Research on the Optimization of Pathological Section Slide-stainer Machine Layout Model

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Abstract. The fully automatic pathological slide-stainer has significant implications for the digitization and simplification of pathology. Given that the current layout of slide-stainer is manually arranged, there are issues with inaccuracy and low time utilization. The purpose of this study is to design an algorithm for optimizing the layout of slide-stainer, aiming to achieve a scientifically arranged layout of staining sites. This enhances the efficiency of pathological section staining and ensures the timely completion of staining tasks. This paper first elaborates on the issue of staining sections using fully slide-stainer and proposes a mathematical model for the optimization design of the slide-stainer layout based on the problem. A multi-objective and multi-constraint optimization function is constructed. By simulating the daily process of section staining with the commonly used HE staining method in medicine, the optimal structure for layout optimization under these conditions is determined. The feasibility of this layout for regular use is verified through a variable neighborhood search algorithm. The results indicate that the optimized layout under this algorithm exhibits better work efficiency.

Keywords: Multi-objective Optimization, Formalization, SA Algorithm, Slide-Stainer, Site Layout Calculation.

1 Introduction

With the global population growth and the continuous rise in medical demands, automated pathology slide staining technology has become an important branch in the field of medical research [1]. The online implementation of remote pathology diagnosis has become feasible, which not only significantly alleviates the shortage of pathologists but also further emphasizes the key role of staining equipment. It simulates the entire process of manual staining by pathologists, thereby replacing the cumbersome manual operation steps. It has advantages such as simple operation, high work efficiency, and stable staining effects[2]. This study focuses on the issue of staining sites path planning during the pathology slide staining process, aiming to find

the optimal layout scheme for staining sites and using advanced simulated annealing algorithms for solving[3]. The automatic staining process of pathology slides is a complex problem involving multi-objective optimization, mainly focusing on staining site configuration, staining environment control, and improvement of the staining process [4].

Ge et al. [5] established a multi-objective optimization model for workshop layout with the objectives of minimizing material handling costs and shortening handling time between work units. An improved genetic algorithm was used for solving, which confirmed the validity of the proposed model and algorithm.

Li et al. [6] incorporated the direct supply and demand relationship between manufacturers and distributors into the research on the location and layout of multiple logistics distribution centers. By introducing a 0-1 variable for the selection and establishment of logistics distribution centers, they improved upon the existing linear programming model for general transportation problems.

Liu et al. [7] took the layout problem of wireless sensor networks as an example, constructed a multi-objective mathematical model to represent the multi-objective optimization problem of wireless sensor network layout, and described the optimization path of genetic algorithms in this problem.

Cui et al. [8] considering the continuous nature of process industry production, established a mixed-flow workshop scheduling model with limited waiting for workpieces from a new perspective. They validated and analyzed the model and algorithm using simulated actual production data.

The current research mainly focuses on the Job Shop Scheduling Problem (JSP), which involves task allocation and sequencing constraints. With a long history of research spanning several decades, it bears a high similarity to the slide-stainer layout optimization problem discussed in this paper[9]. The inherent complexity of JSP means that the computational time required to solve such problems grows exponentially with the increase in problem size, making it difficult for even high-speed computers to produce results within a reasonable timeframe. Consequently, non-numerical methods are typically employed to address the issue [10].

2 Model Construction

2.1 Description and Analysis of the Problem

The arrangement of slide-stainer sites is akin to the problem of selecting locations for logistics distribution centers, primarily based on the number of candidate locations and restrictions on location selection. In discrete location problems, the number of potential facility sites is limited. This applies to situations where only specific candidate locations are available. The layout issue of slide-stainer sites exists solely within a grid of 4 rows and 8 columns, and must exclude fixed sites for the entry and exit of stained sections, thus it falls under the category of discrete location problems [11].

