Vaccine production optimization model based on Monte Carlo algorithm

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Abstract. COVID-19 is ravaging the world. Due to the large scale of vaccine production, the production of vaccines with good quality and quantity is the key to epidemic prevention and control. The problem of vaccine production planning is essentially the same as the problem of assembly line production. Based on the production sequence of a company's vaccine, this paper conducted a normal test on the test data by USING SPSS software and found that it obeys the normal distribution. The shortest processing time and production sequence were obtained by using LINGO software. By using LINGO software, it was found that the processing time was the shortest, 184.778 minutes, in the order of YM4 -- YM5 -- YM10 -- YM7 -- YM8 -- YM1 -- YM2 -- YM3 -- YM9 -- YM6. Based on the above conclusion, monte Carlo experiment was conducted with MATLAB software to find out the maximum probability corresponding to 95% of the production time in the problem, and the result was 1.324%. To mean the lower limit of the 90% confidence interval of each flight reservation production time for each type of vaccine, ignore the machine production of waiting time and each vaccine production after the influence on other types of vaccine production, statistics each vaccine needed to consume the longest flight reservation, the total elapsed time, again will each vaccine consume the longest flight reservation of accumulative sum total production time, The number of production days is 186.189 days under the premise that the reliability is 90%.

Keywords: Vaccine production; Exhaustive search; Monte Carlo algorithm; linear programming.

1. Introduction

COVID-19 has wreaked havoc around the world. In order to control the epidemic, countries are developing COVID-19 vaccines, and the demand for vaccines is now large. Improving production efficiency and ensuring production quality is a key step in epidemic prevention and control. Therefore, it is of practical value to analyze the production efficiency of vaccine flow. Therefore, this paper is based on the production mode of a vaccine production company, that is, according to the sequence of CJ1-CJ2-CJ3-CJ4, the production can be completed only after processing at all four stations. Each process can handle 100 doses of vaccine at a time, and these 100 doses are put into a processing box and sent to the equipment in the station for processing. At the same time, the production sequence of each type of vaccine entering the first station should remain the same once determined, and only after the former type of vaccine leaves the station can the latter type of vaccine enter the station, preventing confusion in the vaccine packaging. There are 10 different types of vaccines, including YM1-YM10, that need to be produced. For safety reasons, each type of vaccine was simulated 50 times per box (containing 100 doses) at each station. It was found that the time required to produce each case of different types of vaccines at each station was not stable due to various reasons such as production equipment and vaccine purification. This paper establishes a mathematical model to improve the production quality and efficiency of the company's vaccine, and optimizes the company's vaccine production mode.

2. Statistical analysis and normality test

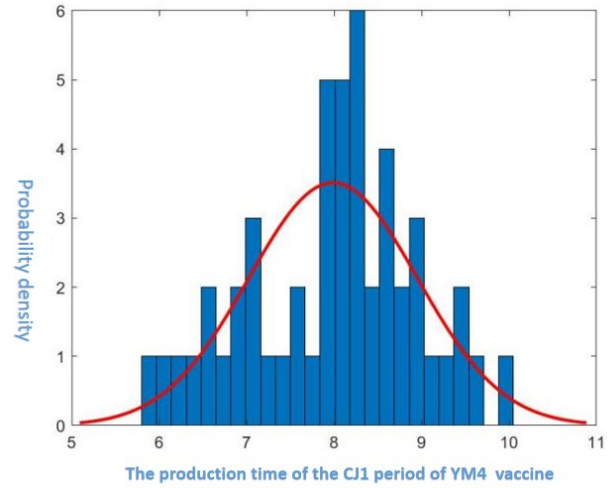
N. Jamshidi [1] conducted experimental research on the heat transfer efficiency of the winding tube heat exchanger at $0.0813<Dc< 0.116$, $13<Pc<18$, and the pipe flow rate was 1 to 4 L/min, and the results showed that the heat exchange efficiency of the heat exchanger could be achieved by increasing the winding diameter, coil pitch and shell distance flow in the winding tube heat exchanger.

Build a heat exchanger geometry model according to the literature, the parameters are shown in Table 1-1.

