JOURNAL OF PURE AND APPLIED MICROBIOLOGY, April 2013. Vol. 7(Spl. Edn.), p. 167-172

# Optimization of Process Parameters in Bone Scaffold Forming of LDM Based on Degree of Grey Incidence

**Liu Yuanyuan[1]*, Han Zhenzhong[1], Fang Shuhui[1], Yu Yongze[1], Liu Ying[1] and Hu Qingxi[1]**

[1]Rapid Manufacturing Engineering Center, Shanghai University, Shanghai, China.

(Received: 03 March 2013; accepted: 14 April 2013)

**LDM process is used for preparing three-dimensional scaffolds for tissue engineering rapid prototyping technologies. Because of its forming process is complex, influenced by a variety of factors caused by processing environment is not stable, the forming of scaffold pore size can not be guaranteed, forming precision is poor. So there is a need for forming parameters to optimize. Aim at LDM process characteristics, the paper determine the main process parameters that affect the bone scaffold forming quality. First, the influence degree of process parameters on one of indexes such as wire width precision and wire height precision is determined by orthogonal experiment. Then, in the problem of a number of process parameters optimization, using the degree of grey incidence method, the number of process indicators of the optimization problem is transformed into the single degree of gray correlation maximization problem, realizing multi-objective parameter optimization. The experiment results show that, using the combined optimization of technological parameters of preparation of bone scaffold, it's forming quality is good, and it can well meet the stem cell growth conditions.**

**Key words:** Low-temperature Deposition Manufacturing (LDM), Scaffold, Degree of Grey, Parameter Optimization.

Rapid[1] Prototyping (RP) technology (Wohlers *et al*., 2003) is a new digital prototyping technology based on discrete/accumulation forming principle. It is under the control of the computer management, according to the CAD model, through the accurate accumulation of materials, then manufacturing of prototypes or parts. RP technology for tissue engineering scaffold fabrication provides a new theory and technology. Low temperature deposition manufacturing (LDM) process (Jin *et al*., 2009) by the Tsinghua University proposed a material extrusion/injection process and thermally induced phase separation process integration of rapid forming technology, which can facilitate the preparation of the rules, through tissue engineering scaffold internal pore structure. In LDM process of bone scaffold, the comparison of important process parameters are (Li *et al*., 2012): stratification thickness, nozzle diameter, nozzle temperature, forming chamber temperature, extrusion speed, filling speed, material concentration, grid spacing. But the primary relationship of the effect of process parameters of each of the process parameters on bone scaffold forming and in comprehensive consideration of the process parameters of circumstances, how to optimize the parameter value is worth further discussion.

As a result of bone scaffold LDM molding process complexity and uncertainty, it has led to the understanding of its one-sidedness and limitation, and the grey system theory to solve the problem has provided a reliable theoretical tool.

* To whom all correspondence should be addressed.
Tel.: +86-15900611572
E-mail: yuanyuan_liu@shu.edu.cn

Degree of grey incidence (Deng *et al*., 2002) is the effective methods of poor information system analysis, and is a kind of important method for gray system method system. Degree of grey incidence is a kind of grey related degree in order to describe the relationships between factors of strength, size and order. The basic idea is: to factor data as basis, by using the mathematical method to analysis the geometrical relationship between factors. Through gray correlation analysis, grey correlation degree was used to measure the process indicators; there will be a number of process indicators of the optimization problem were transformed into a single grey relational degree, thereby realizing the multinomial technology index optimization, and the optimal parameter combination scheme. This paper adopts the method of orthogonal experiment analysis of each process parameter on the influence degree of each index, then using the method of grey relational analysis on experimental data for further processing, to come to consider the process parameters in the absence of process parameters.

**Low-temperature deposition manufacturing (LDM) process description**

Low temperature deposition manufacturing (LDM)process by the Tsinghua University proposed a material extrusion/injection process and thermally induced phase separation process integration of rapid forming technology. The fabrication process of bone scaffolds based on LDM is shown in figure 1.

Compared to other rapid prototyping technology, LDM has the following characteristics (Li *et al*., 2010):

(1) It is material extrusion/injection and thermally induced phase separation process integration technology. This integration is not two kinds of simple process together, but through hardware and software integration, comprehensive two technological advantages, overcome its disadvantage. In the forming chamber, only through a forming process can achieve both contain large hole and comprises a micro-porous hierarchical structure.

