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Genetic Algorithms for Optimising Alginated-Scaffolds for Tissue Engineering

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The increase of the rate of transplants due to damaged or affected tissues or organs by accidents or diseases and also by the aging of the population in many countries, alternative ways of restoring and replacing tissues have been researched and implemented and very successful. Biofabrication by means of rapid prototyping techniques can help in the fashioning and final production of scaffolds devoted to support and stimulate the growth of new tissues. For soft tissues, a biomaterial known as Alginate has been studied and used as raw-material for scaffolds fabrication. A Scaffold should own very dynamical and adaptive characteristics. In this sense, it is fundamental to know better the mechanical and chemical properties since the scaffold must guarantee good strength and stiffness at the same time the material degrades gradually. The present and future of biomedical materials development requires this degree of control prediction in the design, synthesis, and function of next-generation materials. A prediction job is possible and it has already been used so that the scaffold state can be forecasted before its fabrication and, as a good alternative, to know how and how much alginate should be used. A single mathematical model experimentally obtained describes an interesting physical behaviour, that is, in the case of this work, the degradation of alginated-scaffolds. Evolutionary algorithms, like Genetic Algorithms (GA), represent a class of stochastic optimisation procedures based on natural systems according to Darwin's observations, and the modern synthetic theory of evolution. The objective of GA is to find out the best values of alginate amount for scaffold fabrication that maximize the elastic modulus. In summary, the paper presents an optimisation process scheme using Genetic Algorithms to maximize the elastic modulus and therefore to aid the design of scaffolds in alginate. The optimization is very welcome to tissue engineering and Biofabrication.

1. Introduction

Biofabrication by means of rapid prototyping techniques can help in the fashioning and final production of scaffolds devoted to support and stimulate the growth of new tissues. For soft tissues, a biomaterial known as Alginate has been studied and used as raw-material for scaffolds fabrication. A scaffold must own very dynamical and adaptive characteristics in order to be implanted and to take its main roles which are to carry the

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stem live cells inside it, to back the growth of these cells and besides this to biodegradate appropriately since the minimum material should remain after the tissue is reconstructed. In this sense, it is fundamental to be aware of the mechanical and chemical properties since the scaffold must guarantee good strength and stiffness at the same time the material degrades gradually. To know how the mechanical behaviour of the scaffold will be, some time later, is the keyword. And the understanding about the match between biodegradation and young modulus is mandatory.
The present and future of biomedical materials development requires this degree of control prediction in the design, synthesis, and function of next-generation materials (Hutmacher, 2006). A prediction job is possible and it has already been used so that the scaffold state can be forecasted before its fabrication and, as a good alternative, to know how and how much alginate should be used. Other future analyses can be around the best geometry to be adopted during rapid prototyping technique actuation.

2. Genetic Algorithms

Evolutionary algorithms, like Genetic Algorithms (GA), represent a class of stochastic optimisation procedures based on natural systems according to Darwin's observations, and the modern synthetic theory of evolution. The Genetic Algorithms approach starts with a random population of chromosomes that are a set of solutions for the optimization problem. Traditionally, solutions are represented in binary as strings of 0s and 1s, but other encodings are also possible. In each generation, the fitness of every individual in the population is evaluated, multiple individuals are stochastically selected from the current population (based on their fitness), and modified (recombined and possibly randomly mutated) to form a new population. The new population is then used in the next iteration. Usually, the algorithm terminates when either a maximum number of generations has been produced, or a satisfactory fitness level has been reached for the population.

3. The optimisation approach

The optimisation problem is to determine optimal features for the fabrication of optimised alginate scaffolds for tissue engineering. The optimisation goal aims at finding optimal values of alginate composition and initial porosity in order to fabricate scaffolds with, at a pre-determined time, a high mechanical behaviour (elastic modulus). The optimisation problem is given by (Rezende et al., 2007a):

$$\begin{aligned} &\underset{[\alpha,\phi_0]}{\text{Maximize}} && E(\phi_0,\alpha,t) \\ &\text{Subject to:} && 1\% \le \alpha \le 8\% \\ & && 30\% \le \phi_0 \le 80\% \end{aligned} \tag{1}$$

where E is the elastic modulus (shear effects are not considered), α is the alginate composition and ϕ_0 is the initial porosity.

