Optimization of Pharmaceutical Cold Chain Logistics Distribution Path under Time-Varying Network Conditions

Changxi Ma and Xiaoyu Huang

Abstract—**With the rapid growth of demand in the pharmaceutical cold chain market and the increasing traffic congestion in real-world delivery processes, delivery vehicles often cannot maintain constant speed. To address this issue, this paper constructs a vehicle routing problem model that integrates pharmaceutical cold chain logistics characteristics with time-varying road network conditions, with the objective of minimizing total costs. The model is solved using a proposed adaptive hybrid genetic algorithm. Experimental results demonstrate that the algorithm not only effectively solves the problem formulated in the model but also exhibits outstanding performance. Compared with baseline algorithms, the proposed algorithm reduces total costs by 3.4% to 39.1%. Furthermore, compared to models that do not consider time-varying road networks, the proposed model reduces the proportion of customers served during congestion periods by 10.34% to 50.00%. These results indicate that the proposed model can significantly help vehicles avoid congested roads, demonstrating its practical significance.**

Index Terms—**vehicle routing problem, pharmaceutical cold chain logistics, time-varying road network, adaptive hybrid genetic algorithm**

I. Introduction

WITH the development of the national economy and the continuous enhancement of residents' health awareness, the market demand for pharmaceutical cold chain products has soared. Furthermore, driven by national policy initiatives, the pharmaceutical cold chain logistics industry has achieved remarkable development. In the realm of pharmaceutical cold chain products, apart from certain infectious disease vaccines that are in high demand, the market demand for vaccines, biologics, and medications is generally characterized by a wide range of requirements but relatively low dosage volumes. Given this market demand, the transportation process of pharmaceutical cold chain logistics companies typically exhibits the features of small-batch and multi-frequency. Furthermore, as car ownership continues to rise, urban traffic congestion is becoming increasingly severe, often making it difficult for vehicles to maintain optimal speeds during the delivery process [1]. As a result, optimizing pharmaceutical cold chain distribution routes while considering time-varying traffic speeds is not only more realistic but also enables more accurate predictions of delivery vehicle arrival times. This is of paramount importance for scientifically and rationally planning the departure times and distribution routes of delivery vehicles, as well as for controlling distribution costs and other related aspects.

Scholars have conducted in-depth and extensive research on vehicle transportation issues. Research focusing on fuel consumption, carbon emissions[2]-[4], control modes [5], the vehicle routing problem (VRP) [6]-[7], and cold chain transportation [8]-[9] has become a hot topic. With the advancement of VRP research, the optimization of pharmaceutical delivery has garnered increasing attention from researchers. Liu et al. [10] investigated the vehicle scheduling problem in home medical logistics, which encompasses the pickup and delivery of materials among pharmacies, individuals in need of medical care, hospitals, and laboratories. They developed two mathematical models aiming to minimizing costs and solved these models using genetic algorithms and tabu search algorithms. Kramer et al. [11] considered auxiliary depots with wider time windows and hospital depots with stricter time windows in the drug distribution path optimization model, making the drug distribution path more diverse and flexible. Jeanne et al. [12] investigated the delivery methods employed by pharmaceutical delivery companies in response to adverse weather conditions, utilizing Bayesian network methods for modeling and analysis. Zhang et al. [13] integrated epidemic transmission models with multi-period vehicle routing problems to examine their synergistic effects, ensuring that drug allocation meets demand. They applied the ε-global optimization method and a mixed tabu search heuristic to solve instances of varying sizes. Escuin et al. [14] proposed a mathematical model and algorithm to solve the problem of drug logistics distribution path, validating the feasibility of the model and algorithm with practical cases. Pharmaceutical cold chain logistics, an extension of pharmaceutical logistics and includes temperature control requirements, refers to a transportation system engineering approach that requires pharmaceuticals to maintain a certain storage temperature and ensure their quality throughout the production and consumption process. Scholars have also conducted research in this field. Madad et al. [15] studied the cold chain

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Changxi Ma is a Professor at School of Traffic and Transportation, Lanzhou Jiaotong University, Lanzhou 730070, China. (e-mail: machangxi@mail.lzjtu.cn)

Xiaoyu Huang is a postgraduate student at School of Traffic and Transportation, Lanzhou Jiaotong University, Lanzhou 730070, China. (Corresponding author, e-mail: 12231106@stu.lzjtu.edu.cn).

distribution of perishable pharmaceuticals and considered that the travel time exhibits a time dependence. If this time dependence is ignored, it will undermine the effectiveness, applicability, and optimality of the resulting solution. Janga et al. [16] constructed optimization models for drugs and vaccines stored at specific temperatures, and proposed utilizing the Bee-Ant Optimization Algorithm for the optimization model pertaining to drug cold chain logistics distribution paths. Shao et al. [17] proposed a dual distribution method grounded in the vehicle path to address the challenge of reducing overall costs and carbon emissions in cross-regional and multi-seasonal pharmaceutical cold chain logistics processes. In this method, refrigerated trucks or freight cars fitted with refrigerated containers are selected for pharmaceutical delivery. Additionally, a comparison function is designed to calculate the consumption of consumables, enabling a more optimal allocation plan for customer points with diverse demands across multiple temperature zones.