(2) The biological properties of the material can be well maintained, and it has more extensive adaptability for materials. In the process, material at room temperature or below room temperature processing, to ensure the material original physical and chemical properties, biological properties are not affected. Even if it is very sensitive to the temperature of some biologically active proteins through this process, the biological activity would not be affected.

(3) It can form a complicated heterogeneous material scaffold. Through a multi-nozzle technology, it can realize the complex heterogeneous material composition gradient; due to the adoption of the extrusion/injection based on the process principle, without the removal of excess material, can realize the complex heterogeneous materials of fine pore structure gradient.

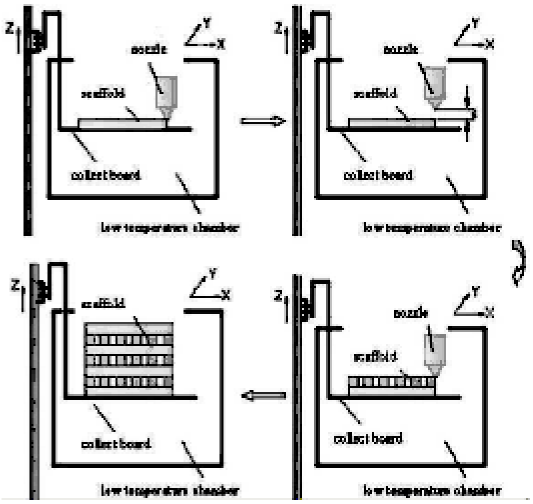



**Fig. 1.** The fabrication process of bone scaffolds based on LDM

**Optimization of process parameters in bone scaffold forming of ldm based on degree of grey incidence**

The forming quality of bone scaffold based on LDM is mainly to see whether it can forming the three-dimensional through and internal pore structure, so the indexes for optimization of process parameters are the forming wire width precision ($W_p$) and height precision ($H_p$). According to the bone scaffold LDM process characteristics, there are many process parameters which can impact the forming quality of bone scaffold, but there are a few parameters that plays a major role, namely the forming chamber temperature, material concentration, extrusion speed, filling speed, grid spacing. Therefore, this paper take the above 5 parameters as control factors, and each control factor choose 4 levels. According to the prior knowledge, the specific values are shown in table 1.

**Table 1**. The control factors and levels

| levels | The control factors | | | | |
|---|---|---|---|---|---|
| | A: the forming chamber temperature/°C | B. material concentration /% | C. extrusion speed /mm/s | D. filling speed /mm/s | E. grid spacing /mm |
| 1 | -10 | 18 | 10 | 12 | 0.6 |
| 2 | -15 | 20 | 13 | 15 | 0.8 |
| 3 | -20 | 22 | 16 | 18 | 1.0 |
| 4 | -25 | 25 | 19 | 21 | 1.2 |

## Orthogonal Experimental Design and Results

The orthogonal design (Ren *et al.*, 2003) is characterized by 'balanced dispersion, comprehensive comparability', so this paper uses orthogonal design to determine the number of experiments, each of 4 levels, 16 sample points. The experiments on rapid manufacturing center of Shanghai University scaffolds for tissue engineering experimental platform, as shown in figure 2.The shaped scaffolds were put into the frozen dryer that bought from German company MartinChrist ALPHAl-2 to freeze drying 20h. The experimental material is B type gelatin, nozzle diameter was 0.4mm, and nozzle temperature was 60 !. Finally, used the optical microscopy to measure the bone scaffold's filament width and height, and its theory value is subtracted from the error value, the experimental results as shown in table 2.

