Wall Shear Stress Based Optimization for Polymeric Scaffolds and its Implication to Degradation Control

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Abstract

Tissue engineering scaffolds are desirable to provide a favorable biological and mechanical environment to stimulate tissue regeneration. Scaffold wall shear stress and degradation influences this environment heavily over time but is usually not taken into account during the design process. A hypothesis proposed in this report is that the scaffolds with homogenously-distributed Wall Shear Stress (WSS) on solid/fluid boundaries will provide better cell attachment and more controllable degradation. Thus to improve the WSS and degradation performance, the void regions of the scaffolds are assumed to be filled with biofluids governed by Navier-Stokes equations. Bidirectional Evolutionary Structural Optimization (BESO) method is used to change the scaffolds in accordance with the local WSS. After shifting the solid elements from the region with the highest WSS to the voids in the region with lowest WSS, a more homogeneous distribution of WSS can be achieved. A number of three-dimensional examples are presented to demonstrate BESO procedure for fluidic WSS uniformity and slowing degradation.
1. Introduction

The design of biodegradable scaffolds is crucial in determining the success of tissue regeneration by providing a certain mechanical and biological environment (Langer et al., 1993). The scaffold is required to have a range of properties to achieve desirable functions. It must for instance have a certain stiffness, to create an appropriate mechanical environment, and a sufficient porosity and permeability, to create a biological environment allowing the nutrients delivery, cell diffusion and the metabolites products removal for tissue growth. It is expected that the degradation of the scaffold should not take place until sufficient tissue has been generated in the pore space (Adachi et al., 2006). As such, the mechanical properties of the tissue-scaffold construct can be remained more or less a constant. In addition to this, these requirements may differ between tissues and tissue sites. Thus it becomes clear that designing an appropriate scaffold is indeed a time-dependent process, which is highly challenging in nature and can be highly laborious when using experimental approaches. Adoption of mathematical modeling techniques offers a new alternative.

The use of periodically-repeated base-celled architecture has become popular in scaffold design in recent years (Hollister et al., 2002; Lin et al., 2004; Hollister, 2005; Lin et al., 2005). Recent developments in solid free-form fabrication are making this approach more and more attractive by providing an effective means to fabricate such special designs (Hutmacher, 2000; Sun et al., 2004; Sun et al., 2005). Together with other methods in computational modelling of the cell spreading and tissue regeneration in porous scaffolds with the consideration of the effect of different parameters on scaffold performance (Sengers et al., 2007; Sanz-Herrera et al., 2009), topology optimization driven by inverse homogenization has been used to scaffold design with biomimetic criteria like bone stiffness and fluid permeability (Sturm et al., 2009; Lin et al., 2004; Hollister, 2005; Lin et al., 2005).

There are two important issues associated with the scaffold design in vitro within a bioreactor. Firstly, scaffold degradation can have a major impact on scaffold performance. The mechanical function and the permeability are both influenced during the degradation process. This implies that there is a need to take degradation into account during the design of the scaffold (Adachi et al., 2006). However, modeling the degradation process of biodegradable polymers proves to be quite complex, which involves a range of chemical, physical and mechanical processes (Siepmann et al., 2001). The factors relating to degradation include (but are not limited to) the rate of water intrusion into the polymer matrix, the types of chemical bonds within the polymer, the pH value of the local environment and autocatalytic effects.

This report adopts a mechanical shear driving degradation mechanism. Under the influence of wall shear stress (WSS), the polymer chains on the scaffold surface can be stretched in the orientation of the flow or entangle with each other. Both cases will lead to polymer chain scission in some stage (Culter et al., 1975; Yu et al., 1979). For this reason, it can be hypothesized that mechanical shear degradation takes place, when the mechanical action on the polymer chain exceeds the activation energy of polymer chain scission (Kim et al., 2000).

Secondly, the wall shear stress itself can directly affect the cell proliferation and tissue differentiation. Most bioreactors are implemented to allow perfusion of culture medium, providing flow mediated mechanical stimuli (Gutierrez, Crumpler 2008).