The path problem of staining pathology sections established in this paper is as follows: given two section inlets, two section outlets, one section buffer center and mul-

tiple reagent stain site centers for transporting a section with a robotic arm. The number of sections to be transported is determined at the beginning of the experiment. The position of the staining reagent site is known and determined after layout. And there is a validity period for section staining, which requires section transfer and allocation within each staining site. Under the constraints of the staining process, the optimal staining path scheme with the minimum total time is sought.

The aforementioned problem involves only one robotic arm for slicing, transporting, and transferring, which is a constrained general transportation problem. In the field of logistics and transportation, whether it's theoretical exploration, model construction, or practical application, a complete and mature system has already been established[12].The research path ultimately determined by the author is to transform the issue of stain site layout in slide-stainers into a problem similar to transportation. On this basis, by considering the unique characteristics of the stain site layout problem in slide-stainers, adjustments and improvements are made to the existing models that solve transportation problems, thereby constructing a mathematical model suitable for addressing the stain site layout problem in slide-stainers.

2.2 Model Construction Related Assumptions

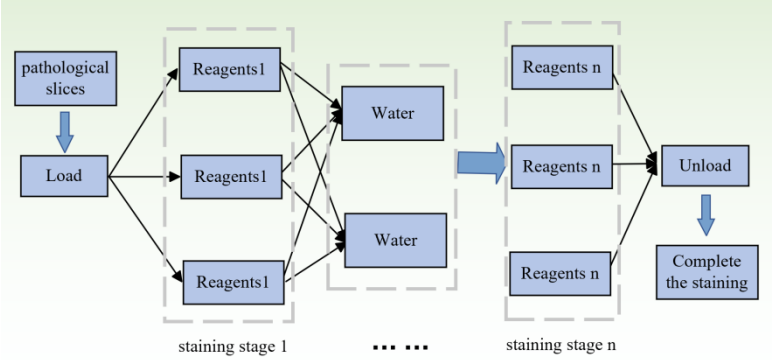

Fig. 1. Slide-stainer section staining process.

Basic Constraints:

(1) Each pathological slide can only be stained by one staining site in each staining process.

(2) The same stain site can only start staining the next slide after the previous one is completed.

(3) The next staining process of the same pathological slide can only begin after the previous one is finished.

(4) The waiting time between staining processes for each pathological slide is limited. The principle of closely connecting between staining processes is to stain continuously without delay as much as possible.

At the same time, it is assumed that:

(1) In the discussion of the staining process, the interruption caused by a certain staining site failure is not considered.

(2) The moment when the first staining site starts staining in the first staining process is always counted as 0.

3 Mathematical Model Variables and Parameter Definitions

3.1 Objective function

In practical applications, traditional job shop scheduling models cannot be directly applied to the optimization of slide-stainer scheduling problems. This is primarily due to the significant differences between industrial manufacturing environments and pathological tissue section staining environments. In the staining process of pathological sections, multiple factors need to be considered simultaneously, including restrictions on the processing flow of sections, limitations within the slide-stainer's internal sites, requirements for continuous loading, and operational constraints of a single robotic arm. Moreover, the layout optimization of slide-stainer requires selecting appropriate optimization objectives based on the specific conditions of medical section staining. In addition to considering the efficiency of traditional three-axis robotic arm transport of sections, it is also necessary to address the constraints of specific staining durations. [13]Therefore, this paper takes the minimum time required for completion of staining as the overall objective:

$$\min \mathrm{G} = \mu_{\mathrm{A}}\omega_1 \sum_{\mathrm{d}_1^{\mathrm{n}}<\mathrm{D_n}<\mathrm{d}_{\mathrm{k}}^{\mathrm{n}}} O_{n,k} + \omega_2 \sum_{0<\mathrm{n}<\mathrm{N}} t_{n,k} \tag{1}$$

In the formula: It includes the total $t_{n,k}$ of the minimum handling time for the robotic arm, as well as the optimization objective for the overall operation duration of slicing and staining at the station. Different weights ω_1 and ω_2 need to be applied to the two objectives, and $\omega_1 + \omega_2 = 1.0$, while μ_{A} used is the dimension of the quality of staining duration.