The mechanical properties vary along time due to degradation and porosity changes. The degradation of alginate structures was determined through the analysis of the shrinkage variation along time as shown in Figure 1 (Rezende et al., 2007b).

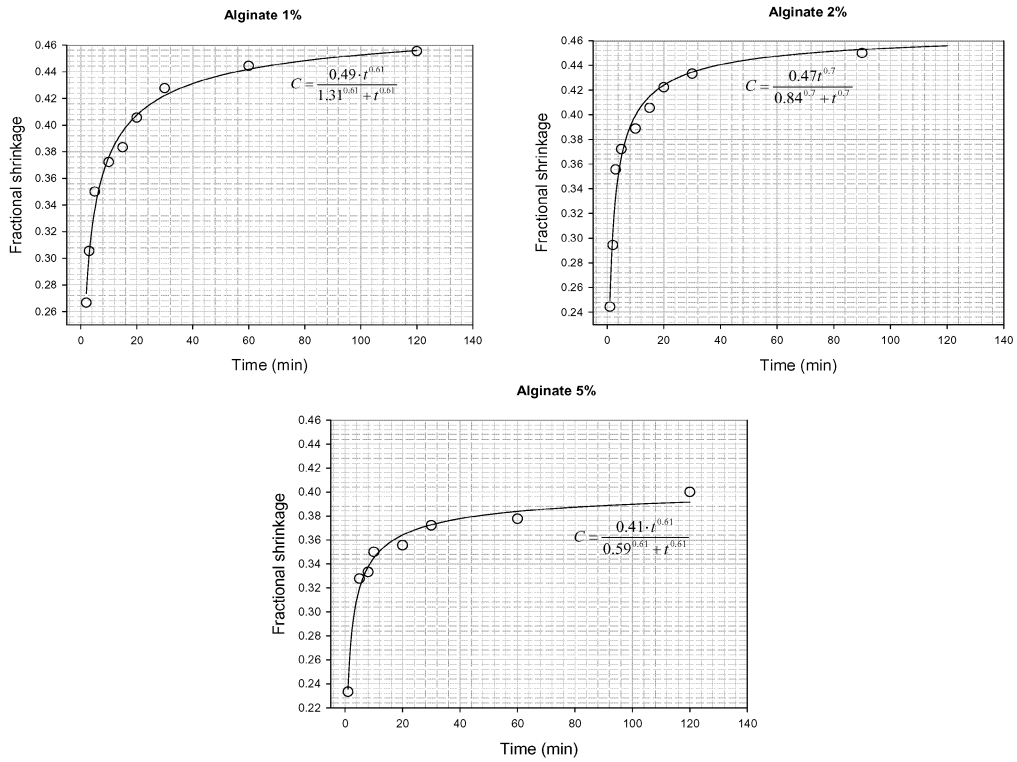

Figure 1 – Fractional shrinkage as a function of time for different alginate compositions.

The shrinkage process can be modeled through a three parameters sigmoidal model given by:

$$C(\alpha,t) = \frac{\varsigma(\alpha) \cdot t^{\vartheta(\alpha)}}{\lambda^{\vartheta(\alpha)} + t^{\vartheta(\alpha)}} \tag{2}$$

where t is the time and $\varsigma, \vartheta, \lambda$ are variables that depend on the alginate composition (α). Porosity at each time is also a function of alginate composition and shrinkage:

$$\phi(\phi_0,\alpha,t) = \phi_0 + \zeta(\phi_0,\alpha) \cdot C(\phi_0,\alpha,t) + \psi(\phi_0,\alpha) \cdot C^2(\phi_0,\alpha,t) \tag{3}$$

where ζ, ψ are constants depending on alginate composition and C is the shrinkage.

