Title: Deep learning-based estimation of iPSC-cardiomyocyte myofibrillar structure from light microscopy

Authors:
Ahola Antti and Jari Hyttinen

Keywords:
Cardiomyocyte, machine learning, biomedical engineering, cell and tissue models

Abstract

The structural immaturity of human induced pluripotent stem cell derived cardiomyocytes (hiPSC-CMs) poses limitations to their use in pharmaceutical and genetic cardiac disease studies. Traditionally, their structure has been evaluated from immunofluorescent staining, which is typically an end-point measurement. Genetically encoded fluorescent reporter lines have enabled live imaging, but generating reporter lines for disease-specific cell lines is not practical. Here, we present a deep learning-based method for generating estimations of a-actinin stain from high resolution microscopy images, enabling label-free continuous evaluation of the culture sarcomeric structure.

We developed a Pix2Pix-based architecture consisting of a residual attention U-Net architecture with squeeze-and-excitation blocks and atrous spatial pyramid pooling, combined with a PatchGAN discriminator. We used a publicly available dataset hiPSC-CM monolayer images, consisting of co-registered brightfield and a-actinin-2-mEGFP images of 1776x1736 px resolution, obtained with 52.29x effective magnification. The data was divided to 382 training and 96 test image pairs. The network was trained to generate 256x256 px images from brightfield image input. The result images were evaluated against ground truth images using CytoSpectre software, commonly used to evaluate sarcomere orientation. Mean resultant length (MRL) was used to quantify the angular difference in main orientation.

The network generated images of the myofibrillar structure with similar orientations as the ground truth. We obtained a MRL of 0.68, indicating a moderate-high relation for the orientation prediction. The results indicate that deep learning methods can be used for label free and continuous estimation of hiPSC derived cardiomyocyte sarcomeres in culture.