3.2 Variable and Parameter Definition

The decision variable parameter symbols used are described as follows:

Table 1. Table for the decision variable parameter symbols.

Project	Symbol	Quantity	Standard Set
Reagent constant	R	I	$\mathrm{R} = \{\mathrm{R}_1, \ldots, \mathrm{R}_{\mathrm{i}}, \ldots, P_{\mathrm{I}}\}$
Staining process	D	N	$\mathrm{D} = \{\mathrm{D}_1, \ldots, \mathrm{D}_{\mathrm{n}}, \ldots, \mathrm{D}_{\mathrm{N}}\}$
section	S	M	$\mathrm{S} = \{\mathrm{S}_1, \ldots, \mathrm{S}_{\mathrm{m}}, \ldots, \mathrm{S}_{\mathrm{M}}\}$
site	V	X	$V = \{v_{1,1}, \ldots, v_{\mathrm{i,j}}, \ldots, v_{\mathrm{I,J}}\}$

Layout	L	Y	$L = \{L_1, \dots, L_y, \dots, L_Y\}$

$$R_I = (dt_k, g_k) \tag{2}$$

R_IReagent constants are constants formed by breaking down the stages of common staining processes. They consist of the reagents used in the staining stage and the precise parameters of the staining time for that stage.

$$D_n = [d_1^n \succ \cdots \succ d_k^n \succ \cdots \succ d_K^n] \tag{3}$$

$$d_k = (P_r, pt_j)$$

D_n represents staining process. There are four common staining techniques involved, namely: Pap return blue staining technique, Pap staining technique, Hematoxylin and Eosin (HE) staining technique, and HE frozen staining technique.Stage d_k is the staining phase, which can be detailed by arranging the staining stages in a specific sequence to complete the expression of staining process D_n. In staining process D_n, the order of execution of the staining stages cannot be changed.The staining stage d_k consists of reagent constant P_r and a precise staining time pt_j, where pt_j represents the staining time for this stage.

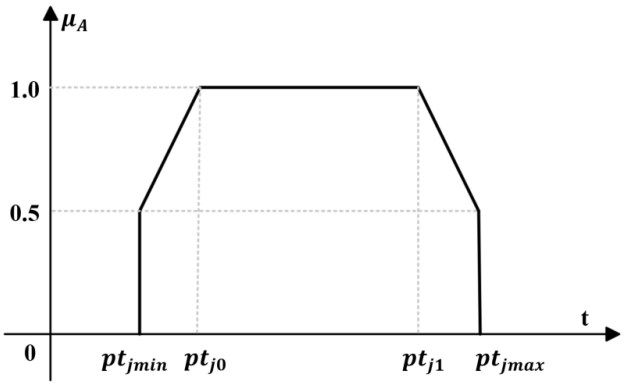

Fig. 2. Trapezoidal fuzzy function $x(pt_{jmin}, pt_{j0}, pt_{j1}, pt_{jmax})$.

$$\mu_A = \begin{cases} \frac{x - pt_{jmin}}{pt_{j0} - pt_{jmin}}, & pt_{jmin} \le x \le pt_{j0} \\ 1, & pt_{j0} \le x \le pt_{j1} \\ \frac{pt_{jmax} - x}{pt_{jmax} - pt_{j1}}, & pt_{j1} \le x \le pt_{jmax} \\ 0, & x < pt_{jmin}, x > pt_{jmax} \end{cases} \tag{4}$$

This paper introduces the concept of trapezoidal fuzzy functions, which are used to represent the range of staining duration changes during the staining stage. Here, pt_{jmin} represents the upper bound of this trapezoidal fuzzy number, pt_{j0} to pt_{j1} corre-

sponds to the optimal staining duration, and pt_{jmax} is the lower bound of this fuzzy number [14].