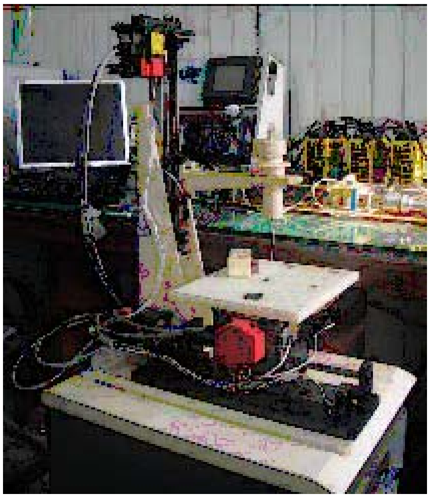


**Fig. 2**. Test platform for bone scaffold

**Table 2**. Orthogonal experimental design and results

| Number | A | B | C | D | E | $W_p$ /mm | $H_p$ /mm |
|---|---|---|---|---|---|---|---|
| 1 | -10 | 18 | 10 | 12 | 0.6 | 0.35 | -0.075 |
| 2 | -10 | 20 | 13 | 15 | 0.8 | 0.32 | -0.090 |
| 3 | -10 | 22 | 16 | 18 | 1.0 | 0.27 | -0.070 |
| 4 | -10 | 25 | 19 | 21 | 1.2 | 0.28 | -0.010 |
| 5 | -15 | 18 | 13 | 18 | 1.2 | 0.32 | -0.073 |
| 6 | -15 | 20 | 10 | 21 | 1.0 | 0.32 | -0.080 |
| 7 | -15 | 22 | 19 | 12 | 0.8 | 0.29 | 0.070 |
| 8 | -15 | 25 | 16 | 15 | 0.6 | 0.27 | 0.050 |
| 9 | -20 | 18 | 16 | 21 | 0.8 | 0.27 | -0.065 |
| 10 | -20 | 20 | 19 | 18 | 0.6 | 0.20 | -0.065 |
| 11 | -20 | 22 | 10 | 15 | 1.2 | 0.18 | -0.050 |
| 12 | -20 | 25 | 13 | 12 | 1.0 | 0.15 | 0.045 |
| 13 | -25 | 18 | 19 | 15 | 1.0 | 0.31 | -0.024 |
| 14 | -25 | 20 | 16 | 12 | 1.2 | 0.25 | 0.040 |
| 15 | -25 | 22 | 13 | 21 | 0.6 | 0.18 | -0.080 |
| 16 | -25 | 25 | 10 | 18 | 0.8 | 0.13 | 0.075 |

**Ash Generated Sequence**

Ash formation process is actually different objectives between dimensional transformation process, due to the difference between target dimension or is orders of magnitude difference, it cannot be compared and analysis. In order to be comparable, it must be analysis of the original data dimensionless processing, so it has the same dimension or is orders of magnitude. According to the formula (Liu *et al.*, 2005):

$$x_{ij} = \frac{\max y_{ij} - y_{ij}}{\max y_{ij} - \min y_{ij}} \qquad ...(1)$$

Where $y_{ij}$ for i index and j test. The calculated results are shown in table 3.

**Table 3.** Dimensionless results

| Number | $W_p$ | $H_p$ |
|---|---|---|
| 1 | 0.00 | 0.19 |
| 2 | 0.14 | 0.00 |
| 3 | 0.36 | 0.25 |
| 4 | 0.32 | 1.00 |
| 5 | 0.14 | 0.21 |
| 6 | 0.14 | 0.13 |
| 7 | 0.27 | 0.25 |
| 8 | 0.36 | 0.50 |
| 9 | 0.36 | 0.31 |
| 10 | 0.68 | 0.31 |
| 11 | 0.77 | 0.50 |
| 12 | 0.91 | 0.56 |
| 13 | 0.18 | 0.83 |
| 14 | 0.46 | 0.63 |
| 15 | 0.77 | 0.13 |
| 16 | 1.00 | 0.19 |

**Single Objective Parameter Optimization Analysis**

According to the results of dimensionless processing, we calculated the sum $K_{ij}$ of the impact factors and the corresponding index value, which i represents the impact factors, j represents the impact factor of the different levels, then calculate each factor of influence on different levels corresponding to the index values and the range R, the calculated results as shown in table 4. When R is bigger, it descript that the control factor of the indexes the degree, one factor at a level corresponding to the index value and the more big, in the level of performance indexes of (Bang SX, *et al.*, 2005), from the values in table 4 are known: the control factor on wire width precision most notable is A, the optimal process parameters is A4B4C2D3E1; the control factor on high precision most notable is E, the optimal process parameters for A4B4C4D2E4.