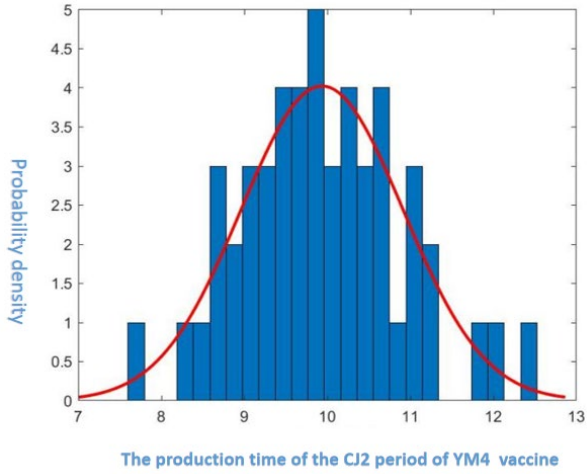
SPSS software was used to conduct statistical analysis on the mean, variance, maximum value and probability distribution of the production time of each box of vaccines at all stations, so that the managers of vaccine production companies could intuitively grasp the capacity level of vaccine production at each station and provide reference for vaccine production. Take YM1 vaccine as an example, the statistical data of production time of its four processes are shown in Table 1.

Table 1. Statistical data on the production time of the four processes of YM1 vaccine

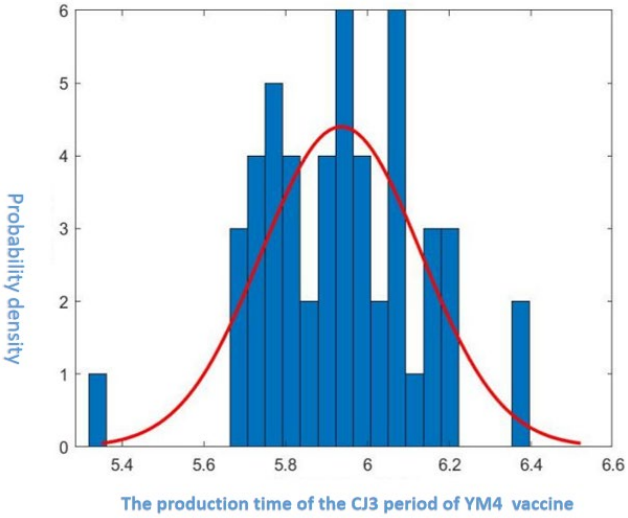
Statistical index	Minimum(Minutes)	Maximum(Minutes)	Mean(Minutes)	Variance
YM1-CJ1	10.056	16.578	13.284	1.263
YM1-CJ2	13.067	17.586	14.962	1.041
YM1-CJ3	17.862	22.908	19.846	1.09
YM1-CJ4	16.505	23.789	20.013	1.375



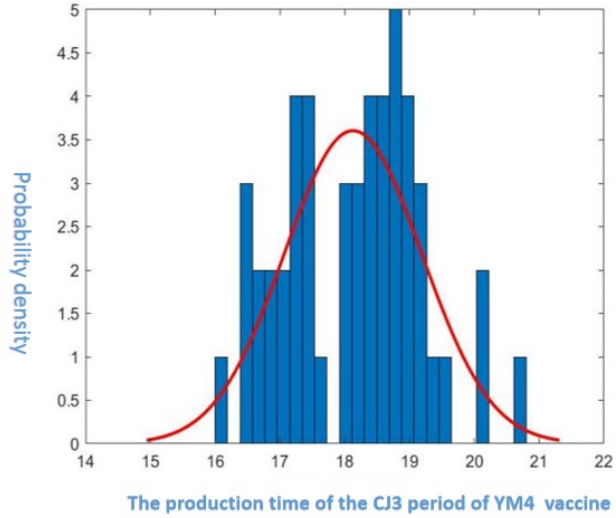
(a)Section 1



(b)Section 2



(c)Section 3



(d)Section 4

Figure 1. The histogram of the time of the four production stages of YM4 vaccine

For all types of vaccines, the production time samples at each site were tested for normality and were found to follow normal distribution. When normal simulation is carried out, simple data cleaning is carried out, and a few invalid values that deviate far from the curve are ignored.

Four stages based on YM4 vaccine, for example, gives the YM4 vaccine on each machine (corresponding to each stage) production and processing on the probability distribution of time, from

the MATLAB software to generate YM4 vaccine in the histogram can be seen in figure 1, the overall distribution among samples is more, on both sides of the distribution is less, the probability density curve to roughly symmetrical inverted U graphics.

Due to the small number of samples, SM method was used for normality test. The results of normality test of YM4 vaccine at four stages were shown in Table 2. It can be seen from Table 2 that the value of significance signal was greater than 0.05, which followed normal distribution.