$$S_m = (id, D_n, Rt_i) \tag{5}$$

S_m represents a pathological section, which contains three types of information. Firstly, it serves as an identifier id for the pathological section, used to distinguish different sections; secondly, D_n indicates the staining process that the pathological section will undergo; Rt_i is the time the section is placed into the slide-stainer, which is generally significant in scenarios where sections are loaded consecutively. When the section is part of the first batch placed into the slide-stainer, the value of Rt_i should be 0.

$$V_{(I\times J)} = \begin{Bmatrix} v_{1,1}, \dots, v_{1,j}, \dots, v_{1,J} \\ \vdots \\ v_{i,1}, \dots, v_{i,j}, \dots, v_{i,J} \\ \vdots \\ v_{I,1}, \dots, v_{I,j}, \dots, v_{I,J} \end{Bmatrix} \tag{6}$$

The distribution of sites within the slide-stainer is represented in the form of a two-dimensional array, where $v_{i,j}$ denotes the internal sites of the slide-stainer. The total number of these is X, and according to functional requirements, they can be set up as reagent sites, water washing sites, loading sites, unloading sites, ovens, etc. Additionally, for the convenience of coding in the algorithms discussed in later chapters of this text, the sites are represented in a one-dimensional form labeled v_x.

$$O_{n,k} = \left(d_k^n, l_y^r, Ht1_{n,k}, Tt_{n,k}, St_{n,k}, Ct_{n,k}, Ht2_{n,k}, Dt_{n,k}\right) \tag{7}$$

Staining operation $O_{n,k}$ corresponds to staining phase d_k^n, and when the sections complete all the staining operations in sequence, they fully execute staining process S_g.

Mechanical arm moves the section to complete the detailed time and timeline of staining in this stage:$Ht1_{n,k}$、$Tt_{n,k}$、$St_{n,k}$、$Ct_{n,k}$、$Ht2_{n,k}$、$Dt_{n,k}$、At_k.These correspond to: initial reset time, execution timeThese correspond to: initial reset time, execution timeing completion time, final reset The relationships between these times and time points can be illustrated as shown in the diagram [15].

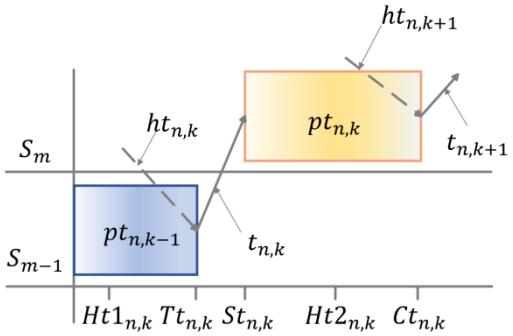

Fig. 3. Graph of staining operation time.

$$t_{n,k}^{x} = t_{xi} + t_x * x \tag{8}$$

$$t_{n,k}^{y} = t_{yi} + t_y * y \tag{9}$$

$$t_{n,k}^{z} = t_z^u + t_z^d + t_z^c + t_z^r \tag{10}$$

The motion of the robotic arm is decomposed into movements in three directions, namely the x-axis, y-axis, and z-axis, including its movement in various stain sites, as well as the operations of clamping and releasing sections by moving the robotic arm up and down.$t_{n,k}^{x}$ and $t_{n,k}^{y}$ represent the horizontal and vertical axes movements of the robotic arm, which include the duration for a single direction motor start and stop as well as the speed of movement per grid. $t_{n,k}^{z}$ is the duration for its vertical movement, which also includes the total time for picking up and releasing sections.

$$t_{n,k} = t_{n,k}^{z} + \max\left(t_{n,k}^{x}, t_{n,k}^{y}\right) \tag{11}$$

The total movement duration of the robotic arm is denoted as $t_{n,k}$. The x-axis and y-axis arms move simultaneously, taking the maximum duration of the two movements, and the z-axis arm must start moving after the x and y axes have completed their movements.