Fluid driven optimization methods have been a topic of research ever since the pioneering works of Pironneau in shape optimization (Pironne, 1973; Pironne, 1974). However,
topology optimization of fluid fields is a relatively young area and is still progressing in different emphases. Steven et al. (Steven et al., 2000) and Borrvall and Petersson (Borrvall et al., 2003) were among the first to conduct topology optimization problems with fluidic criteria. Steven et al proposed flux based evolutionary structural optimization (ESO) procedure to seek topological design for uniform flux distribution, where the element itself was treated as design variable. Borrvall and Petersson (Borrvall et al., 2003) proposed a procedure to minimize energy dissipation, where the elemental density $\rho$ is treated as design variable and coupled with an artificial "inverse permeability". Like a typical isotropic materials with penalization (SIMP) scheme, $\rho$ is penalized by a positive factor to prevent intermediate density values (Bendsøe, 1989; Rozvany et al., 1992). This model was further extended in later studies, to name a few. However, this method usually requires remeshing during optimization and can therefore be time-consuming. Furthermore, local minima cannot always be avoided, leading to non-optimal designs. More recently, the level-set method, first proposed by Osher and Sethian (Osher et al., 2001); has been used in topology optimization of fluidic domains to tackle different objectives (Duan et al., 2008; Zhou et al., 2008).

In this report a bidirectional evolutionary structural optimization (BESO) procedure is proposed for the wall shear stress criterion. The detailed BESO procedure will be presented in section 2 and a number of 3D examples are provided in section 3. Some conclusions will be drawn in section 4.
2. Methods and Materials

The optimization procedure consists of the numerical analysis of fluidic fields and the evolutionary optimization of solid/fluid boundaries. In this section these two components will be discussed in detail. The degradation algorithm is used to justify whether the optimized designs are indeed better than the initials.

2.1 Determination of flow field and wall shear stress (WSS)

Scaffolds actually provide a porous structure allowing nutrient delivery from and metabolite removal into surrounding host tissues. The velocity profiles of the biofluidic flows must be known before a plausible assessment regarding the performance of the scaffold can be made. Without loss of generality, the domain occupied by a representative volume element of a scaffold is mathematically represent as \( \Omega_e \subseteq R^3 \), which is divided into two parts: the solid region \( \Omega_s \) with the volume of solid phase in element \( e \) centered at point \( x \in \Omega_s \) equivalent \( \rho^e(x) = \rho_s^e \), and fluid region \( \Omega_f \) with \( \rho^e(x) = \rho_f^e \). The superscript \( e \) denotes the discretized element in all the formula below. The fluid is assumed to be Newtonian and incompressible, therefore is governed by the steady state Navier-Stokes equations given by

\[
-\mu \nabla^2 u + (u \cdot \nabla)u + \nabla p = f \quad x \in \Omega_f \\
-\text{div} u = 0 \quad x \in \Omega_f 
\]  

(1a) (1b)

where \( u \) denotes the flow velocity, \( p \) the pressure, \( \mu \) the dynamic viscosity and \( f \) the body forces. The nonlinear convective term and classical Hessian matrix are given as \( (u \cdot \nabla)u = \sum_{i=1}^{2} \frac{\partial u}{\partial x_i} \) and \( \nabla^2 u \), respectively. The boundary conditions (BCs) include no-slip BC \(( \uvec = 0 \) on \( x \in \Gamma_0 \)), Neumann BC \(( \sigma n = g \) on \( x \in \Gamma_N \)), input BC \(( p = p_1 \) on \( x \in \Gamma_i \)), output BC \(( p = p_2 \) on \( x \in \Gamma_o \)) and periodic BC \(( u_p |_{x \in \Gamma_p} = u, p_p |_{x \in \Gamma_p} = x \in \Gamma_p \cup \Gamma_p )\). The boundaries \( \Gamma_p \) and \( \Gamma_p \) are opposite surfaces and \( \sigma \) is Cauchy stress tensor defined by \( \sigma(u, p) = \mu \nabla u - p \mathbf{I} \). On the Neumann BC, \( n \) is the normal direction and \( g \) is a constant usually equivalent to zero. The velocity profile and other fluidic characteristics like WSS are obtained by solving the abovementioned Navier-Stokes system with commercial tools (e.g. ANSYS or ABQUES). To reduce computational cost, the design domain for cubic-symmetry microstructure, the geometrical characteristics of most examples in this report, is confined to one-eighth of whole base cell in the design.

