A computational model to describe the collagen orientation in statically cultured engineered tissues

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Introduction
Loading protocols in tissue engineering (TE) aim to improve the deposition of a properly organized collagen network. Cells synthesize the collagen fibers and develop traction forces that play an important role in the fiber alignment. These forces are particularly important in static loading protocols, where no other external force is applied.

Objective: The goal of this study is to investigate the role of cellular traction forces in collagen remodeling of TE constructs developed under static loading conditions.

Methods
The theory of Driessen et al. [1] is extended to include cell stress. The total stress is split in an isotropic matrix part and an anisotropic fiber part.

\[ \mathbf{\sigma} = \mathbf{\sigma}^f + \frac{3}{4\pi} \int \left( \mathbf{\phi}_f \mathbf{\phi}_f + \mathbf{\sigma}_c \right) \mathbf{\varepsilon} \mathbf{d}S \]  

(1)

where \( \mathbf{\sigma} \) represents the matrix stress. \( \mathbf{\phi}_f \) is the collagen fiber content, \( \mathbf{\phi}_f \) is the fiber stress and \( \mathbf{\sigma}_c \) is the cell stress, both acting only in the direction of the fiber \( \mathbf{\phi}_f \). The isotropic matrix stress is modeled as a compressible Neo–Hookean material. The collagen constitutive behavior is described by an exponential law. The constitutive behavior of the cells is described by the theory of Desphande et al. [2]. The cell stress is given by a Hill-like equation and is dependent on the isochoric extension/shortening of the fiber and fiber content \( \eta \).

Discussion
The model successfully predicts the collagen fiber orientation obtained in TE small diameter vessels developed under static loading conditions. Thus cellular traction is an important component in collagen remodeling. Therefore, the model may be a valuable factor in the improvement of loading protocols for TE.