4 Instance Solution Analysis

4.1 Layout Optimization Algorithm

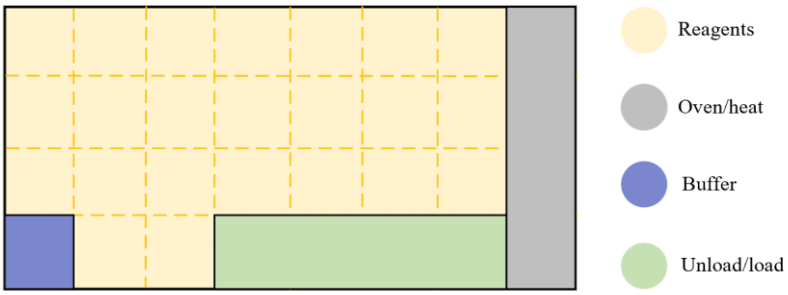

Fig. 4. Layout allocation diagram.

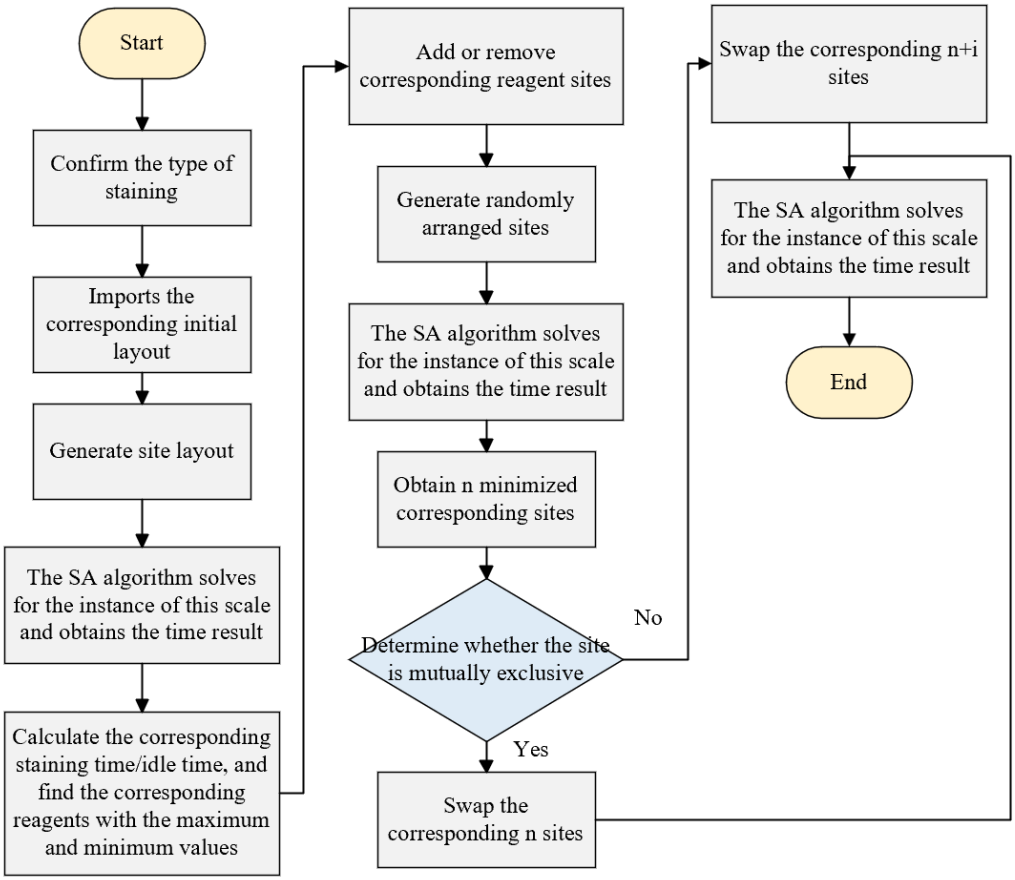

Fig. 5. Slide-stainer layout optimization algorithm flowchart.

