

An In Silico Tool To Simulate Fluid Flow And Shear Stresses On CEP Cells In Tissues And Scaffolds

The cartilage endplate (CEP) is a thin layer of cartilage that separate the intervertebral disc (IVD) from the vertebral body (VB). It is regarded as the main gateway for nutrients and waste in and out of the nucleus pulposus, thus playing a crucial role in keeping the IVD healthy. Yet, it is the spinal tissue receiving the least amount of attention in scientific literature. A key mechanical property is shear stress that has an influence on growth, differentiation, migration, and ECM production. This in turn would also affect the morphology, orientation, metabolic activities, and homeostasis of cells by activating mechanotransducers that regulate gene expression and protein synthesis. Hence, replicating physiologically relevant shear stress levels during cell culture might be beneficial. Here we propose an in silico tool to quantify CEP wall shear stresses for bioreactor experiments whether they are cells in explants or on scaffolds.

The inputs for this in silico tool are CT scans of the CEP explants and/or scaffolds, pressures at the inlet and outlet, and fluid viscosity. It returns inlet and outlet velocities with respect to time and wall shear stresses experienced by the cells at the last time point of the simulation, either at steady state or after a preassigned duration. The tool assumes laminar flow due to the small diameter of pores inside the explant and scaffold but could be changed by the user. In a first step, 3D-slicer was used to create the model of the explant or scaffold, after which MeshLab was run to refine the model before sectioning it into inlet, outlet, and walls. Subsequently, OpenFoam is used, meshing the model using localized mesh controls to fine-tune the transition using SnappyHexMesh and then running the computational fluid dynamics (CFD) analysis using a steady-state solver for incompressible flow following the SIMPLE (Semi-Implicit Method for Pressure Linked Equations) algorithm. Data visualization was performed with Paraview.

The tool was tested on both bovine tail CEP explants and additively manufactured calcium-phosphate base scaffolds with well-defined parametric and morphological characteristics (gyroid, primitive, diamond, and gradient gyroid). The explants were taken from different bovine tails at different locations and CT scanned before being fitted into the fluidic set-up. After fitting into silicon tubes, Dulbecco's Modified Eagle Medium (DMEM) was run through the explants under defined pressure differences and the fluid flow rate was recorded. The additively manufactured scaffolds were CT scanned to have the as-produced geometries for the shear stress calculations.

According to Salinas et al., the optimal range of fluid-induced wall shear stress for chondrocytes is 0.05-0.21 Pa. Passing fluid through a CEP purely under gravitational forces leads to low wall shear stresses throughout the explant mainly less than 0.02 Pa meaning that pumping fluid through the CEP under pressure would be more biologically relevant. The tool presented here enables the calculation of stresses present inside 3D porous biological tissues, allowing a quantification of the required fluid flow rates in bioreactor set-ups to mimic physiological conditions in cell culture.