The dependence between the elastic modulus and porosity for different alginate compositions is given by the following equation:

$$E(\phi_0,\alpha,t) = E_0(\phi_0,\alpha) + k_1(\phi_0,\alpha)\cdot\phi(\phi_0,\alpha,t) + k_2(\phi_0,\alpha)\cdot\phi(\phi_0,\alpha,t)^2 + k_3(\phi_0,\alpha)\cdot\phi(\phi_0,\alpha,t)^3 \quad (4)$$

with E_0 being the initial elastic modulus, k_1, k_2, k_3 constants dependent on both the alginate composition and the initial porosity and ϕ the final porosity of the scaffold.

A single constrained optimisation problem, which maximises the elastic modulus, constraints considers two cases of constraints at shrinkage and final porosity: 1) shrinkage higher than 25% and 2) final porosity higher than 80%.

To solve the constrained problem, a constraint handling method based on the penalty function approach was used, not requiring any penalty parameter (Deb, 2000). In this case, the expression of the fitness function for a minimisation problem, where infeasible solutions are compared based only on their constraint violation, is given by:

$$F(\mathbf{x}) = \begin{cases} f(\mathbf{x}) & \text{if } g_j(\mathbf{x}) \geq 0 \quad \forall j=1,2,...,nc \\ f_{\max} + \sum_{j=1}^{m} \langle g_j(\mathbf{x}) \rangle & \text{otherwise} \end{cases} \quad (5)$$

where $f_{\max}$ is the objective function value of the worst feasible solution in the population.

The GA used in this research work, to solve the formulation indicated above in section 3, is a Fortran binary code (Carroll, 2008). The employed genetic operators are the tournament selection, the uniform crossover, the creep and the jump mutation. Niching and elitism are also employed. The input parameters, chosen by a trial and error method, are indicated in Table 1.

Table 1 - The GA input parameters.

GA input parameters	Value
Population size per generation	50
Maximum number of generations	30
Crossover probability	0.60
Jump mutation probability	0.077
Creep mutation probability	0.077
Initial random number seed for the GA run	-1000

4. Results of the scaffold optimisation using GA

This section presents the results of the scaffolds optimisation using Genetic Algorithms for constrained problem.

4.1 Single objective constrained optimisation problem

The single objective constrained optimization problem which maximises the elastic modulus considers two cases of constraints at shrinkage and final porosity: 1) shrinkage higher than 25% and 2) final porosity higher than 80%.

4.2 Constraint 1: Shrinkage higher than 25%

Results obtained for this case are shown in Table 2:

Table 2 – Optimisation results for the constrained problem (shrinkage > 25%)

Optimisation Variables	Initial Alginate composition (%)	7.06
	Initial Porosity (%)	30.00
Objective Function	Elastic modulus (KPa)	17.52
Constraint	Shrinkage (%)	25.22
Output Variable	Final Porosity (%)	70.97

Figure 2 shows the evolution of the objective function along all the generations. Profiles of the objective function, shrinkage and final porosity are illustrated in Figure 3.

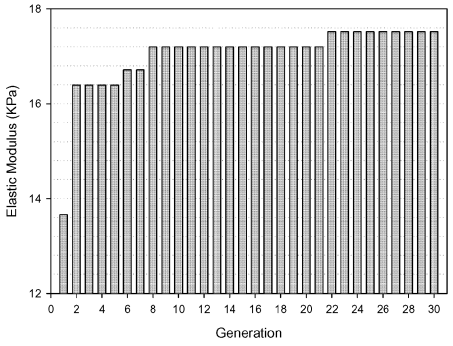

Figure 2 – Evolution of the elastic modulus along all the generations (shrinkage > 25%).

