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Modelling analysis of the effect of fibroblast on ventricular contraction

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Abstract

Introduction

In cardiac tissue, fibroblasts couple to ventricular cardiomyocytes and are known to affect their electrophysiology [1,2]. Electrophysiology controls the active stress in cardiomyocytes, leading to their contraction. Thus, it is likely that fibroblast have an impact on ventricular contraction as well. For its investigation, mechanical analyses of cardiac tissue are performed with the *CellDrum* device [3]. The *CellDrum* is a well with a bottom formed by an ultra-thin circular silicone membrane on which cardiac tissue is cultivated. Clamped in a fixed ring, the displacement and contraction frequency of the auto-contractile tissue construct can be measured using a capacitive sensor. In preliminary experiments with tissues of human-induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CM) co-cultured with fibroblasts at varying proportions of the cells, it was observed that the displacement was enhanced in the presence of fibroblasts making up to 50% of the total amount of cells [4].
The objective of this study is to perform a multiscale FE analysis of the *CellDrum* experiments. The APD90, conduction velocity, and central tissue deflection during contraction are computed as function of the fibroblast cell content.

Methods

Ventricular cell electrophysiology is described by the TenTusscher-Panfilov epicardial model [5] and is coupled with the active fibroblast model published by MacCannel *et al*. [2]. The ventricular-fibroblast cell model is embedded in the monodomain model which computes the propagation of the membrane potential throughout the tissue construct. The Niederer-Hunter-Smith excitation-contraction cell model [6] relates the membrane potential driven calcium concentration of the ventricular cardiomyocytes to their active stress and this is added to the passive stress of the tissue construct characterized by a neo-Hookean strain energy function.

Results

APD90 (307.2ms, 298.8ms, 280.9ms), conduction velocity (0.60m/s, 0.59m/s, 0.59m/s), and central tissue deflection (0.072mm, 0.068mm, 0.059mm) decrease with the relative fibroblast cell content (0%, 25%, 50%).

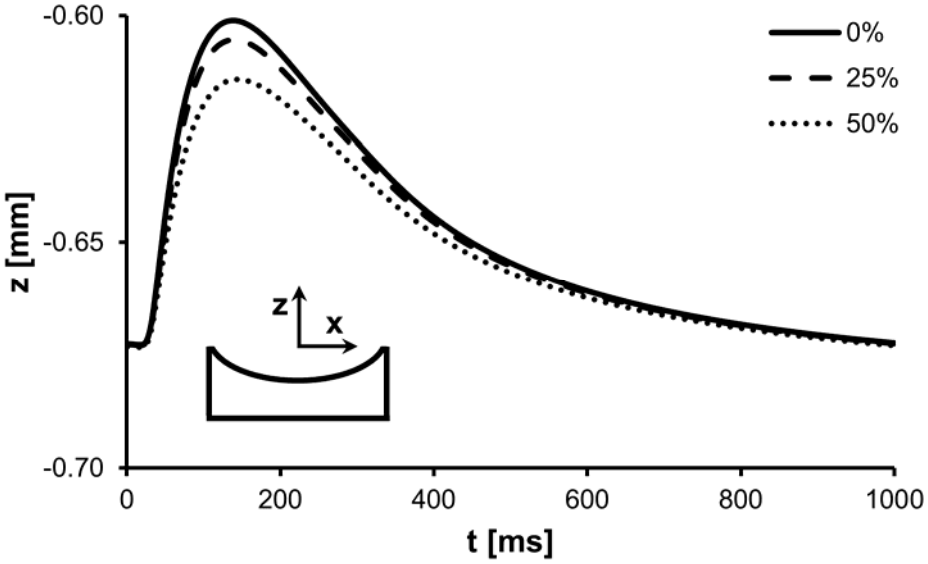

Fig. 1: The z-coordinate of the curved tissue construct center is plotted over time for various fibroblast cell contents.

Discussion

The presented FE analysis cannot explain the experimental findings. Structural analyses and inflation testing will be conducted to investigate whether structural changes or tissue stiffening might be responsible for an enhanced contraction. Except for the formulation of the passive mechanical behavior, the model relates to literature data from human and rat native cardiomyocytes. Comprehensive experimental model parametrization is future work.

References

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