Table2. Results of normality test for YM4 vaccine production time

Statistical index	**Kolmogorov-Smirnov[a]**			**Shapiro-Wilk**		
	Statistical magnitude	Degree of freedom	Significance	Statistical magnitude	Degree of freedom	Significance
YM4-CJ1	.145	50	0.010*	.975	50	.359
YM4-CJ2	.049	50	.200*	.992	50	.982
YM4-CJ3	.069	50	.200*	.977	50	.436
YM4-CJ4	0.081	50	.200*	0.979	50	0.504

*. This is the lower limit of true significance
a. Lilliefors significant level correction

3. The shortest processing order and time are obtained by exhaustive method

$$min\ wt_{10,4} + wb_{10,4};$$

$$\text{s.t.}\begin{cases} \mathrm{T} = \mathrm{wt}_{10,4} + \mathrm{wb}_{10,4} \\ \mathrm{wt}_{\mathrm{i,j}} + \mathrm{wb}_{\mathrm{i,j}} \le \mathrm{wt}_{\mathrm{i,j+1}} \\ \mathrm{wt}_{\mathrm{i,j}} + \mathrm{wb}_{\mathrm{i,j}} \le \mathbf{wt_{i+1,j}} \\ \mathrm{A} = \begin{bmatrix} y_{11} & y_{12} & y_{13} & y_{14} & y_{15} & y_{16} & y_{17} & y_{18} & y_{19} & y_{1,10} \\ y_{21} & y_{22} & y_{23} & y_{24} & y_{25} & y_{26} & y_{27} & y_{28} & y_{29} & y_{2,10} \\ y_{31} & y_{32} & y_{33} & y_{34} & y_{35} & y_{36} & y_{37} & y_{38} & y_{39} & y_{3,10} \\ y_{41} & y_{42} & y_{43} & y_{44} & y_{45} & y_{46} & y_{47} & y_{48} & y_{49} & y_{4,10} \\ y_{51} & y_{52} & y_{53} & y_{54} & y_{55} & y_{56} & y_{57} & y_{58} & y_{59} & y_{5,10} \\ y_{61} & y_{62} & y_{63} & y_{64} & y_{65} & y_{66} & y_{67} & y_{68} & y_{69} & y_{6,10} \\ y_{71} & y_{72} & y_{73} & y_{74} & y_{75} & y_{76} & y_{77} & y_{78} & y_{79} & y_{7,10} \\ y_{81} & y_{82} & y_{83} & y_{84} & y_{85} & y_{86} & y_{87} & y_{88} & y_{89} & y_{8,10} \\ y_{91} & y_{92} & y_{93} & y_{94} & y_{95} & y_{96} & y_{97} & y_{98} & y_{99} & y_{9,10} \\ y_{10,1} & y_{10,2} & y_{10,3} & y_{10,4} & y_{10,5} & y_{10,6} & y_{10,7} & y_{10,8} & y_{10,9} & y_{10,10} \end{bmatrix} \\ B = \begin{bmatrix} t_{11} & t_{12} & t_{13} & t_{14} \\ t_{21} & t_{22} & t_{23} & t_{24} \\ t_{31} & t_{32} & t_{33} & t_{34} \\ t_{41} & t_{42} & t_{43} & t_{44} \\ t_{51} & t_{52} & t_{53} & t_{54} \\ t_{61} & t_{62} & t_{63} & t_{64} \\ t_{71} & t_{72} & t_{73} & t_{74} \\ t_{81} & t_{82} & t_{83} & t_{84} \\ t_{91} & t_{92} & t_{93} & t_{94} \\ t_{10,1} & t_{10,2} & t_{10,3} & t_{10,4} \end{bmatrix}, \mathrm{C} = \begin{bmatrix} \mathrm{wt}_{11} & \mathrm{wt}_{12} & \mathrm{wt}_{13} & \mathrm{wt}_{14} \\ \mathrm{wt}_{21} & \mathrm{wt}_{22} & \mathrm{wt}_{23} & \mathrm{wt}_{24} \\ \mathrm{wt}_{31} & \mathrm{wt}_{32} & \mathrm{wt}_{33} & \mathrm{wt}_{34} \\ \mathrm{wt}_{41} & \mathrm{wt}_{42} & \mathrm{wt}_{43} & \mathrm{wt}_{44} \\ \mathrm{wt}_{51} & \mathrm{wt}_{52} & \mathrm{wt}_{53} & \mathrm{wt}_{54} \\ \mathrm{wt}_{61} & \mathrm{wt}_{62} & \mathrm{wt}_{63} & \mathrm{wt}_{64} \\ \mathrm{wt}_{71} & \mathrm{wt}_{72} & \mathrm{wt}_{73} & \mathrm{wt}_{74} \\ \mathrm{wt}_{81} & \mathrm{wt}_{82} & \mathrm{wt}_{83} & \mathrm{wt}_{84} \\ \mathrm{wt}_{91} & \mathrm{wt}_{92} & \mathrm{wt}_{93} & \mathrm{wt}_{94} \\ \mathrm{wt}_{10,1} & \mathrm{wt}_{10,2} & \mathrm{wt}_{10,3} & \mathrm{wt}_{10,4} \end{bmatrix} \\ AB = C \\ \sum_{i=1}^{10} y_{ij} = 1, j = 1,2,3,4,5,6,7,8,9,10 \\ \sum_{j=1}^{10} y_{ij} = 1, i = 1,2,3,4,5,6,7,8,9,10 \\ \mathrm{wt}_{\mathrm{i,j}} + \mathrm{wb}_{\mathrm{i,j}} \le \mathrm{wt}_{\mathrm{i,j+1}} \begin{cases} \mathrm{i} = 1,2,\ldots,10 \\ \mathrm{j} = 1,2,\ldots,9 \end{cases} \\ \mathrm{wt}_{\mathrm{i,j}} + \mathrm{wb}_{\mathrm{i,j}} \le \mathrm{wt}_{\mathrm{i+1,j}} \begin{cases} \mathrm{i} = 1,2,\ldots,9 \\ \mathrm{j} = 1,2,\ldots,10 \end{cases} \end{cases}$$