**Table 4.** Investigation index values and the range

| index | | $W_p$ | R | $H_p$ | R |
|---|---|---|---|---|---|
| A | $K_{A1}$ | 0.82 | 0.59 | 1.44 | 0.69 |
| | $K_{A2}$ | 0.91 | | 1.09 | |
| | $K_{A3}$ | 1.04 | | 1.68 | |
| | $K_{A4}$ | 1.41 | | 1.78 | |
| B | $K_{B1}$ | 0.68 | 1.91 | 1.54 | 1.18 |
| | $K_{B2}$ | 1.42 | | 1.07 | |
| | $K_{B3}$ | 2.17 | | 1.13 | |
| | $K_{B4}$ | 2.59 | | 2.25 | |
| C | $K_{C1}$ | 1.91 | 0.51 | 1.01 | 1.49 |
| | $K_{C2}$ | 1.96 | | 0.90 | |
| | $K_{C3}$ | 1.45 | | 1.69 | |
| | $K_{C4}$ | 1.45 | | 2.39 | |
| D | $K_{D1}$ | 1.64 | 0.73 | 1.63 | 0.87 |
| | $K_{D2}$ | 1.45 | | 1.83 | |
| | $K_{D3}$ | 2.18 | | 0.96 | |
| | $K_{D4}$ | 1.59 | | 1.57 | |
| E | $K_{E1}$ | 1.81 | 0.22 | 1.13 | 1.59 |
| | $K_{E2}$ | 1.77 | | 0.75 | |
| | $K_{E3}$ | 1.59 | | 1.77 | |
| | $K_{E4}$ | 1.69 | | 2.34 | |

**Table 5.** Gray relational coefficient and degree of grey

| Number | Gray relational coefficient | | Degree of grey |
|---|---|---|---|
| | $W_p$ | $H_p$ | |
| 1 | 1.00 | 0.72 | 0.86 |
| 2 | 0.78 | 1.00 | 0.89 |
| 3 | 0.58 | 0.67 | 0.63 |
| 4 | 0.61 | 0.33 | 0.47 |
| 5 | 0.78 | 0.70 | 0.74 |
| 6 | 0.78 | 0.79 | 0.76 |
| 7 | 0.65 | 0.67 | 0.66 |
| 8 | 0.58 | 0.50 | 0.54 |
| 9 | 0.58 | 0.62 | 0.60 |
| 10 | 0.42 | 0.62 | 0.52 |
| 11 | 0.39 | 0.50 | 0.45 |
| 12 | 0.35 | 0.47 | 0.41 |
| 13 | 0.74 | 0.38 | 0.56 |
| 14 | 0.52 | 0.44 | 0.48 |
| 15 | 0.39 | 0.79 | 0.59 |
| 16 | 0.33 | 0.72 | 0.53 |

**Table 6.** Degree of grey and the range R of different levels of the affect factors

| index | A | | | | B | | | | C | | | | D | | | | E | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $r_{A1}$ | $r_{A2}$ | $r_{A3}$ | $r_{A4}$ | $r_{B1}$ | $r_{B2}$ | $r_{B3}$ | $r_{B4}$ | $r_{C1}$ | $r_{C2}$ | $r_{C3}$ | $r_{C4}$ | $r_{D1}$ | $r_{D2}$ | $r_{D3}$ | $r_{D4}$ | $r_{E1}$ | $r_{E2}$ | $r_{E3}$ | $r_{E4}$ |
| CI | 2.15 | 2.70 | 1.98 | 2.86 | 2.66 | 2.75 | 2.33 | 1.95 | 2.60 | 2.63 | 2.25 | 2.13 | 2.41 | 2.44 | 2.42 | 2.42 | 2.51 | 2.68 | 2.36 | 2.14 |
| R | 0.81 | | | | | | 0.87 | | | | | 0.50 | | | 0.03 | | | 0.54 | | |

**Multi-objective Parameter Optimization Analysis Calculation of Gray Relational Coefficient and Degree of Grey (Kuo *et al*., 2008)**

In order to make the parameter combination scheme can make the forming bone scaffolds with high forming quality, selection of grey generating sequences to the reference sequence for Xo= ( xo1, xo2 ), respectively, said wire width error and height error optimal value. According to the gray relational degree analysis method for smaller-the-better, choose the reference sequence Xo= (0, 0), then:

Gray relational coefficient is

$$r(x_{oj}, x_{ij}) = \frac{\min\left|x_{oj} - x_{ij}\right| + \zeta \max\left|x_{oj} - x_{ij}\right|}{\left|x_{oj} - x_{ij}\right| + \zeta \max\left|x_{oj} - x_{ij}\right|} \quad ...(2)$$

Where $\zeta$ is 0.5(Lv F , *et al*., 1997).