The vehicle routing problem (VRP) is a classic NP-hard problem. Most large-scale VRP instances are addressed using heuristic intelligent algorithms, such as the ant colony algorithm [18]-[19], genetic algorithm [20]-[21], and tabu search algorithm [22]. However, the genetic algorithm exhibits limited local search capability, resulting in suboptimal overall quality of feasible solutions. Additionally, the tabu search algorithm heavily depends on the initial solution. Combining these two algorithms can, to some extent, compensate for their individual shortcomings. Based on this, this paper proposes an adaptive hybrid genetic algorithm with a dynamically adjusted cross-mutation probability formula. This formula intelligently regulates the cross-mutation probability, thereby avoiding premature convergence of the algorithm. Furthermore, the proposed algorithm combines the genetic algorithm with the tabu search algorithm, employing a tabu list to record and prevent redundant exploration previously searched solutions. This integration prevents repeated calculations and enhances the search capability of the overall search capability.

A review of relevant literature reveals that research on optimizing the distribution path of pharmaceutical cold chain logistics under time-varying road network conditions is relatively scarce. Most studies assume a constant vehicle speed when addressing this issue, but in reality, speeds vary dynamically based on road conditions. Furthermore, most studies only consider hard time window constaints or focus on the time impact when assessing a time window penalty cost. In actual delivery situations, uncontrollable factors such as traffic congestion and vehicle failures, often prevent deliveries at the customer's requested time. The use of hard time windows may not align with actual delivery scenarios. Additionally, the penalty cost is not exclusively determined by time. Therefore, soft time window models that consider factors such as time and demand can be designed to more accurately measure a time penalty cost.

The main contributions of this paper are summarized as follows. (1) This paper proposes a total cost model for distribution in pharmaceutical cold chain logistics. To enhance the realism of the model, the time-varying road network problem is considered during the research process. The speed of delivery vehicles constantly changes during the distribution process, and the impact of speed differences at different time periods on delivery time is taken into account. (2) Nowadays, logistics delivery has entered the minute level, and delivery time will affect user satisfaction, thereby affecting company profits. Therefore, in terms of time penalty cost, this paper designs a special time window, and the calculation of penalty cost is not only related to delivery time but also to the value of the products requested by customers. (3) An adaptive hybrid genetic algorithm is developed to address the problem of delivery paths in pharmaceutical cold chain logistics.

The remainder of this paper can be described as follows. In Section 2, a detailed introduction to the mathematical model is provided. In Section 3, the proposed algorithm is described in detail. In Section 4, we conduct experimental evaluation and analysis using large-scale examples. Finally, our conclusions and insights are presented in Section 5.

II. Problem Description and Modeling

A. Problem Description

Under time-varying urban traffic conditions, the optimization of distribution routes in pharmaceutical cold chain logistics can be characterized as follows. A distribution center uses vehicles to provide delivery services to various customer nodes. The vehicles depart from the distribution center, complete all delivery tasks, and subsequently return to the distribution center. Each customer node has a specified time window for delivery. If the delivery cannot arrive within the designated time window, penalties will be incurred. Under these conditions, develop a delivery plan with the goal of minimizing the total distribution cost. Considered the complexity and operability of real-world problems, this paper proposes the following assumptions: (1) There is only one distribution center, and the delivery vehicles are homogeneous, i.e. identical in vehicle model, load capacity, and specifications. (2) The vehicle's load capacity is fixed and cannot exceed the specified limit, and the demand for each customer point can be met by one vehicle through one-time delivery. (3) The locations of the distribution center and customer points are known, along with the respective requirements, time windows, and customer-specific data. (4) The vehicle speed exhibits time-varying characteristics, and it may fluctuate depending on the driving period. (5) The travel cost is only proportional to the mileage traveled. (6) The quantity of goods at the distribution center exceeds the total demand at the customer nodes.

B. Notations

The parameters related to the model are established as follows. It is assumed that N is the set of customer points, and V is the set of all nodes, where V = {0} ∪ N, with 0 representing the distribution center. Additionally, K is the set of delivery vehicles, where K = {0, 1, ..., k}, and k denotes the vehicle number. The relevant variables and parameters of the model are detailed in Table I.

C. Time-Varying Road Network Analysis

In general, when constructing a VRP model, it is assumed that the vehicle travels at a constant speed. However, in reality, the vehicle's speed may vary due to various factors. This paper considers only the influence of driving time periods on vehicle speed and adopts the piecewise function based on speed studied by Ichoua et al. [23] to describe the time-varying characteristics. The driving speed function for each time period throughout the day is shown in (1).

$$v_{ij}(t)=\begin{cases} v_{ij1}, & t\in T_1 \\ v_{ij2}, & t\in T_2 \\ \cdots & \\ v_{iju}, & t\in T_u \end{cases} \tag{1}$$

Within a single time period, the vehicle speed remains constant but may change in different time periods. The calculation process of vehicle travel time in a time-varying network is analyzed as follows:

(1) Determine the corresponding vehicle speed during the given travel time period. Proceed to (2).

(2) Calculate the distance traveled by the vehicle at the corresponding speed during the remaining time of the current period, add the distance already traveled by the vehicle, and check whether the total distance obtained exceeds the road distance.

(3) If the total distance exceeds the road distance, the travel time is the sum of the travel time spent before entering the current time period and during the current time period. The driving time within the current period is calculated as follows: the remaining road distance, obtained by subtracting the distance already traveled from the total road distance, divided by the corresponding speed in the current period.

(4) If the total distance does not exceed the road distance, the vehicle will continue driving into the next period. Proceed to (2) and repeat.