A vaccine testing department in a country urgently needs 100 doses of YM1-YM10 vaccine for testing. It needs to establish a mathematical model and formulate the epidemic production sequence so as to deliver the vaccine in the shortest time. The final analysis results are based on the average time for each station to produce each case of vaccine, with the initial time being 00:00. The simplest solution is to permutations and combinations of 10 production sequences, using 0-1 programming model to solve the problem. A total of 3,628,800 possible production sequence combinations of 10 vaccines were exhaustively selected, and a 0-1 matrix of 10×10 was constructed. The LINGO algorithm was used to traverse all production sequence and it was found that the production sequence was YM4-YM5-YM10-YM7-YM8-YM1-YM2-YM3-YM9-YM6.The shortest time is 184 minutes. The established integer programming model is as follows:

The notations involved in this problem are described in Table 3.

Table 3. Symbol notation for model 1

Parameters of the symbol	parameter specification
$wt_{i,j}$	The time required to produce the no. J slot of the no. I processed vaccine
$wb_{i,j}$	Start time of production of the no. J slot of the no. I processed vaccine
$Y_{i,j}$	Introduce the 0-1 variable, $Y_{i,j}=\begin{cases}0, \text{Vaccine no. I was produced before vaccine no. J}\\ 1, \text{Vaccine no. I was produced after vaccine no. J}\end{cases}$
T	Total production time
t_{ij}	Processing time of vaccine processed no. I at slot no. J
YM_i	The no. I vaccine produced by the company

The constraint conditions and objective function were realized by LINGO statement and imported into LINGO to run. The optimal production sequence was obtained as YM4-YM5-YM10-YM7-YM8-YM1-YM2-YM3-YM9-YM6, and the production time needed was 184 minutes. Assume that the production starts from 0:00, the production schedule is shown in Table 4, and the schematic diagram of the production plan is shown in Figure 2.

Table 4. Production time schedule for model 1

Vaccine production serial number	Processing order (Vaccine Serial number)	Enter the first slot (Hour: Minutes)	Enter the fourth slot (Hour: Minutes)
1	YM4	0: 00	0: 44
2	YM5	0: 07	0: 55
3	YM10	0: 16	1: 11
4	YM7	0: 29	1: 31
5	YM8	0: 40	1: 47
6	YM1	0: 56	2: 07
7	YM2	1: 10	2: 26
8	YM3	1: 20	2: 41
9	YM9	1: 40	2: 50
10	YM6	1: 55	3: 04

