Estimating active tension in cardiac micromuscles

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Introduction: Microphysiological systems (MPSs) provide a well-defined environment for the formation and monitoring of cardiac micromuscles, and provide a powerful platform for both disease and drug development studies. Such devices can replicate key features of the heart's electromechanical behavior, giving a detailed in vitro testbed for investigating cardiac function, both biomechanics and electrophysiology. In an MPS, quantities like displacement and velocity can be identified based on optical measurements of the tissues during contraction [1]. While useful for evaluating relative changes in muscle twitch, it remains difficult to quantify and characterize the underlying active tension that causes displacement during contraction.

Methods: In this work, we applied an inverse modeling approach to estimate the active tension generated during contraction, as well as the fiber directions in a cardiac micromuscle. Cardiomyocytes differentiated from human induced pluripotent stem cells (hiPSC-CMs) were loaded into MPSs and self-assembled into a uniaxial beating microtissue. High-speed microscopic videos were recorded over several contractions and changes in displacement were calculated. Finally, we used a computational mechanical model in combination with an optimization algorithm, similar to the one used in [2], to find the active tension and fiber directions likely to cause the tissue displacement.

Results: Using the displacement recorded for a single chip (Fig 1A), the active strain (Fig 1C), varying over time and space, and the fiber direction (Fig 1D), varying over space, can be estimated. The model, depending on these two variables, was able to closely reproduce (Fig 1B) the displacement given as input. The corresponding mean active tension for this specific experiment at peak contraction value is given by 0.059 ± 0.043 (active strain) and the corresponding fiber direction angle 3.3° ± 25.8°.

Discussion: Through our framework we can identify regions of active contraction, and fiber direction alignment, both known to be important metrics from a physiological perspective. We can also quantify the active tension generated. This approach can be used to quantify differences and changes in a range of experiments where mechanical properties are critical metrics, including but not limited to screening of drugs that alter contractility, and tissue structural development in different maturation protocols.

References:

[1] Huebsch, N et al. Metabolically-Driven Maturation of hiPSC-Cell Derived Cardiac Chip. Biorxiv (preprint). 2020. https://doi.org/10.1101/485169.

[2] Finsberg, H. et al: Estimating cardiac contraction through high resolution data assimilation of a personalized mechanical model. Journal of Computational Science. 2018;24:85–90. https://doi.org/10.1016/j.jocs.2017.07.013

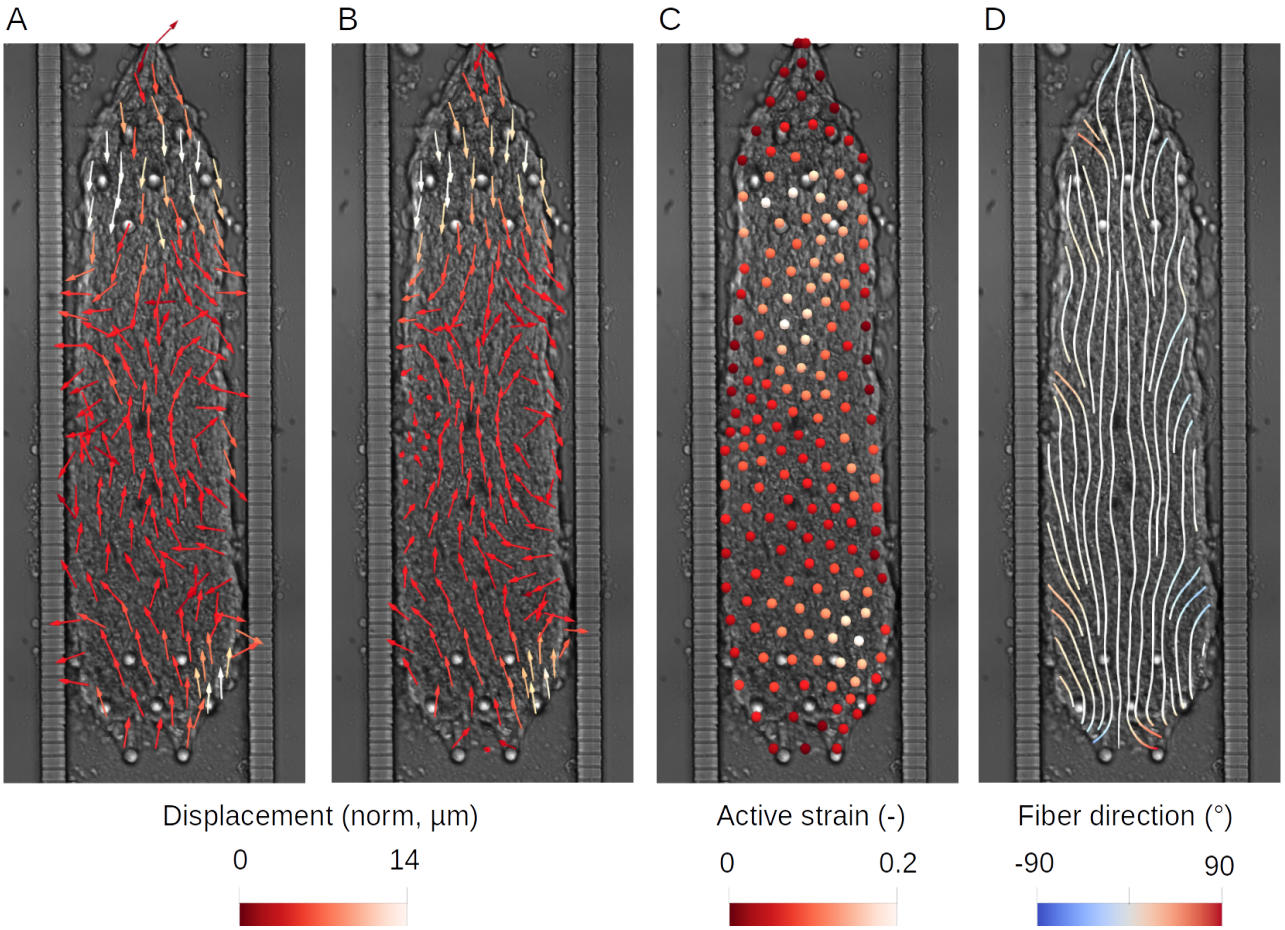

Fig 1: Results for a single chip, at maximum contraction values. **A**: Original displacement obtained from optical measurements. **B**: Corresponding model displacement resulting from the active tension and fiber direction calculated by the optimization algorithm. **C**: Optimized active tension, given as active strain, returned by the method. **D**: Optimized fiber orientations returned by the method.