TABLE I
SYMBOLS AND DESCRIPTIONS

Notations	Descriptions
F	Fixed cost per vehicle (CNY/ vehicle)
c	The travel cost per unit distance traveled by the vehicle (CNY/km)
d_{ij}	Distance from customer point i to customer point j (km)
q_i	The demand for customer point i (kg)
Q	Vehicle capacity (kg)
a_1	The refrigeration costs incurred during transportation per unit time (CNY/h)
a_2	The refrigeration costs incurred during service per unit time (CNY/h)
t_{ij}	The time required for the vehicle to travel from point i to point j (min)
t_{si}	The service time of the vehicle at point i (min)
λ	The environmental cost per unit of carbon emissions (CNY/kg)
g	The fuel consumption per unit distance (L/km)
η	The carbon emission coefficient per unit fuel consumption of vehicles (kg/L)
τ	The deterioration rate of pharmaceuticals
δ	The speed at which pharmaceuticals deteriorate
b	The unit cost of transporting pharmaceuticals (CNY/kg)
θ	The adjustment parameters for time penalty cost
$[e_i, l_i]$	The expected delivery time window for customers
P	Unit price of transported pharmaceuticals (CNY/(min*kg))
α	Penalty coefficient for vehicles arriving early
β	Penalty coefficient for vehicles arriving late
ω	Profit coefficient of pharmaceuticals
t_i	The time when the vehicle arrives at point i
x_{ijk}	The binary variable x_{ijk} is 1 when the vehicle k is driving on road (i,j) and 0 otherwise
y_{ki}	The binary variable y_{ki} is 1 when the vehicle k is servicing customer point i and 0 otherwise

D. Cost analysis in cold chain logistics

The total distribution cost includes fixed cost, travel cost, refrigeration cost, carbon emission cost, damage cost, and time penalty cost. Based on this, a model for optimizing the distribution paths in pharmaceutical cold chain logistics is developed.

(1) Fixed cost (C_1)

In the process of logistics distribution, delivery vehicles incur certain fixed costs, including vehicle depreciation, driver's driving expenses, and wages for loading and unloading workers. This cost solely depends on the number of delivery vehicles.

$$C_1=|K|F \tag{2}$$

(2) Travel cost (C_2)

Vehicles need to consume a certain amount of fuel when delivering pharmaceuticals, resulting in travel cost. This cost is linearly related to the vehicle's mileage, with longer distances leading to higher travel cost.

$$C_2=c\sum_{k\in K}\sum_{i\in V}\sum_{j\in V}x_{ijk}d_{ij} \tag{3}$$

(3) Refrigeration cost (C_3)

The total refrigeration cost includes the refrigeration cost during transportation and the refrigeration cost during service [18].

$$C_3=a_1\sum_{k\in K}\sum_{i\in V}\sum_{j\in V}x_{ijk}t_{ij}+a_2\sum_{k\in K}\sum_{i\in V}\sum_{j\in V}y_{ki}t_{si} \tag{4}$$

(4) Carbon emission cost (C_4)

Vehicles need to consume fuel during operation, accompanied by a significant amount of carbon dioxide emissions, which results in a corresponding cost known as carbon emission cost. Carbon emission cost is primarily related to the amount of energy burned; that is, this cost is closely linked to the vehicle's fuel consumption and increases with the cumulative increase in driving mileage.

$$C_4=\lambda g\eta\sum_{k\in K}\sum_{i\in V}\sum_{j\in V}x_{ijk}d_{ij} \tag{5}$$

(5) Damage cost (C_5)

The cost of goods damage refers to the expenses incurred due to changes in the quality of pharmaceuticals.

$$\tau=1-e^{-\delta t_{ij}} \tag{6}$$

$$C_5=b\tau\sum_{k\in K}\sum_{i\in V}\sum_{j\in V}y_{ki}q_i \tag{7}$$

(6) Time penalty cost (C_6)

The time window adopted in this paper is represented by $[e_i, l_i]$, which signifies the customers' expected delivery time range. The relationship between delivery time and penalty cost is illustrated in Fig. 1.

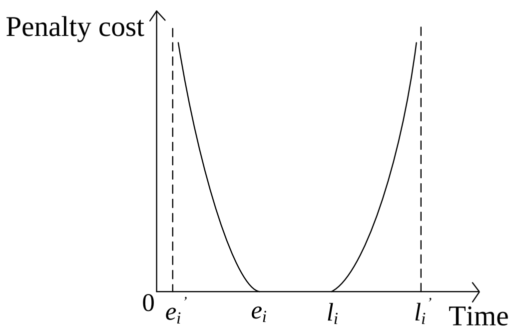

Fig. 1. Time penalty cost

In Fig. 1, e_i' represents the set time upper bound; l_i' represents the set time lower bound. The time window calculation for penalty cost, designed in this paper, is related not only to the vehicle's delivery time but also to the weight and value of the goods. Therefore, there are three types of penalty costs related to demand points.

The first type is when the vehicle arrival time is within the customer's acceptable range, but the delivery occurs before the customer's expected delivery time. At this point, corresponding penalty cost is incurred.

$$C_6(i) = \alpha P q_i \omega (e_i - t_i)^\theta \quad e_i^{'} \le t_i < e_i \tag{8}$$

The second type is when the delivery time is within the time window, at which point the customer is most satisfied and can immediately use the service without incurring penalty cost.

$$C_6(i) = 0 \quad e_i \le t_i \le l_i \tag{9}$$

The third type is when the delivery time exceeds the customer's expected delivery time, but it is still within an acceptable time range, resulting in corresponding penalty cost.

$$C_6(i) = \beta P q_i \omega (t_i - l_i)^\theta \quad l_i < t_i < l_i^{'} \tag{10}$$

In summary, the time penalty cost incurred can be formulated as follows.

$$C_6(i) = \begin{cases} \alpha P q_i \omega (e_i - t_i)^\theta, & e_i^{'} \le t_i < e_i \\ 0, & e_i < t_i < l \\ \beta P q_i \omega (t_i - l_i)^\theta, & l_i < t_i < l_i^{'} \end{cases} \tag{11}$$