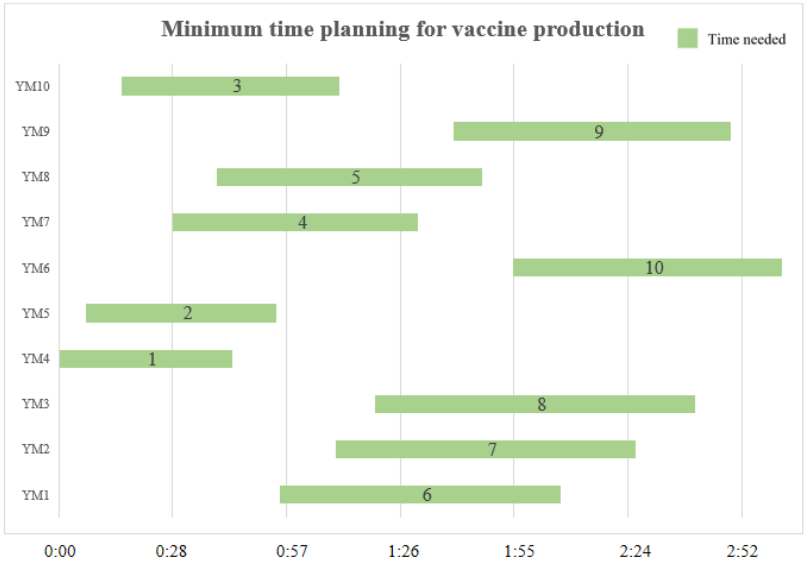


Figure 2. The Gantt chart of the production plan corresponding to Model 1

4. Monte Carlo algorithm to solve the production plan

The shortest time based on the previous model becomes the maximum probability of a 5% reduction in the satisfied time. The random normal distribution function of the production time was fitted based on the original data of the random sample of the production time of each vaccine and each machine. Then the 0-1 matrix model of the production time in the previous question was constructed and imported into LINGO for implementation. The outer loop of the algorithm builds the model, and the inner loop carries out monte Carlo experiments for each sample several times to save the optimal solution. Sortrows function is used in MATLAB software to sort the optimal solutions in order from small to large, and find out the maximum probability corresponding to the time when the production time is 95% of the production time solved by the previous model, that is, the highest point of the vertical coordinate of the scatter plot. Dozens of times and monte carlo simulation, based on the experimental data in different cuts than the distribution of the observations, get the optimal solution based on big data, using the nonlinear simulation of the least-squares get shorter time ratio and the relation between the probability distribution and relation curve and the results showed that the total time of 170.153 minutes, corresponding to the maximum probability of 1.324%, as shown in figure 3.

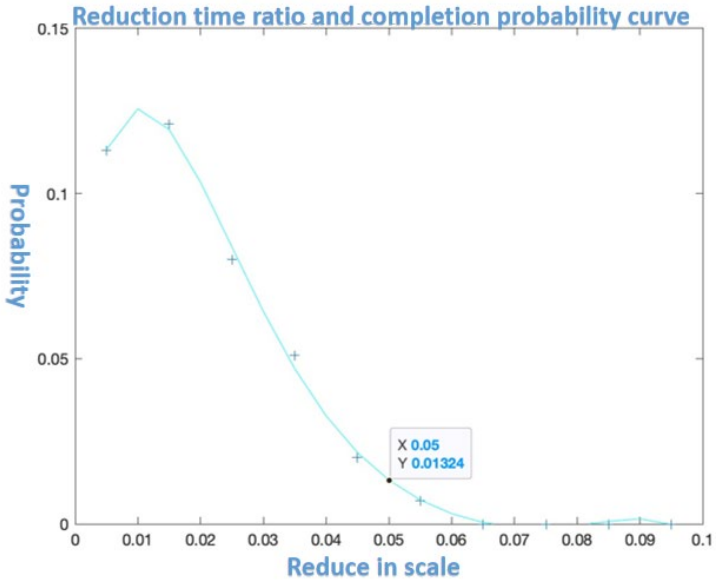


Figure 3. The reduction time ratio and completion probability curve

The production sequence for model 2 was YM7-YM2-YM10-YM1-YM8-YM4-YM3-YM6-YM5-YM9, as shown in table 5.

Table 5. Production time schedule for model 2

Vaccine production serial number	Processing order (Vaccine Serial number)	Enter the first slot (Accumulated Minutes)	Enter the fourth slot (Accumulated Minutes)
1	YM7	0	43.282
2	YM2	8.8435	56.197
3	YM10	16.526	69.8156
4	YM1	27.9899	89.1356
5	YM8	38.4723	104.7327
6	YM4	52.0476	114.7716
7	YM3	58.7584	132.5856
8	YM6	76.5724	149.0212
9	YM5	93.0080	157.3295
10	YM9	103.3925	170.1532