To improve staining efficiency and reduce the maximum staining duration, a set of slide-stainer layout optimization algorithms was designed. The specific operational steps are as follows:

Step 1: Confirm the medical type of the slide-stainer for this staining session and import the initial layout parameters corresponding to that type.

Step 2: Based on the parameters, generate the arrangement of the original sites. This includes reagent sites, loading and unloading sites, heating oven sites, etc.

Step 3: On the initial layout, use the established mathematical model to perform path analysis with the simulated annealing algorithm, and obtain the time results under the initial layout.

Step 4: Analyze the reasonableness of the reagent site distribution based on the proportion of each stage's staining duration and idle duration in the time results. Adjust the corresponding sites accordingly.

Step 5: Perform random permutation distribution among the aforementioned sites. Conduct pairwise exchanges for each site. Obtain the time results after pairwise exchanges.

Step 6: Compare the time results from step five, obtain the smallest n time values corresponding to the mutually exclusive sites, and retain the exchange results.

Step 7: Iterate steps 5 and 6 ten times.

Step 8: Obtain the final Gantt chart, output the results, and end the program.

4.2 Application of Simulated Annealing Algorithm

The simulated annealing algorithm simulates the changes in the internal state of matter during the solid annealing process, establishing a correlation between optimization problems and the annealing process. The objective function aimed at minimizing time is correlated with the energy E of the internal state of matter. The cooling schedule parameter is used to control the progression of the algorithm, allowing it to produce an approximate optimal solution to the problem within polynomial time. This paper proposes a modified Metropolis criterion for the established dynamic optimization model, which is constrained and uses the difference between two numbers as the objective function, thereby expanding the feasible determination of the Metropolis criterion.

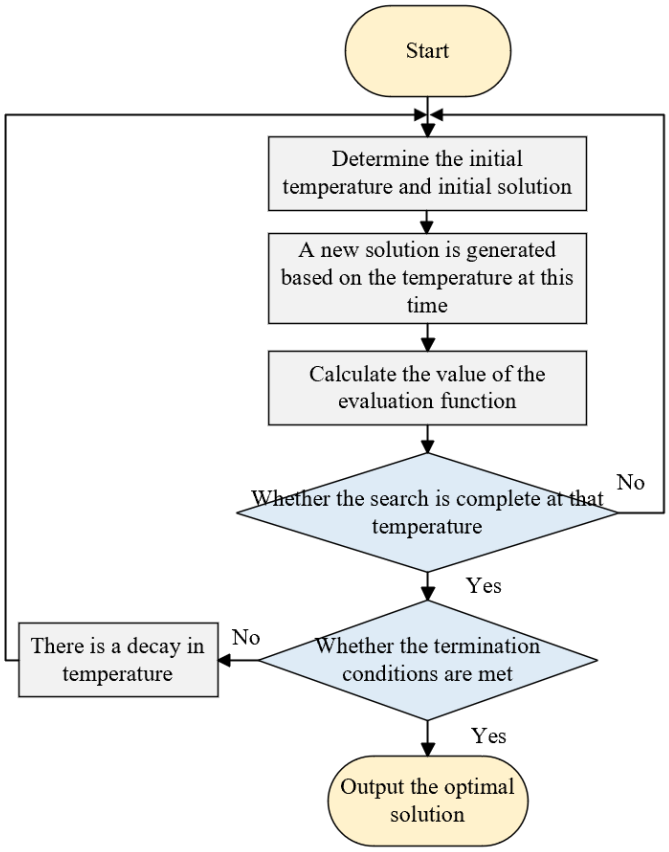

Fig. 6. Simulated annealing algorithm basic flowchart.

4.3 Comparison of Experimental Results

For the aforementioned mathematical model, a simulated annealing algorithm was employed to solve this specific problem. The simulation experiment was conducted on a computer equipped with an Intel i7-11800H processor (frequency of 2.30GHz) and 32GB of memory, using Python version 3.8.8 for implementation.

