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# CFD modelling of a mixing chamber for the realisation of functionally graded scaffolds

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ABSTRACT

Biological tissues are characterised by spatially distributed gradients, intricately linked with functions. It is widely accepted that ideal tissue engineered scaffolds should exhibit similar functional gradients to promote successful tissue regeneration. Focusing on bone, in previous work we proposed simple methods to obtain osteochondral functionally graded scaffolds (FGSs), starting from homogeneous suspensions of hydroxyapatite (HA) particles in gelatin solutions. With the main aim of developing an automated device to fabricate FGSs, this work is focused on designing a stirred tank to obtain homogeneous HA–gelatin suspensions. The HA particles transport within the gelatin solution was investigated through computational fluid dynamics (CFD) modelling. First, the steady-state flow field was solved for the continuous phase only. Then, it was used as a starting point for solving the multi-phase transient simulation. CFD results showed that the proposed tank geometry and setup allow for obtaining a homogeneous suspension of HA micro-particles within the gelatin solution.



## 1. Introduction

Biologically inspired approaches have been widely accepted in designing better implants as well as in manufacturing artificial tissues. In general, tissues are characterised by hierarchical structures with spatially distributed gradients of properties and composition, that are intimately linked with functions (Miyamoto et al., 1999). For instance, bone tissue, with its stiff external region (i.e. cortical bone) gradually changing to a porous spongy honeycombed internal one (i.e. cancellous bone), demonstrates how the functional gradation has been used in biological adaptation to optimise the material response to external loadings. The current consensus is that an ideal tissue-engineered scaffold should recapitulate most of the native tissue characteristics to provide cells with an optimal micro-environment promoting cell growth and differentiation. Therefore, functionally graded scaffolds (FGSs) are critical for the successful engineering of biological tissues. A variety of manufacturing methods for the fabrication of FGSs have been proposed, including multiple tape casting (Werner et al., 2002), injection moulding (Zhang et al., 2007), multiple and differentiated impregnations (Tampieri et al., 2001), modified sponge replication (Hsu et al., 2007) and freeze-casting (Macchetta et al., 2009). However, the development of new manufacturing methods that can tightly control the gradient of properties in a cost-effective way is still a challenge (Miao and Sun, 2009). Focusing on bone tissue, which is mainly composed by hydroxyapatite (HA) and collagen (Col), we have recently investigated simple methods to obtain osteochondral FGSs with either discrete or continuous gradient profiles. In particular, discrete FGSs were prepared by stacking homogeneous HA–gelatin (HA/Gel) suspensions with different HA/Gel weight ratios (Jelen et al., 2013), while continuous FGSs were obtained using the gravitational sedimentation of HA particles that occurs during the controlled cross-linking of homogeneous HA/Gel suspensions (Mattei et al., 2012). These methods are very suited for developing an automated device to realise either discrete or continuous FGSs for tissue engineering applications. Mechanical agitation is widely used in industrial processes involving solid–liquid flows, with the typical requirement of suspending the solid phase for dissolution, enhanced reaction, or to obtain uniform suspensions, as in our case. Among the various approaches to provide mechanical agitation (e.g. sonication, vortexing, stirring, etc.) we chose to suspend particles through mixing in a small stirred tank. Understanding the fluid dynamics in the stirred tank is critical to properly design a mixing chamber that ensures a homogeneous suspension of HA micro-particles (secondary solid discrete phase) within the gelatin solution (primary liquid phase) prior to be transferred into a mould. Multi-phase computational fluid dynamics (CFD) modelling significantly helps in designing

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**Nomenclature**

| | |
|---|---|
| $\alpha_q$ | ***q***th phase volume fraction |
| $\rho_q$ | ***q***th phase density |
| $\vec{v}_q$ | ***q***th phase velocity |
| $\dot{m}_{pq}$ | mass transfer from phase ***p*** to phase ***q*** |
| $S_q$ | ***q***th phase source term |
| $p$ | pressure (shared by all phases) |
| $\bar{\bar{\tau}}_q$ | ***q***th phase stress-strain tensor |
| $\vec{g}$ | acceleration due to gravity |
| $\vec{R}_{pq}$ | interphase force |
| $\vec{v}_{pq}$ | interphase velocity |
| $\vec{F}_q$ | external body force |
| $\vec{F}_{lift,q}$ | lift force |
| $\vec{F}_{vm,q}$ | virtual mass force |
| $\mu_q$ | ***q***th phase shear viscosity |
| $\lambda_q$ | ***q***th phase bulk viscosity |
| $K_{pq}$ | interphase momentum exchange coefficient |
| $\bar{\bar{I}}$ | identity tensor |
| $d_s$ | ***s***th solid phase particle diameter |

the stirred tank, limiting the expensive and time-consuming *trial-and-error* experimental approach. CFD modelling has become a powerful tool for the prediction of flow fields and mixing in stirred tanks, being very helpful for estimating important process parameters such as the homogenisation time ($t_H$, i.e. the time required to achieve a fully-mixed state) and the requested power input. Several approaches to modelling solids transport were proposed, including both Lagrangian and Eulerian techniques. The Eulerian multiphase model is of particular interest, since it uses separate sets of Navier–Stokes equations for the liquid and the solids (or granular) phases, coupling the interactions between them. Using Eulerian–Eulerian models, Micale et al. predicted particle distribution at low particle concentrations in single and multiple impeller stirred vessels (Micale et al., 2000). Even though their results were in good agreement with experimental axial measurements of solids concentration, they used correction factors to fit the numerical predictions to experimental data, concluding that improved single-phase simulations and incorporation of the so-called four-way interactions (i.e. fluid-particle, particle-fluid, particle-particle and particle-turbulence) would enhance model applicability and reliability. The Eulerian Granular Multiphase (EGM) model accounts for the four-way coupling between and within phases, providing a fully predictive solution of the solids transport in the stirred tank. The strongly coupled momentum equations of granular and liquid phases require a transient solution (Massah and Oshinowo, 2000).