E. Modeling

The goal of optimization is to minimize the total delivery cost. In this model, the total distribution cost, including fixed cost, travel cost, refrigeration cost, carbon emission cost, damage cost, and time penalty cost, is shown in (12).

$$\min C = C_1 + C_2 + C_3 + C_4 + C_5 + \sum_{i \in N} C_6 \tag{12}$$

Subject to:

$$\sum_{k \in K} \sum_{i \in N} x_{0ik} - \sum_{k \in K} \sum_{j \in N} x_{j0k} = 0 \tag{13}$$

$$\sum_{k \in K} \sum_{i,j \in N} x_{ijk} = \sum_{k \in K} \sum_{i,j \in N} x_{jik} = 1 \tag{14}$$

$$\sum_{k \in K} \sum_{i,j \in N} x_{ijk} q_i \le Q \tag{15}$$

$$\sum_{k \in K} \sum_{i \in N} x_{0ik} \le |K| \tag{16}$$

$$x_{ijk} \in \{0,1\} \quad \forall i, j \in V, k \in K \tag{17}$$

$$y_{ki} \in \{0,1\} \quad \forall i \in V, k \in K \tag{18}$$

Equation (13) represents that each delivery task starts and ends at the delivery center; Equation (14) represents that each customer point can only be serviced once; Equation (15) represents that the total amount of goods required by each customer served by the vehicle is less than the rated load capacity of the vehicle; Equation (16) states that the total number of vehicles serving customers shall not exceed the total number of vehicles owned by the distribution center; Equations (17) and (18) represent decision variables, which are binary variables.

III. Adaptive Hybrid Genetic Algorithm

The above model is a typical NP-hard problem. When the node size is small, mathematical programming methods can yield exact solutions. However, as the node size increases, the solution space grows exponentially, and mathematical programming methods cannot solve it. Therefore, heuristic methods are generally employed to find approximate solutions. Traditional genetic algorithms with fixed crossover and mutation probabilities are prone to premature convergence. Therefore, a dynamically adjusted crossover and mutation probability formula is designed to intelligently regulate the crossover and mutation probabilities with iterative formulas, thereby mitigating premature convergence of the algorithm. By integrating the improved adaptive genetic algorithm with the tabu search algorithm, this approach exhibits excellent global and local search capabilities. The algorithm steps are as follows.

A. Encoding Operation

The length of the chromosome is n+k+1, where n represents the number of customer points, k represents the number of delivery vehicles. The encoding for the distribution center is 0; the numbers 1, 2, 3, ..., n represent the natural number sequence assigned to each customer point. For example, if there are 3 vehicles in the distribution center providing delivery services to 10 customers, and one of the delivery sequences (or routes) represented by a chromosome is: 0-3-5-9-0-6-10-1-2-0-8-4-7-0, then the indicated delivery routes can be interpreted as follows: The first vehicle's driving route is 0-3-5-9-0, signifying that it departs from the distribution center, visits customer points 3, 5, and 9,and then returns to the distribution center. The second vehicle's driving route is 0-6-10-1-2-0, indicating that it departs from the distribution center, visits customer points 6, 10, 1, and 2 sequentially, and then returns to the distribution center. The third vehicle's driving route is 0-8-4-7-0, showing that it departs from the distribution center, visits customer points 8, 4, and 7, and subsequently returns to the distribution center.

B. Population Initialization

Firstly, randomly arrange all customer point codes in a column, where q_i represents the demand for goods at the i-th customer point in the chromosome. Further adjustments will be made based on the constraints of vehicle load, retaining those chromosomes that meet the constraints and eliminating those that do not, in order to construct a chromosome that fully satisfies the constraints.

C. Fitness Calculation

Fitness value is a measure of evaluating an individual. In general, the larger the fitness value of an individual, the higher the probability that they will be selected and retained for the next generation. The model established in this paper is a problem of minimizing the objective function, so the selection of the fitness function is measured by the reciprocal of the objective function.

$$f(x) = \frac{1}{Z(x_i)} \tag{19}$$

Where $Z(x_i)$ represents the objective function value corresponding to individual x_i.

D. Individual Selection

The roulette wheel selection method is employed to retain the best chromosome from the parent generation and replace the worst one in the offspring generation [24]. The specific steps are as follows.

(1) Calculate the fitness of each chromosome in the current population.

$$fit(i) \tag{20}$$

(2) Calculate the sum of fitness of all chromosomes in the population.

$$sumfit = \sum_{i \in N} fit(i), \quad i = 1, 2, \cdots, n \tag{21}$$

(3) Calculate the selection probability of each chromosome in the current population.

$$p(i) = \frac{fit(i)}{sumfit}, \quad i = 1, 2, \cdots, n \tag{22}$$

(4) Calculate the cumulative probability of each chromosome in the current population.

$$ps(i) = \sum_{i \in N} p(i), \quad i = 1, 2, \cdots, n \tag{23}$$

A real number r within the interval [0,1] is randomly generated. If $ps(i) > r$, select the first chromosome. Otherwise, select the i-th chromosome that satisfies $ps(i-1) < r < ps(i)$.