To verify the effectiveness of the experiment, the pathological sections used in this experiment were stained with HE staining, which involves a variety of reagents in its process. The staining stages are as follows. Three sections were entered, and the time intervals at which the sections entered the stain site site were used as initial data. Adjustments were made to this data, and the minimum maximum completion time was calculated.

Table 2. HE staining method

S_g	st_k	pt_j
1	oven	7min
2	Xylene	5min
3	Xylene	5min
4	Xylene	5min
5	absolute alcohol	2min
6	absolute alcohol	2min
7	95% alcohol	2min
8	75% alcohol	2min
9	water	2min
10	Hematoxylin	5min
11	water	1min
12	1% acid alcohol	0.1min
13	water	1min
14	alkaline water	1min
15	water	5min
16	eosin	2min
17	water	0.5min
18	75% alcohol	1min
19	85% alcohol	1min
20	95% alcohol	1min
21	absolute alcohol	1min
22	Xylene	2min
23	Xylene	2min
24	Xylene	2min

Based on the above staining process, a comparative analysis of the results between the layout before optimization and after optimization.

75% athanol	95% athanol	absolute alcohol	absolute alcohol	Xylene	Xylene	Xylene	oven
alkaline water	75% athanol	water	water	water	water	water	oven
Hematoxylin	1% acid alcohol	Xylene	absolute alcohol	95% athanol	85% athanol	Eosin	heat
Buffer	Xylene	Xylene	unload	unload	load	load	heat

Fig. 7. Optimized pre-Layout.

75% athanol	95% athanol	1% acid alcohol	absolute alcohol	Xylene	Xylene	alkaline water	oven
Xylene	75% athanol	water	water	water	Hematoxylin	water	oven
Hematoxylin	85% athanol	Xylene	absolute alcohol	95% athanol	85% athanol	Eosin	heat
Buffer	alkaline water	Eosin	unload	unload	load	load	heat

Fig. 8. Optimized layout.

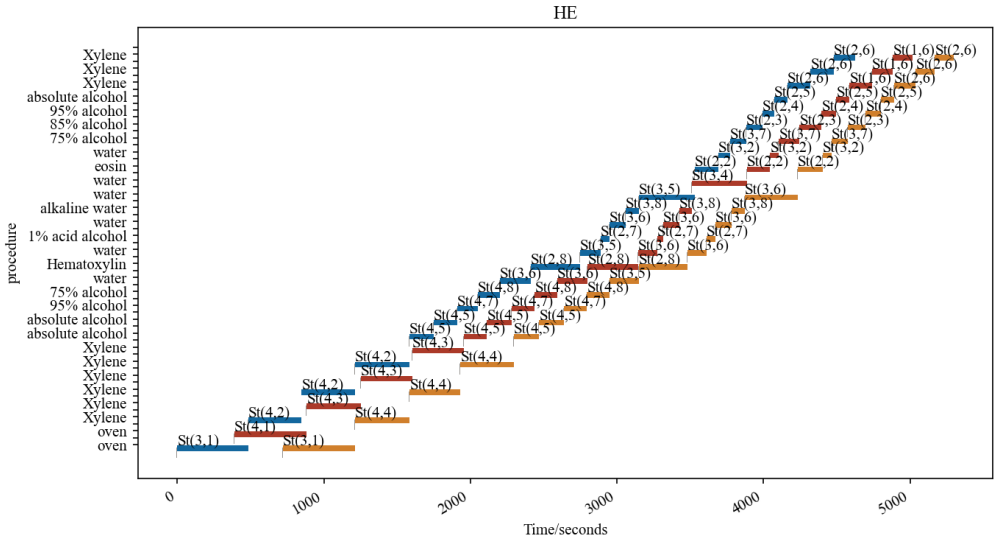

Fig. 9. Gantt chart before layout optimization.

