A mathematical model of tissue-engineered cartilage development under cyclic compressive loading

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The major challenge associated with tissue engineered cartilage is the difficulty to approximate the mechanical properties of the new tissues to the native ones. When implanted, these inferior tissues are detrimental due to cell damage and degradation of extracellular matrix. In order to increase the production of extracellular matrix and mechanical properties of the cultured tissues, mechanical stimulation in bioreactors has provided good results. Computational modelling techniques are useful to establish protocols for mechanical stimulation of tissue engineered cartilage, as well as to provide further insights on outputs not easily measurable experimentally. In this work a coupled model of solute transport and uptake, cell proliferation, extracellular matrix (ECM) synthesis and remodeling of mechanical properties accounting for the impact of mechanical loading in is presented as an advancement of a previous coupled model validated for free swelling tissue engineered cartilage cultures. Tissue engineering constructs were modeled as biphasic with a linear elastic solid and relevant intrinsic mechanical stimuli in the constructs were determined by numerical simulation for use as inputs of the coupled model. The mechanical dependent formulations were derived from a calibration and parametrization dataset and validated by comparison of normalized ratios of cell counts (Fig 1), total glycosaminoglycans (Fig 2) and collagen after 24h continuous cyclic unconfined compression from another dataset. The model successfully fit the calibration dataset and predicted the results from the validation dataset with good agreement, with average relative errors up to 3.1 and 4.3% respectively. Temporal and spatial patterns determined for other model outputs were consistent with reported studies. The results suggest that the model describes the interaction between the simultaneous factors involved in in vitro tissue engineered cartilage culture under dynamic loading. This approach could also be attractive for optimization of culture protocols, namely through the application to longer culture times and other types of mechanical stimuli.

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FIGURE 1
Comparison between numerical predictions and experimental averages of cell densities. Open circles – numerical averages. Open squares – experimental averages with +/- standard deviation bars. A – 5% amplitude. B – 10% amplitude.

FIGURE 2
Estimated ratio of released GAGs vs total GAGs. Blue circles – 5% amplitude. Red circles – 10% amplitude. Green circles – 15% amplitude.

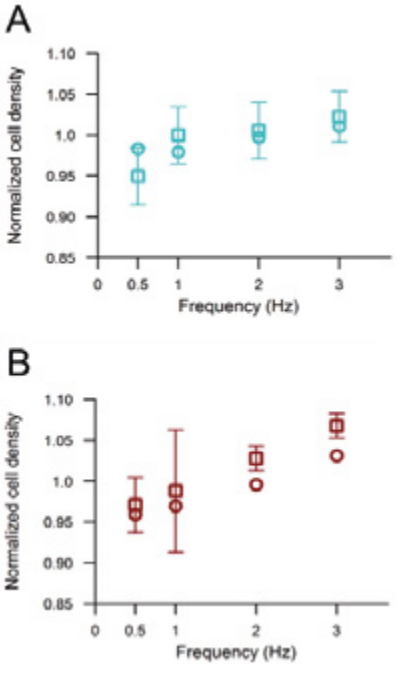

Figure 1

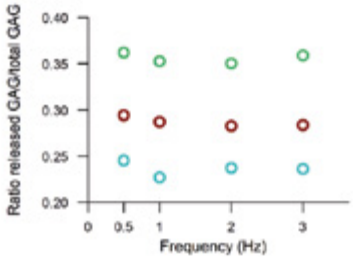

Figure 2