E. Crossover Operation

The crossover operation in genetic algorithms involves the exchanging certain gene segments between two paired chromosomes in a specific manner, thereby generating two new offspring. This process enables the population to explore a wider range of the search space and potentially identify better solutions [25]. Setting a fixed crossover probability can ensure the emergence of new individuals, but when the population evolves to a certain extent, it is easy to destroy individuals with higher fitness [26]. Because the crossover factor needs to decrease with the increase of iteration times, more crossover operations are performed in the early stages of the algorithm to explore more solution space, while in the later stages, crossover operations are reduced to focus on finer local search. The cosine function can fully satisfy this changing relationship and can decrease at a slower speed in the early stages, gradually accelerating in the middle and late stages. Therefore, this paper introduces a dynamic crossover probability based on the cosine formula and sets the individual crossover probability.

$$P_c = P_{c\min} + \left(P_{c\max} - P_{c\min}\right) \cdot \frac{1 + \cos\left(\pi \cdot \dfrac{g}{G}\right)}{2} \tag{24}$$

where P_c represents the crossover probability, $P_{c\min}$ represents the lower limit of the crossover probability, $P_{c\max}$ represents the upper limit of the crossover probability, g is the current iteration count, and G is the maximum iteration count.

The specific operation of the crossover method used in this paper is as follows.

(1) Randomly select a segment of the daughter pathway on each of the two parental chromosomes, as shown in Fig. 2.

(2) The selected sub section is placed in front, as shown in Fig. 3.

(3) Include Path A of Parent Chromosome 1 as part of Offspring Chromosome 1, and append the codes that are not present in Path A of Parent Chromosome 2 to the end of Path A in Offspring Chromosome 1, in the order they appear in Parent Chromosome 2. Finally, add the code 0 at the end of the Offspring chromosome. As shown in Fig. 4.

(4) For offspring chromosome 1, insert a code 0 at one of the seven positions following the A pathway, resulting in a total of seven scenarios. Calculate the fitness for each of these seven scenarios and select the one with the highest fitness value as offspring chromosome 1. Similarly, obtain offspring chromosome 2.

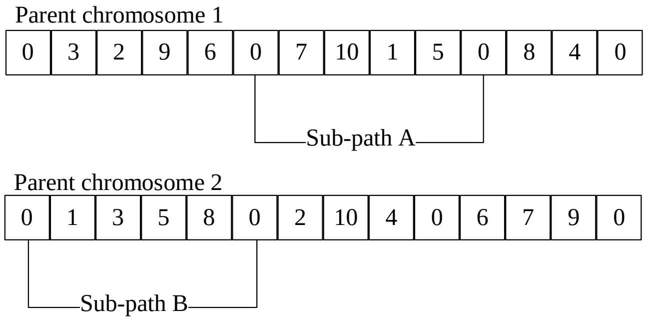

Fig. 2. Parent chromosomes

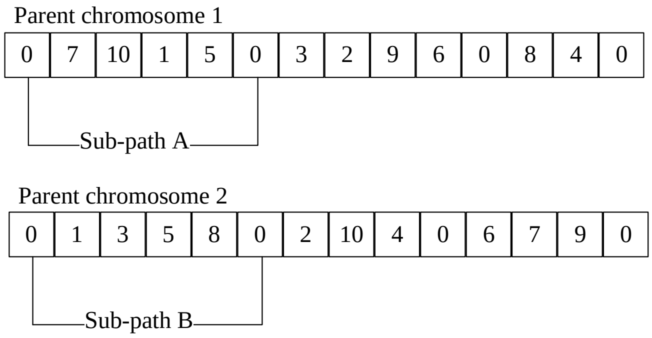

Fig. 3. New parent chromosomes

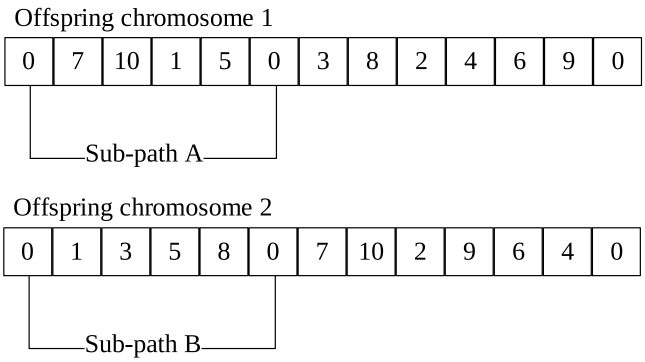

Fig. 4. Offspring chromosomes

F. Mutation Operation

Similarly, to safeguard the continuity of excellent individuals within the population and to enhance diversity in the early stages of the search, the mutation probability gradually decreases as the number of iterations increases. The dynamic mutation probability, which is based on a cosine function, has been set as follows.

$$P_m = P_{m\min} + \left(P_{m\max} - P_{m\min}\right) \cdot \frac{1 + \cos\left(\pi \cdot \dfrac{g}{G}\right)}{2} \tag{25}$$

where P_m represents the crossover probability, $P_{m\min}$ represents the lower limit of the crossover probability, $P_{m\max}$

represents the upper limit of the crossover probability.

The mutation operation described in this paper employs the swapping operator, which randomly selects two positions in the parent chromosome for exchange [27]. To prevent the destruction of the best individual by mutation operation, the top 30 excellent individuals are retained, and the mutation operation is applied to the remaining individuals. A simple example is shown in Fig. 5.

Parent	0	3	2	9	6	0	7	10	1	5	0	8	4	0
Offspring	0	3	2	8	6	0	7	10	1	5	0	9	4	0

Fig. 5. The example of exchange mutation

G. *Tabu Search Strategy*

The tabu search operation is incorporated after the crossover step of the genetic algorithm and before updating the population.

First, compare the genes of the offspring generated by crossover with the existing population to check for any historical operation records. Then, use tabu lists to remove duplicated or ineligible genes. Subsequently, preserve the optimized offspring genes. Next, merge these optimized offspring genes, which have undergone tabu search, with the current population to form a new population.

