Estimating active strain in micromuscles

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MOTIVATION

Cardiac microphysiological systems (MPSs) can be used to mimic key features of cardiac functionality. They highly controlled environment for the formation and monitoring of cardiac micromuscles, formed from stem cell derived cardiomyocites that self-assemble into beating microtissues. Microscopic videos can then be used to monitor movement over time, and image analysis technicques used to quantify this as displacement and velocity [1]. While these are useful as metrics of changes in cardiac functionality, they cannot directly be used to quantify the underlying active tension driving the contraction.

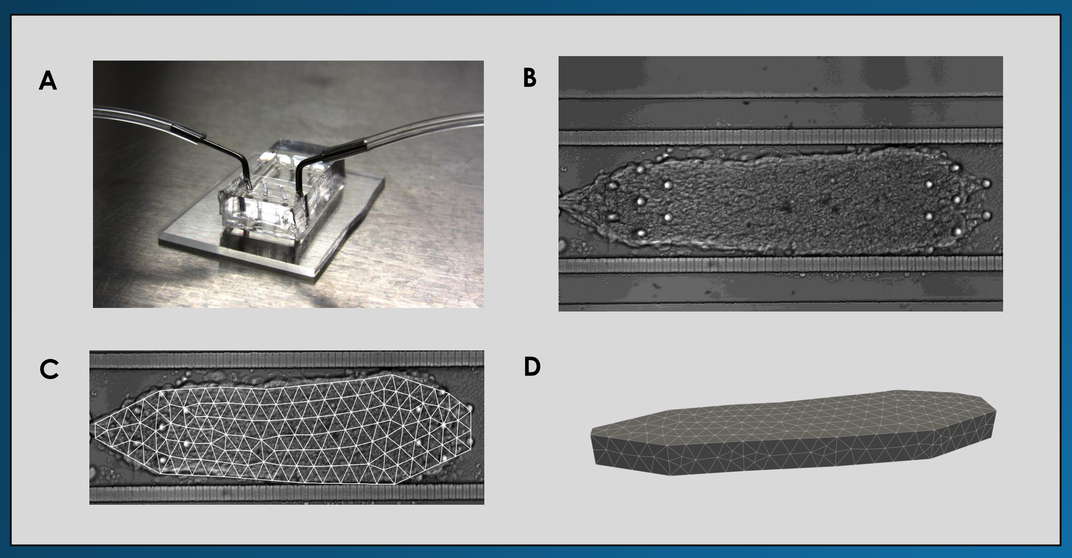

Fig. 1. Cardiac microphysiological systems (A) are small devices in which cardiac micromuscles (B) can develop. We trace the outline of the microtissue and create an experiment-specific mesh to represent the domain (C & D).

METHODS

We get a displacement field from recorded brightfield images using Farnebacks motion tracking algorithm [2]. This will be used as the true solution, the original displacement field.

The model the underlying mechanics of the microtissue, we model it as an incompressible, hyperelastic anisotropic material. Our model is dependent on

- The active strain **γ**; the active tension generated by the tissue
- The fiber direction **θ**; the longitudial cellular orientation

and we consider both as spatially variable continuous functions. With these given as input, we get the resulting model displacement as an output of our forward model.

For our case, we have the displacement – while the active strain and fiber direction distributions are unknown. To find these, we solve a PDE-constrained optimization problem:

$$\begin{aligned} \min & ||u_{data} - u_{model}(\gamma, \theta)|| \\ s.t. \quad \gamma & \in [0, 0.3] \\ \theta & \in [-\frac{\pi}{2}, \frac{\pi}{2}] \end{aligned} \qquad \text{and} \qquad \nabla \cdot P(\gamma, \theta) = 0$$

where u_{data} is the displacement found based on the motion tracking and $u_{model}(\gamma, \theta)$ the displacement found by the forward model. The PDE is solved using the Finite element method, and the gradient is found solving the adjoint problem, both implemented in Pyadjoint [3]. The optimization problem itself is solved using IPOPT [4].