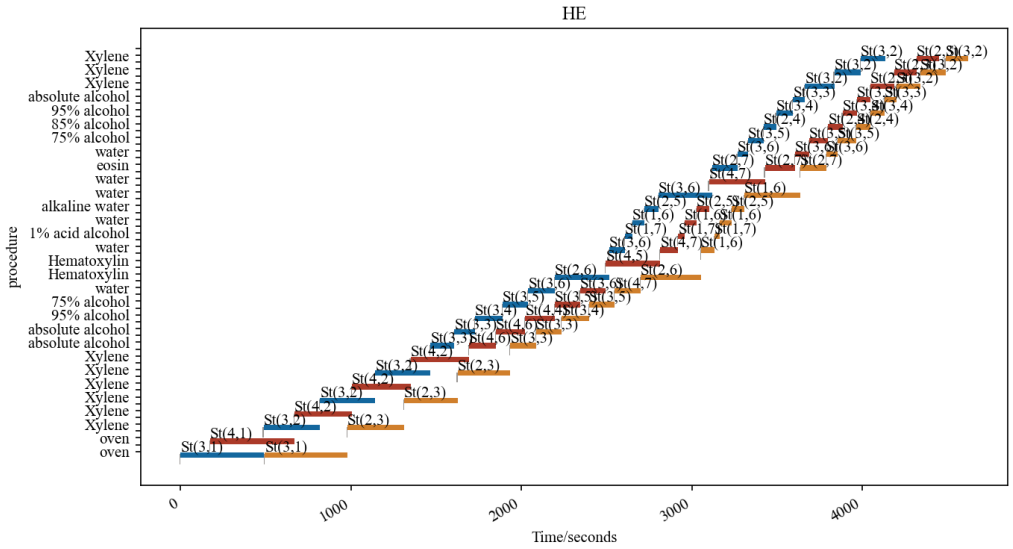

Fig. 10. Optimized layout gantt chart.

By comparing the Gantt chart, the experimental results can be obtained. As shown in the figure above, the total time required for a slide-stainer to continuously complete the staining of three pathological sections is 5179 seconds. After optimizing the layout of the stain site, the duration was reduced to 4513 seconds, a decrease of 12.9%. The entire staining process ran smoothly, with each section's staining phase reaching the required duration, and there were no instances of competition among robotic arm drives. This proves that this staining layout can adapt to environments where multiple sections are loaded continuously for staining.

5 Conclusion

In the process of advancing pathology towards digitalization and streamlining, the fully automatic tissue section slide-stainer plays a crucial role. Addressing the prevalent issue of manual arrangement in current machine layouts, an algorithm has been developed to optimize the layout of slide-stainers, with the aim of enhancing the efficiency of tissue section staining and ensuring timely task completion. Upon thorough analysis of the tissue section staining process by the fully automatic stainer, issues with existing layouts have been identified by us, including insufficient precision and low time-utilization efficiency.

To address these issues, a multi-objective, multi-constraint mathematical optimization model was constructed to determine the optimal layout for stain sites. The optimization design problem of the slide-stainer layout was deeply explored, emphasizing the importance of constructing a model with low computational complexity. Building upon improvements to the current transportation problem, a nonlinear programming model was established for the optimization design of the slide-stainer layout. The

effectiveness of the proposed algorithm was tested by simulating the routine tissue section staining process using the widely employed HE staining method in the medical field. Through simulation experiments, the optimal layout structure under these conditions was obtained. Among other things, a reversal operation was introduced to reconsider the layout and finally, the feasibility of solving the multi-objective tissue section slide-stainer layout problem using the simulated annealing algorithm was verified. The effectiveness of the model and algorithm was demonstrated through practical examples.The overall duration has been reduced by over 600 seconds, decreasing by more than 10%.

The experimental results show that the optimized layout significantly improves work efficiency. This proves that our algorithm can effectively solve the existing issues with slide-stainer layouts, enhance the efficiency of tissue section staining, and ensure that staining tasks are completed promptly.

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