It was widely accepted that the hydrodynamic environment plays an important role in affecting the in vitro proliferation and osteogenic differentiation within tissue scaffolds (Silvia et al., 2008). For
example, it was interesting to observe that the tissue grew much faster in outboard surfaces of a
single disc shaped scaffold where the WSS is maximum (Neitzel et al., 1998). As the fast growth
of tissue in some areas might finally block the pore space and compromise the nutrient delivery in
other areas, it is therefore desirable that the scaffold could provide a uniformly-distributed WSS,
thereby enabling the tissue growth more uniformly. Another important feature of WSS is that it
could drive the degradation of polymeric scaffolds. It is expected that the degradation can
proceed uniformly throughout the entire domain such that the topological features can be
maintained as long as possible to avoid suddenly-change in physical properties affecting the
tissue further generation.

Being the total shear force per unit area, WSS $\tau$ can be defined as

$$\tau = \sqrt{\tau_{xy}^2 + \tau_{xz}^2 + \tau_{yz}^2}$$

(2)

with three components equal to

$$\tau_{xy} = \mu \left( \frac{\partial u_1}{\partial y} + \frac{\partial u_2}{\partial x} \right) \quad \tau_{xz} = \mu \left( \frac{\partial u_1}{\partial z} + \frac{\partial u_3}{\partial x} \right) \quad \text{and} \quad \tau_{yz} = \mu \left( \frac{\partial u_2}{\partial z} + \frac{\partial u_3}{\partial y} \right),$$

respectively.

To mathematically describe WSS uniformity, a cost function of the squared difference between
local WSS $\tau^e$ and an averaged WSS $\bar{\tau}$, can be formulated as

$$\begin{cases}
\min J = \sum_e \left( \frac{\tau^e - \bar{\tau}}{\bar{\tau}} \right)^2 \\
s.t. \quad \sum_e V^e = V_0
\end{cases}$$

(3)

where NE is the number of discretized elements and $V_0$ is prescribed as the volume constraint
for solid phase.

Since wall shear stress is a localized quantity, a topological solution to Eq. (3) is by no means
easy. The typical mathematical programming method requires to calculate the sensitivity and may
confront significant challenge (Zhou et al., 2008). Nevertheless, a non-gradient bidirectional
evolutional structural optimization (BESO) procedure allows driving the design towards an
optimum without sensitivity. This technique has well proven to be effective and powerful for many
solid mechanics design problems (Huang X, 2008). In fact, BESO can easily accommodate both
a gradient and non-gradient procedure, thus making it particularly suitable for the cases, in which
the determination of the sensitivity is difficult or impossible.

To achieve a uniform WSS distribution, the stress deviation on each surface element,

$$\left( \tau^e - \bar{\tau} \right),$$

will be directly used as an indicator to measure its contribution toward the objective
function. In the BESO procedure, the wall shear stresses on all elements are first ranked
according to their magnitude. If the volume of solid domain in the current iteration exceeds the
desired value, i.e. $\sum_e V^e > V_0$, the surface solid elements $\rho^e(x) = \rho_s^e$, $x \in \Omega_1$ with the highest
WSS deviations (positive maximum) will be changed to fluid, $\rho^f(x) = \rho_f^e$, $x \rightarrow \Omega_2$, aiming to
reduce the local WSS peak. If the volume fraction is below the desired volume fraction, \( \sum e V^e < V_0 \), the surface elements in fluid domain \( \rho^e(x) = \rho_f^e, \ x \in \Omega_2 \) with the lowest WSS deviations (negative maximum) will be changed to solids \( \rho^e(x) = \rho_s^e, \ x \to \Omega_1 \), aiming to increase local WSS. As such the topology evolves towards a more uniform distribution of WSS. At the same time, the volume will converge to the desired value \( V_0 \) by adopting the following numerical technique.

Firstly, the number of elements to be removed or added may not be a constant but progressively reduces. In such a way the design is allowed to quickly approach a rough optimized topology in the beginning and then be gradually tweaked towards an optimum. Secondly, to prevent the formation of ‘islands’ (isolated solid elements), the element is allowed to alter only when it directly connects to a solid element.

The BESO optimization will not terminate until the objective converges. The standard deviation of the objective values over the last ten iterations will be adopted to assess the convergence. Mathematically a convergence is considered attainable as Eq. 4 holds true:

\[
\sqrt{\frac{1}{5} \sum_{j=1}^{10} (J_j^{n+1} - J_j^n)^2} < \delta
\]

(4)

where the superscripts \( n \) and \( n+1 \) denote the iteration steps and \( \delta \) is a small value to be decided experimentally.

2.2 Degradation algorithm

Polymer degradation can be accelerated when WSS exceeds the threshold (Culter et al., 1975). Therefore, the first step in the degradation assessment is to calculate WSS. When WSS in all surface solid elements is calculated, they will be compared against the threshold \( \vartheta \). If \( \tau^e(x) \geq \vartheta, \ x \in \Omega_1 \), this element will become a void, signifying local degradation or erosion.