The tabu search algorithm is widely used to find optimal solutions due to its effective local search method [28]. By increasing the diversity of the search space and enhancing local search capabilities, tabu search aids in accelerating the convergence speed of algorithms [29]-[30]. The integration of tabu search into genetic algorithms has significantly improved their performance. This is particularly advantageous when tabu search is positioned after crossover operations, as it allows newly generated genetic individuals to serve directly as starting points for the tabu search process. This, in turn, facilitates further optimization and selection through tabu-based filtering. The candidate neighborhood solution with the best target value and not in the tabu list can be selected as the current best solution. However, there is an aspiration criterion: if the optimal solution selected from the neighborhood candidates is prohibited by the tabu list but is still better than the current best solution, the optimal neighborhood solution can be accepted to replace the current best solution, thereby achieving efficient global optimization search [31]. Algorithm 1 shows the specific steps of tabu search.

IV. Computational Experiments

A. *Experiment setup*

The instances used in this paper originate from Solomon's [32] datasets. And all instances are classified into three types: Cluster (C), Random (R), and Random Cluster (RC). The datasets utilized in this paper are large-scale, with 101 nodes in each group, and certain parameters from the Solomon instances can be directly adopted, including the site location, time window, and service time. Additionally, time periods can be segmented according to the time scale provided in the dataset, and different speeds can be assigned for each segment. In actual distribution, nodes are connected by multiple, non-straight, roads; hence, the straight-line distance can greatly diverge from the actual distance.

This paper introduces the circuitous coefficient δ ($\delta \approx 1.5$) [33] and defines d_{ij} as the product of this coefficient and the straight-line distance between two points. The other parameters are shown in Table II.

The parameters for the algorithm are shown in Table III. The algorithm is implemented using Python programming and runs on a computer with a CPU of 2.40 GHz and 16GB of memory.

Algorithm 1: Tabu Search

Input: the list of all genes (genes), the list of genes generated after cross operation (crossedGenes)

Output: the updated gene list that has been filtered through tabu lists and treated with amnesty (new_Genes)

```
Compute the current best solution: P_b ← max (gene.fit for gene in genes)
Construct the tabu list: tabu_list ← {gene.fit for gene in genes}
Initialize the list of filtered solutions: new_Genes ← []
for i = 1 to len(crossedGenes) do
    Let g_i = crossedGenes[i]
    if g_i.fit in tabu_list then
        if g_i.fit > P_b then
            Amnesty for this gene. Add g_i to new_Genes
        else
            Skip this gene (mark as tabu)
        end if
    else
        Add g_i directly to new_Genes
    end if
end for
Output new_Genes
```

TABLE II
MODEL PARAMETERS

Parameters	Description	Value
F	Fixed cost per vehicle (CNY/ vehicle)	100
c	The travel cost per unit distance traveled by the vehicle (CNY/km)	2
Q	Vehicle capacity (kg)	200
a_1	The refrigeration costs incurred during transportation per unit time (CNY/h)	0.025
a_2	The refrigeration costs incurred during service per unit time (CNY/h)	0.1
λ	The environmental cost per unit of carbon emissions (CNY/kg)	0.2
g	The fuel consumption per unit distance (L/km)	0.15
η	The carbon emission coefficient per unit fuel consumption of vehicles (kg/L)	2.62
δ	The speed at which pharmaceuticals deteriorate	0.01
b	The unit cost of transporting pharmaceuticals (CNY/kg)	1
P	Unit price of transported pharmaceuticals (CNY/(min*kg))	1
θ	The adjustment parameters for time penalty cost	0.5
ω	Profit coefficient of pharmaceuticals	0.18
α	Penalty coefficient for vehicles arriving early	0.2
β	Penalty coefficient for vehicles arriving late	0.2

TABLE III
ALGORITHM PARAMETERS

Parameter	Description	Value
Popsize	Population size	100
G	Maximum number of iterations	500
P_{cmin}	Lower limit of crossover probability	0.9
P_{cmax}	Upper limit of crossover probability	0.6
P_{mmin}	Lower limit of mutation probability	0.01
P_{mmax}	Upper limit of mutation probability	0.2

B. Comparison Analysis of Time-Varying and Static Road Network

Three sets of experiments are conducted on the R204, C107, and RC107 datasets: two with a static road network and fixed vehicle speeds, and the other with a time-varying scenario accounting for changes in vehicle speeds over time. The setting of vehicle speeds in the time-varying road network is based on the time window of each dataset. Taking the R204 dataset as an example, the limits are set at 0 minutes (corresponding to 7:00) and 1020 minutes (corresponding to 24:00). The congestion periods are set from 30 minutes to 120 minutes (corresponding to the morning peak from 7:30 to 9:00) and from 630 minutes to 720 minutes (corresponding to the evening peak from 17:30 to 19:00), during which the speed is set at 20 km/h. For other time periods, the speed is set at 30 km/h. The time-varying road network conditions is called option I; The set speed in the static road network is 30km/h, which is called option II; The other group is set to 40km/h, known as option III. Table IV shows the experimental results for three datasets, where I represents the time-varying road network conditions, II represents the static road network conditions, TC represents the total cost, CPUT represents the running time, TD is the total delivery distance, R represents the proportion of customers served by vehicles during congestion periods to the total number of customers.

