SARC-GRAPH: AUTOMATED SEGMENTATION, TRACKING, AND ANALYSIS OF SARCOMERES

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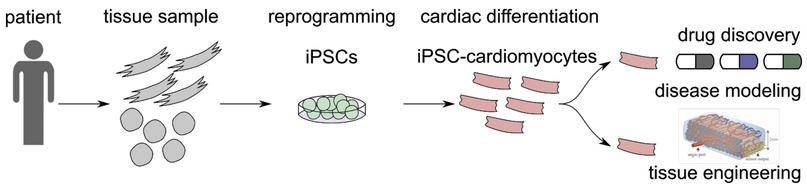
Abstract

Heart Disease is the leading cause of death worldwide. This has led to an increase of research on human induced Pluripotent Stem Cell-Derived Cardiomyocytes (hiPSC-CMs). Being able to gain a better understanding of this has the potential to lead to the advancement of numerous medical applications. The Sarc-Graph is a computational framework created to segment, track, and analyze sarcomeres in fluorescently tagged hiPSC-CMs. Within the code are functions that allow us to segment and track z-discs and sarcomeres in beating heart cells and perform automated spatiotemporal analysis and data visualization.

Background

What Are hiPSC-CMs?
Human induced pluripotent stem cells are derived from human tissue samples. Those cells are then reprogrammed to a pluripotent stage.
In mature cardiomyocytes, sarcomeres have a highly ordered regular structure. As opposed to Sarcomeres in hiPSC-CMs, which are typically immature and disordered.
It is this irregular structure and the large variation between cells, that makes quantitative analysis difficult. This is where the sarc-graph comes in. This framework is used for analyzing beating hiPSC-Cms with the hope that it will help advanance drug discovery, genetic cardiac disease, and cardiac repair.



Synthetic and Experimental Data

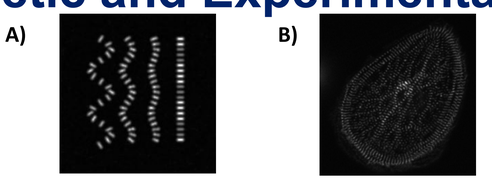
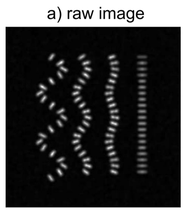


Figure A: This is an example of synthetic data. Synthetic data is used for software validation.
Figure B: This is an example of experimental data. Experimental data is used for software demonstration. This image is a single paced hiPSC-CMs cultured on a fibronectin-coated glass substrate. A noticeable challenge for analysis of this image is the low spatial resolution and the and small deformation.

Segmentation

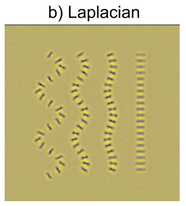
Raw 2D image

- **Raw two-dimensional input image**
- **Synthetic data is used to test the image analysis code**



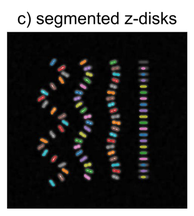
Laplacian

- **Removed noise using Gaussian blur**
- **Used laplacian operator to detect high gradients at the edge of every z-disc**



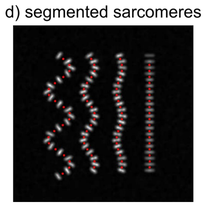
Z-discs

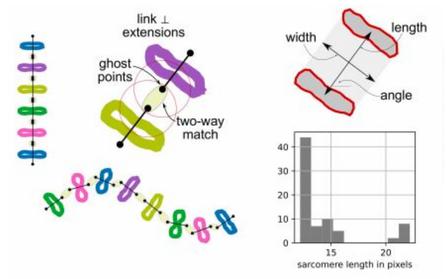
- **The command *measure.find_contours()* is used.**
- **Z-discs are identified as closed contours**