5. Linear programming solves vaccine production schedule under certain reliability

Every time the vaccine production line production 100 doses of vaccine, dose and actual requirements in the production of tens of thousands of agents, from a macro perspective, dangdang began producing a vaccine, four slots are at work at the same time, each station production time can't more than 16 hours a day, each type of vaccine production task can split appropriately, which can be done only part of each type of vaccine. The processing time of each process is the lower limit of 90% confidence interval of the mean, and the processing time of each vaccine is equal to the sum of the processing time of each machine; The total production time is equal to the total production time of each vaccine. The company plans to select a number of vaccines for production within 100 days to meet the production schedule for maximum sales. The model 3 was as follows:

$$\text{s.t.}\begin{cases} AB = C \\ t_i = \mathrm{n}\sum_{j=1}^{4} tm_{ij} \\ \mathrm{T} = \sum_{\mathrm{i}=1}^{10} \mathrm{t_i}\,, \mathrm{i} = 1,2,\ldots,10 \\ \textit{Obey all the constraints in question two} \end{cases}$$

The model 3 was realized by LINGO software, whose notation of symbol refers to table 5. As a result, the production sequence was as follows: YM1-YM2-YM3-YM4-YM5-YM6-YM7-YM8-YM9-YM10, whose details are shown in figure 4. And the total production time was at least 187 days under the premise of ensuring 90% reliability;

Table 6. Symbol notation for model 3

Parameters of the symbol	parameter specification
n_i	Number of vaccines processed for production no. I
tm_{ij}	The time required for the no.J machine to produce the vaccine for production no.I
t_i	Total time required to produce vaccine for production no. I
T	The time required to produce all vaccines

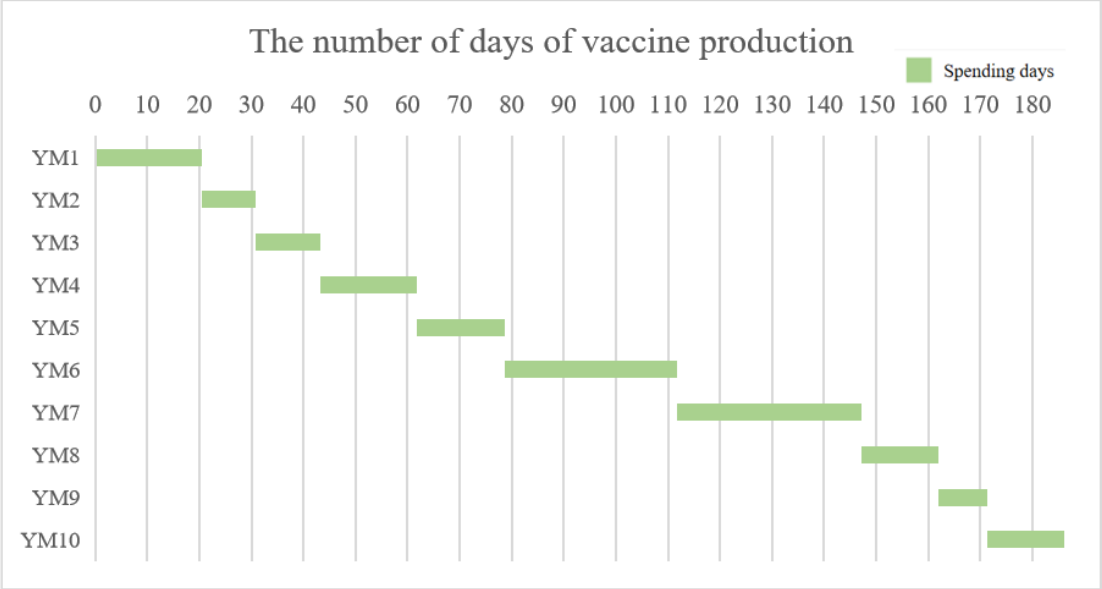


Figure 4. The Gantt diagram of production time for model 4

6. Conclusion and discussion

In this paper, SPSS software was first used for statistical analysis and normality test of experimental data, and it was found that the production time of each stage of various vaccines followed the normal distribution. After that, LINGO software was used to enumerate all production modes to get the shortest production time and the corresponding production sequence. It was found that it took 184 minutes to produce in the sequence of YM4-YM5-YM10-YM7-YM8-YM1-YM2-YM3-YM9-YM6. Then, monte Carlo model is used to solve the production sequence of YM1-YM2-YM3-YM4-YM5-YM6-YM7-YM8-YM9-YM10 in which the maximum probability of time reduction of 5% is 1.324% and the reliability is 90%. The total production time should be at least 187 days on the premise that the reliability is 90%.

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