TABLE IV
EXPERIMENTAL RESULTS USING THREE DATASETS

Instance	Option	TC	TD	CPUT(s)	R
R204	I	10,918	4,083	56	0.19
	II	10,571	3,976	50	0.26
	III	10,176	3,697	50	0.25
C107	I	16,144	4,324	48	0.06
	II	15,931	3,633	43	0.09
	III	15,900	3,534	47	0.09
RC207	I	15,333	5,246	46	0.29
	II	14,012	5,182	43	0.33
	III	13,399	5,080	43	0.32

Table IV shows the following: (1) Under time-varying road network conditions, the total cost across the three datasets is higher than that under static road network conditions, with an increase of 1.33% - 9.42%. Similarly, the total traveled distance under time-varying conditions is also higher, increasing by 1.23% - 19.02%. However, the proportion of customers served during congestion periods (R) under time-varying conditions is lower than that under static conditions, decreasing by 10.34% - 50.00%. These results indicate that while delivery under time-varying conditions increases costs and distances, it also helps vehicles avoid congestion, thereby reducing traffic pressure and demonstrating significant practical value. (2) Comparing option II and III, as the speed decreases, the total cost increases accordingly, indicating an inverse relationship between cost and congestion speed. This highlights that considering the time-dependent nature of vehicle travel speed is both effective and meaningful for research.

C. Experiment on Different Customer Distribution Examples

Different types of examples are used to address the issues raised in this paper. Table V shows the experimental results, where TMC represents the time penalty cost of the vehicle, TRC is the travel cost, RC is the refrigeration cost, DC is the damage cost, CEC is the carbon emission cost, and VN is the vehicle numbers.

TABLE V
EXPERIMENTAL RESULTS OF DIFFERENT EXAMPLES

IN	TC	TMC	TRC	RC	DC	CEC	VN
C106	17,335	1,095	9,736	3,348	1,771	382	10
C108	17,015	1,215	9,316	3,323	1,794	366	10
R205	12,662	489	8,124	1,519	1,409	319	8
R206	12,361	377	8,128	1,448	1,287	319	8
RC207	15,333	396	10,492	1,371	1,660	412	10
RC208	14,857	156	10,712	1,003	1,563	421	10

From Table V, it can be seen that: (1) Among all types, the total cost of type C is the highest, with 17,355 in the C106 dataset, which is 13.0% -36.9% higher than that of the other dataset types. The time-related costs, including time penalty cost, refrigeration cost, and damage cost, are also the highest, with the sum of these costs reaching 6,332 in the C108 dataset. Compared to other types of datasets, this is 84.9% -85.3% higher. This is mainly because the service time for all C-type is 90 minutes, whereas for R-type and RC-type it is only 10 minutes, resulting in a longer distribution process. Consequently, the costs associated with delivery time are relatively high. (2) Compared with the C-type, the R-type and RC-type have lower total costs, time penalty costs, refrigeration costs, and loss costs. This is mainly attributed to the 10-minute service time for these two types of customer nodes, which is significantly shorter than the C-type's 90-minute service time. The time window requirements of the customer are relatively relaxed, allowing the vehicle to visit more customers in a shorter period, thus reducing the total delivery time. Meanwhile, the shorter service time also leads to a reduction in the required refrigeration time, which in turn lowers the refrigeration cost. Overall, special attention should be paid to service time during actual delivery. (3) For all types of examples, TRC accounts for a relatively high proportion of the total cost, with the highest proportion in the RC208 dataset at 10,712, accounting for 72%. In the remaining datasets, it accounts for 54.7% - 64.1%. This indicates that travel costs are one of the main sources of logistics and distribution costs. These costs can be reduced by minimizing the total delivery distance. Additionally, time penalty cost, refrigeration cost, and damage cost are also important components, accounting for 26.9% - 37.2% of the total cost across all datasets. These costs are closely related to travel time. Therefore, to reduce costs, it is important to minimize travel time as much as possible. (4) The proportion of carbon emission cost is very low, with only 319 in the R-type dataset, accounting for 2.5%, and around 3% of the total cost in the other datasets. This indicates that solely considering the cost of carbon emissions is not sufficient to effectively incentivize logistics companies to adopt energy-saving and emission-reduction measures.

D. Algorithm Performance Tests

To validate the effectiveness of the improved genetic algorithm, we conducted experimental verification on three datasets: C107, R107, and RC107. The experiment employes the adaptive hybrid genetic algorithm (AHGA) proposed in this paper, with the basic genetic algorithm (GA), adaptive genetic algorithm (AGA), and hybrid genetic algorithm (HGA) serving as baseline algorithms. Each algorithm is executed ten times to determine the average result for each instance. The crossover probability in the GA and HGA is 0.7; and the mutation probability in both algorithms is 0.01. The iteration of experiments on three datasets is shown in Fig. 6-8.

