Virtual Particle Tracking Based In Silico Model of Engineered Heart Tissue Contractility

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Context: Engineered heart tissue (EHT) is a novel *in-vitro* modeling platform for studying cardiac diseases and drug responses. Human induced pluripotent stem cell derived cardiomyocytes (hiPSC-CMs) are cultured between bending pillars, enabling the measurement of force. However, the pillar deflection does not represent the intrinsic contraction force generated by the CMs. New methods for analyzing tissue contractility on EHT platforms are needed.

Aim: To address the need, we combined optical flow-based data leveraging virtual particles and biomechanical spring/damper model to estimate the EHT contraction mechanics and cellular active forces.

Methods: Video microscopy recordings of beating hiPSC-CM EHTs were quantified using TV-L1 optical flow estimation to generate velocity vector fields. Virtual particles were generated in a grid pattern on top of each EHT. With the optical flow fields, the particle trajectories were estimated during contraction cycle providing particle trajectory shape and length.

To explain the particle trajectory data, we created a 2D *in-silico* model of EHT contraction. The model consists of parallel spring-mass-dampers with active and passive force components, connecting the particle locations and their trajectories in a 2D mesh. Pillar movement connected with springs acted as a model boundary condition. Using the model, the active force component was estimated.

Results: Particle-based tracking revealed unsynchronized onset of contraction and motion perpendicular to the axial contraction due to displacement of mass. The biomechanical model provides quantitative cardiac force generation measures throughout the analyzed EHT.

Conclusion: Our trajectory data and biomechanics based model provides a novel view to EHT biomechanics. With the proposed *in-silico* framework, we can better estimate the actual cellular active forces with an improved view to cell biophysics. Combining the developed model with structural 3D imaging data will further improve our understanding of 3D cardiac structure-function relation and bridge the gap between EHT *in-vitro* and *in-silico* studies.