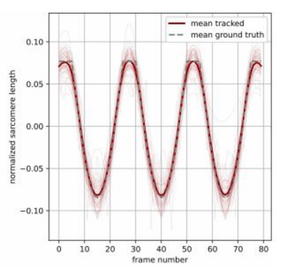
Sarcomeres

- **Now that the Z-disc are segmented, sarcomeres are procedurally identified.**



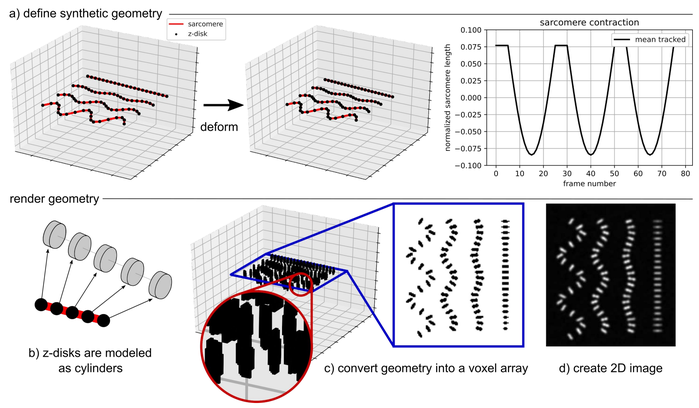


The algorithm illustrated above links approximately parallel z-discs

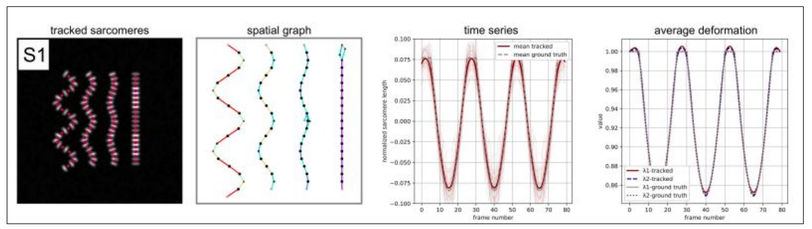


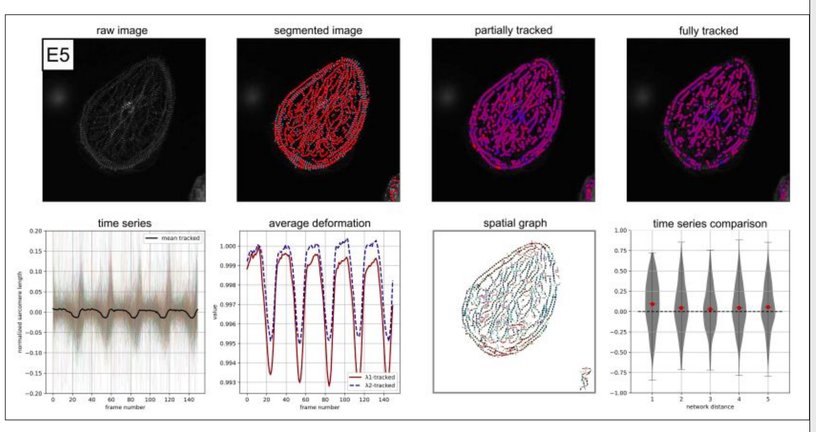
individual sarcomeres, 76/80 recovered

How synthetic data is created



Results





In figure E5, red corresponds to contracted state. Blue corresponds to a relaxed state.

Conclusion

The Objective of the "sarc-graph" is to allow the computational framework to be open source and accessible for researchers looking for an automated quantitative analysis of hiPSC-CM behavior. In order to achieve this, code was written to create a tool that can segment and track z-discs and sarcomeres in beating cells. Thus allowing data visualization to be performed. The future goal of the sarc-graph is that it will be used as an vital tool by researchers studying hiPSC-CMs behavior.

References

[1] Zhao, Zhang, Chen, Lejeune, "SARC-GRAPH: AUTOMATED SEGMENTATION, TRACKING, AND ANALYSIS OF SARCOMERES IN HIPSC-DERIVED CARDIOMYOCYTES" (2021):1-6.

Acknowledgements

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