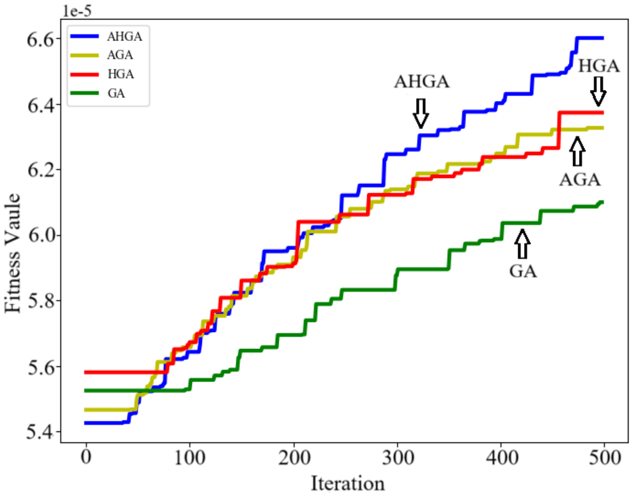

Fig. 6. Comparison of C107 example iterations

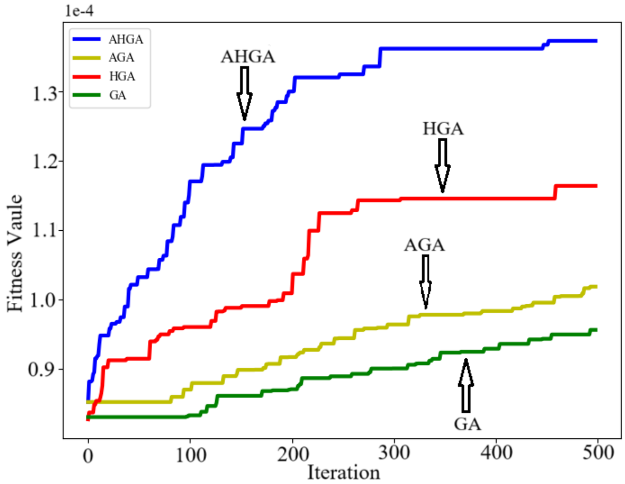

Fig. 7. Comparison of R107 example iterations

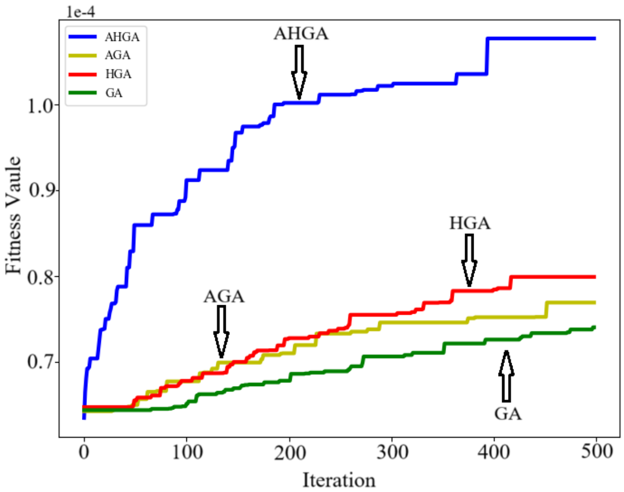

Fig. 8. Comparison of RC107 example iterations

From Fig. 6-8, it can be intuitively observed that GA, AGA, and HGA fall into local optima during the optimization process, from which they cannot escape in a timely manner. In contrast, the AHGA designed in this paper demonstrates earlier convergence and significantly higher accuracy. This enhancement is attributed to the introduction of dynamic crossover and mutation operators, coupled with the application of tabu search algorithms for local search operations. These innovations have improved the convergence speed and accuracy of AHGA, bolstering its global search capability, and thereby enabling it to reach convergence more rapidly and generate more reasonable paths. The results of the three comparative experiments are shown in Table VI.

TABLE VI
COMPUTATIONAL RESULTS BY FOUR ALGORITHMS ON THREE INSTANCES

Instance	Algorithm	TC	CPUT(s)	TD
C107	AHGA	16144	48	4324
	HGA	16691	42	4647
	AGA	16807	48	4660
	GA	17394	39	4958
R107	AHGA	8088	56	2475
	HGA	9394	34	3167
	AGA	10618	51	3755
	GA	11251	42	4122
RC107	AHGA	10291	53	3258
	HGA	13514	31	4974
	AGA	14000	46	5253
	GA	14504	29	5478

The data in Table VI reveals that: (1) In terms of total cost, the AHGA algorithm outperforms GA, AGA, and HGA across all examples. Specifically, compared to GA, AHGA achieves a maximum savings of 39.1% and a minimum savings of 7.7%. When compared to AGA, AHGA can save between 4.1% and 36.0%. Compared to HGA, AHGA can save between 16.1% and 3.4%. (2) Regarding runtime, the AHGA algorithm primarily focuses on dynamically adjusting crossover probability and mutation probability, as well as incorporating a tabu search. However, the computation time for all four algorithms remains relatively similar, with no significant differences observed. (3) In terms of driving distance, the AHGA algorithm also performs better in all examples. Specifically, compared to GA, AHGA reduces the distance by a maximum of 66.5% and a minimum of 14.7%. When compared to HGA, the maximum reduction is 27.8%, and the minimum reduction is 7.4%. Compared to AGA, the maximum decrease is 51.7% and the minimum decrease is 7.8%. (4) Among all the algorithms, GA performs the worst and yields the highest total cost. AGA and HGA outperform GA, indicating that incorporating dynamic crossover-mutation factors or tabu search can enhance algorithm performance to some extent. AHGA has the best performance, with the lowest total cost and total distance. This algorithm combines the advantages of dynamic crossover mutation factors and tabu search, and can therefore obtain better results than AGA and HGA.

V. CONCLUSIONS

To enhance the precision of travel time estimation in pharmaceutical cold chain logistics route optimization, this study integrates time-dependent vehicle speeds into the model. A time-variant speed function is formulated to reflect this variability. Under the constraints of time windows, customer demand, and maximum vehicle load capacity, a pharmaceutical cold chain vehicle routing problem model is developed, with the objective of minimizing total costs. Finally, the AHGA is subsequently employed to solve for the optimal path of the model. Calculations, analyses, and comparisons are then carried out to evaluate the solution. When comparing results obtained from the model presented in this paper with those obtained under constant speed conditions in a static road network, it is found that considering a time-varying road network can, to some extent, assist delivery vehicles in avoiding congested periods and thereby alleviating traffic pressure. To verify the improvement effect of the AHGA, a comparison of the solution results obtained using the GA, AGA, and the HGA is conducted. This comparison demonstrates that the AHGA exhibits superior performance. However, there are some shortcomings. The study only focused on a single type of product and a single vehicle model, and only considered the impact of morning and evening rush hours on speed. In future research, more factors can be incorporated into the model to enhance its applicability.

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