciding the routes' schedules required to move highly perishable commodities on a health care network— and an efficient solution algorithm with optimality guarantees.

Our model presents a great advantage with respect to previous models for this problem: it optimizes the **number** and the **timing** of the pickup decisions, while respecting the life span of the samples. Moreover, samples' life spans are defined between the time at which they are generated at each SCC (collected from patients) and their arrival time at the Lab for analysis. This detailed consideration of the perishability of the samples, and its individual tracking, causes a strong and difficult interdependency between the pickup times at each centre and the global routing plan. This highly complex reality has been modeled as a service network design problem on a time-expanded network, which allowed us to remove precedence and synchronization constraints by explicitly setting the life span of the samples in the origin and destination of each transportation request. In addition, we have introduced a dynamic discretization discovery algorithm with optimality guarantees to alleviate the computational complexity of the problem. The strength of the algorithm is in reducing the full problem to a series of easier problems on smaller networks with a lesser number of nodes and a smart group of commodities.

Our computational campaign shows that the new formulation is useful to provide non-trivial dual and primal bounds, as compared to a recent mathematical model from the literature, while being richer and capable to capture more features from the real application that inspires our study. Indeed, the new mathematical program allows us to solve with a commercial solver a much harder problem, as the detail of the perishability of each transportation request is tracked individually and the optimal number of pickups is part of the optimization output. A state-of-the-art commercial solver is able to find solutions for our formulation with less than 13% gap in less than an hour (on average). Therefore, our model could allow managers of a health care network to decide the optimal number of visits that will need to be performed at each SCC, the optimal routes (timing and sequence) for a given fleet, and the optimal size of said fleet (optimal numbers of vehicles), all of it with the certainty that the samples' life spans will be respected.

Finally, the proposed algorithm also proves efficient at solving larger problems in moderate computing times. It is able to solve to optimality 18 of the 20 instances tested, with a time granularity of one minute and with a total of more than 200 transportation requests.

As an avenue of future research, we believe that our iterative framework may be combined with decomposition methods to cope with the complex attributes of the network design structure this problem raises, and to potentially scale and solve larger instances. Also, a capacitated variant of the problem may be relevant in cases where the products use a significant portion of the trucks' capacities.

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A Detailed computational results

In this appendix we report detailed computational results for the mathematical model and the different algorithm variants introduced in this article. In all these tables, the columns are the same and reflect the following data. Column *Instance* reports the problem name. Column *Routes* is used to report the total number of vehicles used in the best feasible solution. Column *Pickups* is used to report the total number of pickups performed at the different SCCs. Columns *Upper Bound* and *Lower Bound* are used to report the primal and dual bounds at the end of the optimization. Column *gap* reports the relative gap between these two values, computed as $(UB - LB)/UB * 100$. Finally, column *time* is used to report the total elapsed time. When the solver is unable to find a feasible solution of reasonable quality, we leave some boxes blank as the values reported by the solver are not representative of an optimal or a near-optimal solution.

Instance	Routes	Pickups	Upper Bound	Lower Bound	gap	time
01	4	5	510	510	0.00	68
02	4	6	612	612	0.00	135
03	4	4	396	396	0.00	117
04	1	3	168	168	0.00	52
05	3	3	311	311	0.00	58
06	4	9	672	672	0.00	2286
07	3	5	283	283	0.00	185
08	6	8	784	784	0.00	943
09	3	6	270	270	0.00	445
10	19	20	2847	2005	29.57	22344
11	3	9	289	289	0.00	1808
12	3	9	311	311	0.00	4764
13	3	8	270	270	0.00	426
14	6	9	771	771	0.00	4515
15	6	8	780	780	0.00	11692
16	6	10	789	789	0.00	10492
17	3	7	312	312	0.00	703
18	3	8	405	405	0.00	1137
19	4	9	447	447	0.00	1566
20	5	14	679	453	33.28	2169
Average	4.65	8			3.14	3295

Table 4: Proposed method on problems with $\Delta k = 15$ and $\Delta t = 1$

Instance	Routes	Pickups	Upper Bound	Lower Bound	gap	time
01	4	1	510	510	0.00	130
02	4	1	612	612	0.00	136
03	4	1	396	396	0.00	334
04	1	1	168	168	0.00	87
05	3	1	311	311	0.00	168
06	4	1	672	672	0.00	19344
07	3	1	283	283	0.00	1081
08	6	2	784	784	0.00	1012
09	3	2	270	270	0.00	6324
10				0	100.00	23140
11			4763	0	100.00	23732
12			2401	0	100.00	23240
13	3	1	270	270	0.00	15427
14	6	2	711	711	0.00	11745
15	6	2	780	780	0.00	12050
16			6702	789	88.23	22811
17	3	2	312	312	0.00	21700
18	3	2	405	405	0.00	11018
19			6424	0	100.00	23499
20			7099	0	100.00	24700
Average	3.79	6.36			29.41	12084