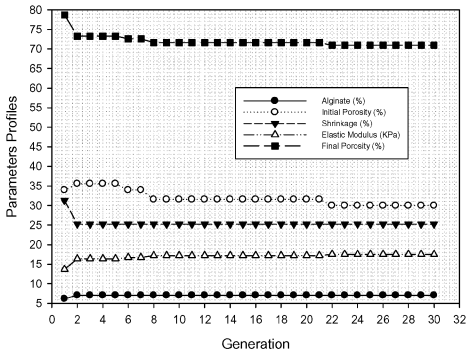

Figure 3 – Profiles of the objective function, shrinkage and final porosity obtained with the best values of the optimisation variables at each generation (shrinkage > 25%).

4.3 Constraint 2: Final porosity higher than 80%

Results obtained for this case are shown in Table 3:

Table 3 – Optimisation results for the constrained problem (final porosity > 80%).

Optimisation Variables	Initial Alginate composition (%)	5.79
	Initial Porosity (%)	32.38
Objective Function	Elastic modulus (KPa)	12.99
Output Variable	Final Porosity (%)	80.01
Constraint	Shrinkage (%)	33.29

Figure 4 shows the evolution of the objective function along all the generations. Profiles of the objective function, shrinkage and final porosity are illustrated in Figure 5.

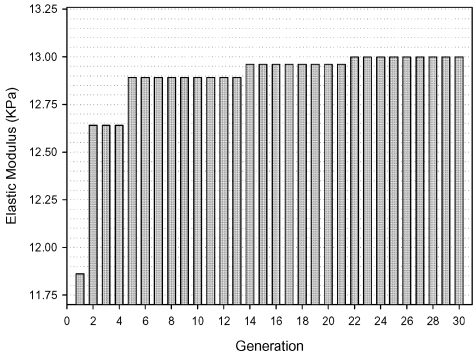

Figure 4 – Evolution of the elastic modulus along all the generations (final porosity > 80%).

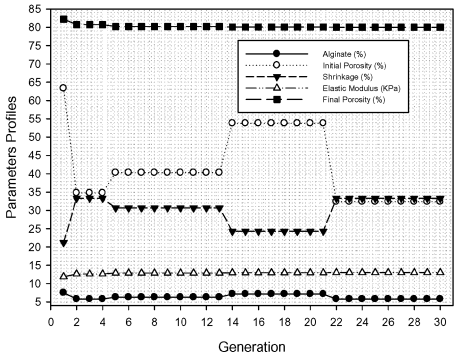

Figure 5 – Profiles of the objective function, shrinkage and final porosity obtained with the best values of the optimisation variables at each generation (final porosity > 80%).

5. Conclusions

This research uses Genetic Algorithms to optimise the mechanical behaviour of alginate scaffolds for tissue engineering. The mathematical model was experimentally obtained and the best values for both alginate composition and initial porosity of the scaffold allowing the constrained maximisation of the elastic modulus were determined through the optimisation code. The next work is to extend this tool to perform topological optimisation considering shear effects and compressive modulus variation, integrating them with a broader simulation code.

References

Carroll, D., 2008, Carroll's FORTRAN Genetic Algorithm Driver. In http://cuaerospace.com/carroll/ga.html accessed in November 16th , 2008.

Deb, K., 2000, An efficient constraint handling method for genetic algorithms. *Computer Methods in Applied Mechanics Engineering*, 186, 311-338.

Hutmacher, D. W., 2006, Scaffold-based tissue engineering– design and fabrication of matrices using solid freeform fabrication techniques. Adv. Manufact. Tech. for Medical Applications, Ed. by I. Gibson, 163-189.

Rezende, M. C. A. F., Rezende, R. A., Bartolo, P. J. S., Costa, A. C., Maciel Filho, R., 2007a, Evolutionary Optimisation for Soft Tissue Engineering. 3rd VRAP 2007,

Rezende, R. A., Bártolo, P.J., Mendes, A., Maciel Filho R., 2007b, Experimental characterisation of the alginate gelification process for rapid prototyping, Chemical Engineering Transactions. ICheaP-8.

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