In this paper, multiphase CFD modelling is used to study the distribution of HA micro-particles in a gelatin solution at 40 °C (modelled as water) within a stirred tank. In particular, the transient start-up of a purposely designed mixing tank driven by a 4 blade radial paddle (RP4) is presented, considering the HA secondary phase initially located at the bottom of the tank, at a given homogenous concentration. The rest of the domain is composed of HA–free gelatin solution. This case is of particular interest for the realisation of discrete FGS by stacking different homogeneous HA/Gel layers, as we proposed. In fact, the FGS fabrication can be automated by designing a device which integrates and controls a small stirred tank with an actuated bottom that can be opened and closed to transfer the HA/Gel suspension to an underlying mould. In particular, first a homogeneous HA–rich suspension is prepared in the stirred tank and partially transferred into the mould, realising the subchondral bony layer of the osteochondral FGS. Then, the remaining HA/Gel mixture in the stirred tank is sequentially diluted with a HA–free gelatin solution, obtaining less HA-rich suspensions for intermediate FGS layers. The latter are sequentially cast into the mould towards a HA-free region, resembling the cartilaginous layer. The stirred tank should be properly designed to guarantee a homogeneous particle suspension after each dilution. The pre-processor MixSim 2.0 (Fluent Inc., USA) was used to create the computational grid with multiple reference frames (MRF), while numerical calculations in the agitated vessel were solved using ANSYS FLUENT (Ansys Inc., USA). Computations were performed assuming a standard $k-\varepsilon$ model of turbulence and modelling the multiphase flow using the EGM. First the steady-state flow field was solved for the continuous phase only (i.e. gelatin solution), and then used as a starting point for the multi-phase transient simulation. Steady-state flow field in the stirred tank and time-varying concentrations of HA particles obtained from the numerical simulations will be presented and discussed.

## 2. Material and methods

### 2.1. Experimental problem description

According to the experimental protocols showed in (Jelen et al., 2013; Mattei et al., 2012), a mixing chamber with a volume of about 2 mL was designed and modelled to prepare the homogeneous HA/Gel suspension to realise discrete or continuous FGS. The stirred tank has a flat bottom and an inner diameter of $T$ = 14 mm (Fig. 1). The liquid level is $T$ = $H$ = 14 mm. The off-bottom clearance is $C$ = $T$/4 = 3.5 mm. The custom made centric shaft has a diameter of 2 mm and ends with an integrated 4 blade radial paddle impeller (RP4). The latter moves in clockwise direction at a constant rotational speed $N$ = 240 rpm, chosen on the basis of experimental tests previously performed in our laboratory with a similar setup. The RP4 impeller has a diameter of $D$ = 9 mm ~0.64 $T$, in agreement to the typical dimensions reported in the literature, i.e. 0.5–0.8 $T$ (Inglezakis and Poulopoulos, 2006). Blades are $B$ = 3 mm in height and 1 mm in thickness. The 2 mm cylindrical core at the centre of the impeller (Fig. 1b) guarantees a geometrical continuity with the shaft, enhancing the overall mechanical stability of the rotating elements and improving the fluid dynamics at the blades crossing point, avoiding any zone of stagnation, with respect to sharp perpendicular angles.

According to the geometry described, the resultant volume of liquid within the stirred tank was 2.0742 mL. Since we used the multiple reference frame (MRF) approach for CFD calculations (Section 4), this volume was divided in two domains: a rotating zone around the impeller (*radial paddle*) and an external region (*continuum*) with no assigned motion. Considering the sequential dilution approach to obtain discrete FGSs previously described, we studied the transient mixing between a HA–rich gelatin suspension initially located in the *radial paddle* region only and a HA–free gelatin solution located in the rest of the stirred-tank liquid volume (i.e. *continuum* zone). The primary liquid phase was represented by a 5% w/v gelatin solution at 40 °C, here modelled as water (density, 1 g/cm$^3$; viscosity, 1 cP). The volume fraction of HA micro-particles (density, 3.157 g/cm$^3$; average diameter, 10 μm) in the *radial paddle* region was set to 0.037, resembling the remaining portion of a 70/30 HA/Gel suspension, previously prepared for the bony layer of the ostechondral FGS (Mattei et al., 2012; Tampieri et al., 2008).

### 2.2. CFD calculations

The software package from Fluent Inc. was used for the CFD simulations. In particular, MixSim 2.0, a specialised pre-processor for mixing applications, was used for defining the mixing tank