RESULTS

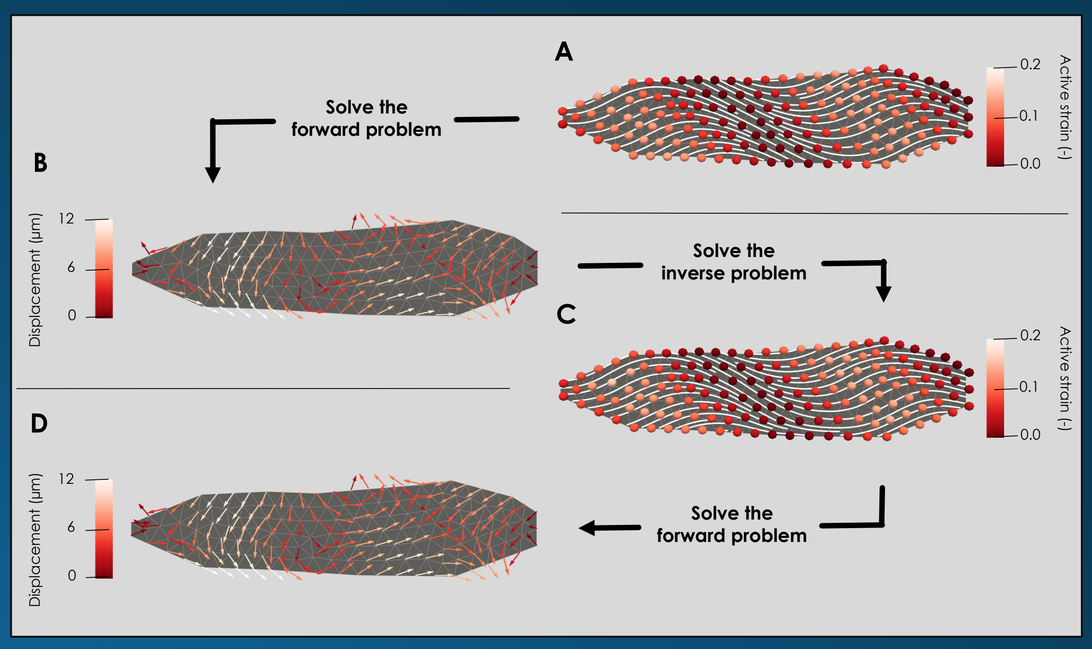

Fig. 2. In a synthetic data experiments, we knew the orignal active strain and fiber direction distributions (A), The active strain is represented using scalar glyphs, colored according to magnitude, while the fiber direction is displayed with streamlines. We next solved for displacement (B), represented with vector glyphs; the magnitude is again displayed in colors. Using the displacement data, we then solved the inverse problem. The active strain and fiber direction distributions found (C), which again results in the model displacement (D), closely resembles (A) and (B).

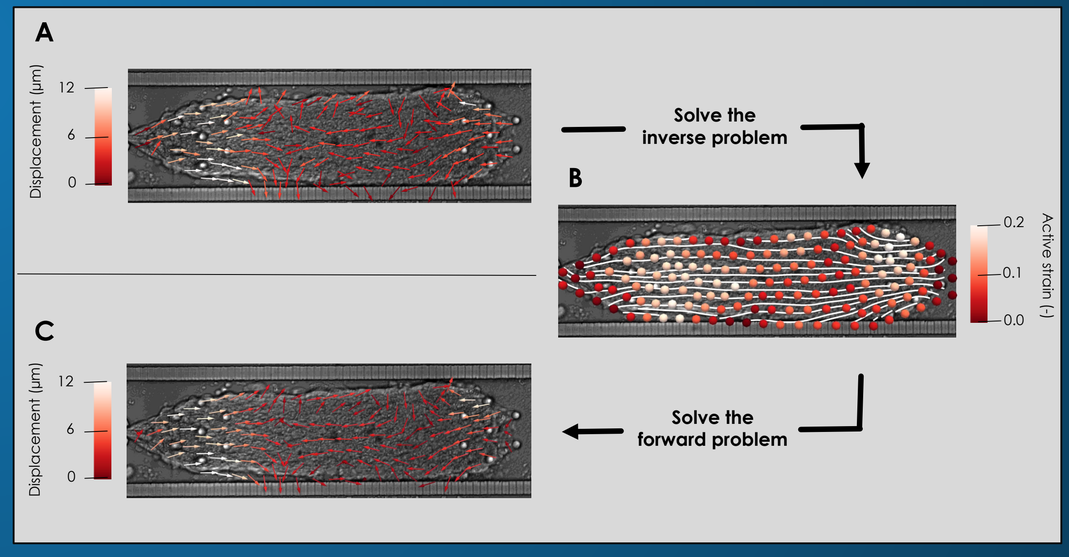

Fig. 3: From original displacement data (B), obtained from the motion tracking, we solved the inverse problem to find optimal active strain and fiber direction distributions (C). The resulting active strain is strong in two different regions, while the resulting fiber direction is fairly well aligned everywhere. The model displacement (D) using these distributions as input is observed to be very similar in regions of high displacement, and somewhat smoother in regions with low displacement.

REFERENCES

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