Table 5: Time expanded formulation on problems with $\Delta k = 15$ and $\Delta t = 1$

Instance	Routes	Pickups	Upper Bound	Lower Bound	gap	time
01	6	7	760	760	0.00	22
02	5	7	783	783	0.00	22
03	6	6	610	610	0.00	22
04	2	3	195	195	0.00	22
05	4	5	372	372	0.00	23
06	5	11	855	855	0.00	23
07	3	6	283	283	0.00	23
08	8	10	945	945	0.00	28
09	4	8	270	270	0.00	22
10	9	25	2940	2940	0.00	30
11	4	13	340	340	0.00	24
12	5	9	395	395	0.00	25
13	4	9	345	345	0.00	23
14	7	11	984	984	0.00	32
15	7	11	990	990	0.00	32
16	7	12	1000	1000	0.00	32
17	4	9	325	325	0.00	23
18	5	9	535	535	0.00	26
19	5	10	565	565	0.00	31
20	5	15	635	635	0.00	31
21	6	14	1355	1355	0.00	33
22	5	15	680	674	0.00	78
24	6	14	590	590	0.00	80
25	6	15	1555	1555	0.00	46
26	6	16	2350	2343	0.00	112
27	7	25	1060	1060	0.00	2032
28	10	21	3590	3590	0.00	128
29	7	22	1110	1089	1.89	3699
30	7	14	1645	1645	0.00	74
31	7	31	1190	1167	1.93	3724
32	7	35	1170	1163	0.00	2357
34	9	20	2330	2330	0.00	126
35	10	28	1985	1953	1.61	4065
36	42	45	1250	1118	10.56	3969
37	10	33	2145	2072	3.40	4169
38	11	31	2125	2076	2.31	4140
39	11	49	2405	2093	12.97	4009
40	13	41	2520	2410	4.37	4113
Average	7.50	17.50			1.03	986

Table 6: Time expanded formulation on problems with $\Delta k = 180$ and $\Delta t = 5$

Instance	Routes	Pickups	Upper Bound	Lower Bound	gap	time
01	4	5	510	510	0.00	68
02	4	6	612	612	0.00	135
03	4	4	396	396	0.00	117
04	1	3	168	168	0.00	52
05	3	3	311	311	0.00	58
06	4	9	672	672	0.00	2286
07	3	5	283	283	0.00	185
08	6	8	784	784	0.00	943
09	3	6	270	270	0.00	445
10				2005	100.00	22277
11	3	9	289	289	0.00	1808
12	3	9	311	311	0.00	4764
13	3	8	270	270	0.00	426
14	6	9	771	771	0.00	4515
15	6	8	780	780	0.00	11692
16	6	10	789	789	0.00	10492
17	3	7	312	312	0.00	703
18	3	8	405	405	0.00	1137
19	4	9	447	447	0.00	1566
20				493	100.00	23240
Average	3.83	7			10.00	4345

Table 7: Proposed model without the upper bound heuristic on problems with $\Delta k = 15$ and $\Delta t = 1$

Instance	Routes	Pickups	Upper Bound	Lower Bound	gap	time
01	4	5	510	510	0.00	199
02	4	6	612	612	0.00	161
03	4	4	396	396	0.00	260
04	1	3	168	168	0.00	67
05	3	3	311	311	0.00	133
06	4	9	672	672	0.00	410
07	3	5	283	283	0.00	198
08	6	8	784	784	0.00	385
09	3	6	270	270	0.00	159
10	30	20	6179	0	100.00	22277
11	3	9	289	289	0.00	9570
12	3	9	311	311	0.00	10036
13	3	8	270	270	0.00	3363
14	6	9	771	771	0.00	3992
15	6	8	780	780	0.00	6643
16	6	10	789	789	0.00	4912
17	3	7	312	312	0.00	649
18	3	8	405	405	0.00	1496
19	4	9	447	447	0.00	9520
20	24	14	2352	463	80.31	22277
Average	6.15	8			9.02	48.35

Table 8: Proposed model without the commodity grouping on problems with $\Delta k = 15$ and $\Delta t = 1$