It is noted though that the degradation is a time-dependent process. For each intermediate topological design, the degradation process can be run to assess its performance relative to other topologies. This actually forms an inner loop in the degradation-based topology optimization (outer loop). Since this report aims to achieve a uniform WSS, it is unnecessary to run the inner loop in each iteration step. Instead, we monitor the degradation in a passive way to assess the performance during the topology optimization. The flowchart of the entire optimization and degradation process is depicted in Fig. 1.
Fig. 1. Flowchart of optimization and degradation process
3. Results and discussion

The design domains for all the examples are unit cubes homogeneously discretized into a 60×60×60 mesh with brick elements. In the examples below, the void regions are occupied by laminar and incompressible flows with unit density (kg/m³) and dynamic viscosity (Pa·s). To investigate the validity of the proposed method, the examples with different boundary conditions and initial designs were explored. All initial microstructures should allow the fluids pass through them. Unless stated otherwise, the volume fraction constraint \( V_0 \) and the initial volume fraction are 0.5. It must be noted that a sophisticated topology consisting of a limited number of brick elements will inevitably yield jagged boundaries. Therefore all the final topologies were post-processed to provide smoother structural boundaries below.

3.1 Vertically squared bars in three directional flow (Example 1)

A pressure was applied to three sides of the base cell whilst the pressure on the opposing sides was kept zero. In this way a three dimensional flow field was created. Four identical columns placed at the four corners were adopted as an initial design (shown as in Fig. 2a). The evolution process of the topologies can be seen in Figs. 2b-d. It is observed that as the design progresses, the solid elements were shifted from areas with the highest wall shear stress to those with a lowest shear stress to reduce the resistance to the flow. As such the four columns evolve into a microstructure similar to the well-know Schwarz-P structure, which corresponds to the optimization results for minimal energy dissipation (Zhou et al., 2008) and maximum permeability (Guest 2007).

Fig. 3a illustrates a clear convergence of the objective function. It shows the objective value drops drastically in the first 20 iterations (corresponding to Figs. 2a-c), then it gradually converges to a minimum (corresponding to Fig. 2d). As plotted in Fig. 3b plots the WSS spectrum of nodal WSS, in which the optimal design presents a sharper distribution in the stress domain. The number of elements with relative high or low WSS in the initial structure reduced gradually and a narrower WSS distribution was finally achieved. It is also note that the volume of the final design is very close to the constraint.
Fig. 2. Topology evolution of the first example
To explore the degradation performance, both the initial and optimized microstructures were tested. The value of the threshold is chosen in such a way that a gradual degradation takes place. All elements will degrade if the threshold is too high and no elements will degrade if the threshold is too low. The degradation results are plotted in Fig. 4 in which the degradation values 0 and 1 denote nil and full degradation, respectively. It is clearly shown that the optimized design degrades much more slowly than the initial microstructure, in line with the *in vivo* need that the scaffold should keep adequate stiffness in the beginning otherwise it will be too weak to support the tissue growth under mechanical stimulus.

**Fig. 3.** Objective function and wall shear stress distribution of the first example

**Fig. 4.** Degradation curves of the initial and optimized design of the first example
3.2 Vertical bars in horizontal flow (Example 2)

The second example starts with the same initial design. However, the volume fraction in this case is not 0.5 but 0.1. Along the direction parallel to the squared columns, a certain pressure drop is applied to those two opposite surfaces, leading to a flow perpendicular to the vertical columns. The snapshots of initial, intermediate and optimized designs are displayed in Fig. 5. Due to the horizontal flow the columns “elargate” firstly along the direction of the flow during the initial optimization stage, gradually forming two thin plates parallel to the flow direction. Then these two plates are slowly transformed into two thick bars, still keeping parallel to the flow direction. Finally these two bars merge together, forming a single rectangular bar orientated in the flow direction.
The variation of the objective function vs the iteration is plotted in Fig. 6a. Although the objective function seems to fluctuate a lot mainly due to the jagged surface formed by the cubic elements, an evident decrease and convergence can be observed around 200 iterations. Furthermore, it must be noted that the objective function stays relatively high due to the roughness of the design surface. After applying a smoothing algorithm the objective value can drop to 0.008. Fig. 6b shows a spectrum of the initial design and the optimized design after applying a smoothing algorithm. Like the previous example, both the high and low WSS decrease, leading to a very narrow distribution, indicating a nearly uniform wall shear stress. Again, the volume converges to the targeted volume fraction well.