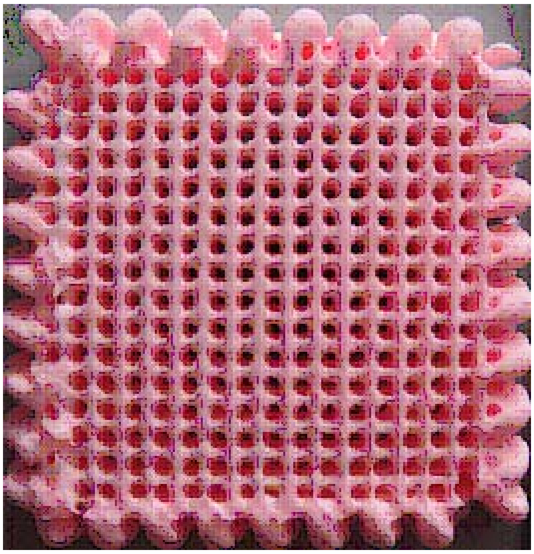
Degree of grey that comparative sequence $X_i$ of the reference sequence $X_o$ is:

$$r(X_o, X_i) = \frac{1}{n}\sum_{j=1}^{n} r(x_{oj}, x_{ij}) \quad ...(3)$$

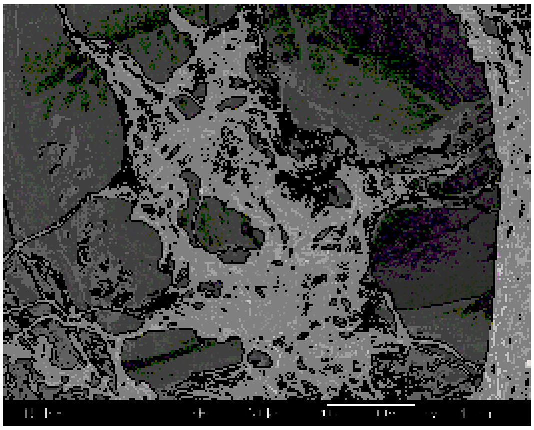
The results as shown in table 5.

**Determined the Optimal Combination of Process Parameters to Satisfy the Two Indicators**

According to the grey relational degree, we have calculated the sum $r_{ij}$ of the level associate degrees of impact factors, where i represents the impact factors, j represents the impact factors of the different levels, and then calculate each factor of influence on different levels corresponding to the index values and the range. Table 6 shows, the comprehensive process index (CI) influence orders for B,A,E,C,D, and the best parameter combination for bone scaffolds forming is B2A4E2C2D2.



(A)



(B)

**Fig. 3**. The forming scaffold after parameter optimization and cell morphology

## CONCLUSIONS

LDM process can be easily prepared through rules, the tissue engineering scaffold internal pore structure, but because of its forming process is complex, influenced by a variety of factors caused by processing environment is not stable, the forming of scaffold pore size can not be guaranteed, forming precision is poor. In this paper, through the analysis of orthogonal, we tested the effects of scaffold forming quality of several main parameters, and analysis the various factors affecting the individual process index sequence, and the optimal parameter combination scheme. In a number of process parameters optimization problem, using the degree of grey incidence method, the number of process indicators of the optimization problem is transformed into the single degree of gray correlation maximization problem, realizing multi-objective parameter optimization. The results show that, using the combined optimization of technological parameters of preparation of bone scaffold, it's forming quality is good, and it can well meet the stem cell growth conditions.

## ACKNOWLEDGEMENTS

This work is supported by National Natural Science Foundation of China (Grant No.51075253) and the National Science Foundation for Young Scientists of China (Grant No.51105239).

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