![Fig. 5. Topology evolution of the second example](image)

![Fig. 6. Objective function and wall shear stress distribution of the second example](image)

The degradation of the initial and optimized design can be seen in Fig. 7, which clearly shows the optimized design outperforms the initial design in terms of degradation speed over the entire process. It can be claimed that within the new microstructure, the lifetime of the optimized design is three times than that of the initial design.
3.3 Truss-like structure in horizontal flow (Example 3)

A truss-like structure was chosen as an initial design in this example (Fig. 8a). The flow field is the same as the one used in Example 2. Fig. 8 illustrates the topological evolution during the design. It is observed that the voids in the side walls parallel to the flow direction become solid elements as the optimization progresses. Simultaneously, the voids in the front and back faces perpendicular to the flow direction grows, leading to a larger area of the flow. This process continues until a design with a through-hole is fully taken a shape as shown in Fig. 8d.
The objective function is plotted in Fig. 9a, and once again a significant drop of the objective function is shown. Similar to the previous example, the objective function can be further reduced by applying a smoothing algorithm, leading to an objective value of 0.16. The nodal WSS spectrum, as plotted in Fig. 9b, displays the same patterns as in the previous examples, reflecting a more uniform WSS distribution.
Fig. 10 depicts the degradation behavior of the initial and optimized designs. Up until the twentieth iteration steps, this behavior is very similar for both designs. After this period the difference between these two designs becomes apparent, in the end leading to a two-fold lifetime of the optimized design.

![Degradation Curve](image)

**Fig. 10.** Degradation curves of the initial and optimized design of the third example

### 3.4 A pipe bend (Example 4)

The pipe bend problem has often been used a benchmark problem in previous studies (Steven et al., 2000; Duan et al., 2008; Zhou et al., 2008), but is often confined to two dimensions. The pipe bend problem in this example is very similar to 2D. A nearly empty initial design, with a volume fraction of only 0.05 and solid material on the edges of the cubic design domain, was chosen as the initial microstructure. Unit pressure drop was applied to the input and output, which are located on the bottom and right hand side of the initial (Fig. 11).

![Schematic Drawing](image)

**Fig. 11.** Schematic drawing of boundary conditions
In this way a bending flow is generated. The formerly-used symmetry conditions were dropped because the problem is no longer symmetrical in three orthogonal axes. The desired volume fraction was expected to be 0.95. The results of the optimization process along with the initial design can be seen in Fig. 12, in which the fluid domain is shown instead of the solid one. It can be observed that the open design domain converges to a single pipe whilst material is being added. Once the volume fraction of 95% is reached the BESO method continues to optimize the design resulting in a structure as shown in Fig. 12c. When observed from the side, the optimized design shows a good resemblance to the benchmark problems in the aforementioned two-dimensional works. The objective value of the final design is 0.16, which is in the same order of magnitude as the previous examples. The WSS spectrum, plotted in Fig. 13, shows a relatively narrow distribution, confirming that it becomes uniform.

Fig. 12. Topology evolution of Example 4
Fig. 13. wall shear stress distribution of the optimized design in the fourth example
4. Conclusions

This report proposed a Bidirectional Evolutionary Structural Optimization (BESO) method in fluid problems to control the degradation of biodegradable tissue scaffolds. The BESO method shifts solid elements with a high wall shear stress to voids with a low wall shear stress, as such a more uniform wall shear stress can be obtained. The number of shifted elements decayed during the optimization procedure, allowing the design to quickly approach a rough optimized topology and then be gradually tweaked the shape towards an optimum. In addition, island formation was prevented by allowing only the void elements with solid neighbours to become solids themselves. A number of examples were explored, showing that the proposed BESO procedure leads to a more uniform wall shear stress.

A degradation algorithm based on shear degradation was developed; both the initial and optimal designs were tested by using this algorithm. It was shown that the optimized scaffolds outperformed the initial designs, these scaffolds degrade more slowly and therefore have a longer lifetime. This means that the favorable mechanical environment will last longer allowing more time to regenerate neo-tissue.

It is noted that degradation involves a range of chemical, physical and mechanical factors which have not been included in the degradation algorithm and the design process presented. Future studies into degradation may allow these factors to be taken into account during design.
References


