Computer analysis of calcium cyclings of stem cell-derived cardiomyocytes

As any organ, the heart of an individual is built of an innumerable number of cells called cardiomyocytes. Traditionally our understanding of human cardiac cells is based on animal studies, but with the aid of new stem cell technologies, we are now able to study human cells. Now, computer-aided technologies are developed to improve and speed-up the analysis of cardiomyocytes.

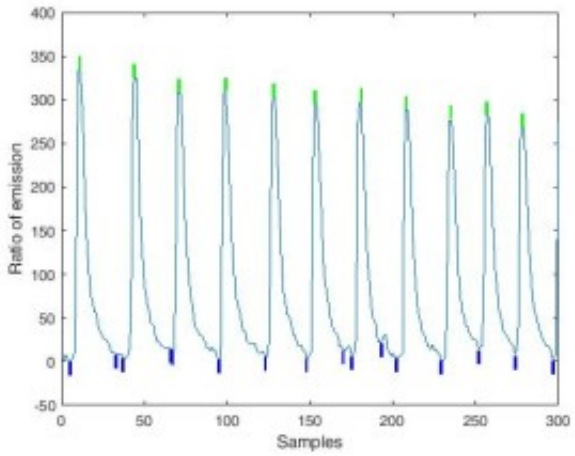

Fig. 1. Cardiomyocytes were exposed to two different wavelengths of light and emissions recorded. For calcium analysis, regions of interest were selected from a video stream of spontaneously beating cells. A 12-second signal with all peaks detected normal (green marker) represents normal, valid calcium cyclings of a cardiomyocyte. The normal signal is harmonious and includes pretty regularly repeating peaks.

In our research, we utilize induced pluripotent stem cell (iPSC) technology where e.g. skin cells are reprogrammed into pluripotent stem cells (iPSCs). iPSCs carry the whole genome of the individual who donated the skin sample. These iPSCs can be differentiated e.g into cardiomyocytes. iPSCs derived from an individual having a genetic cardiac disease carry the same disease information as the patient and thus the disease can be studied in laboratory without predisposing the patient to any risks.

Calcium cycling is very important in cardiomyocytes. It is the link between the electrical signaling and the contraction of cardiomyocytes. Changes and irregularity in calcium cyclings can been analyzed with special fluorescent markers and the effects of different drugs on this process can be visualized.

To improve the analysis of cardiomyocytes, we developed computer methods based on signal analysis and classification that detect peaks or cyclings (transients) in cardiomyocyte signal data and classify entire signals into either a normal or abnormal group. Our objective is to create computer software for detection of normal or abnormal calcium cyclings and analysis of drug responses or adverse side effects. Additionally the software is useful when studying genetic cardiac diseases.

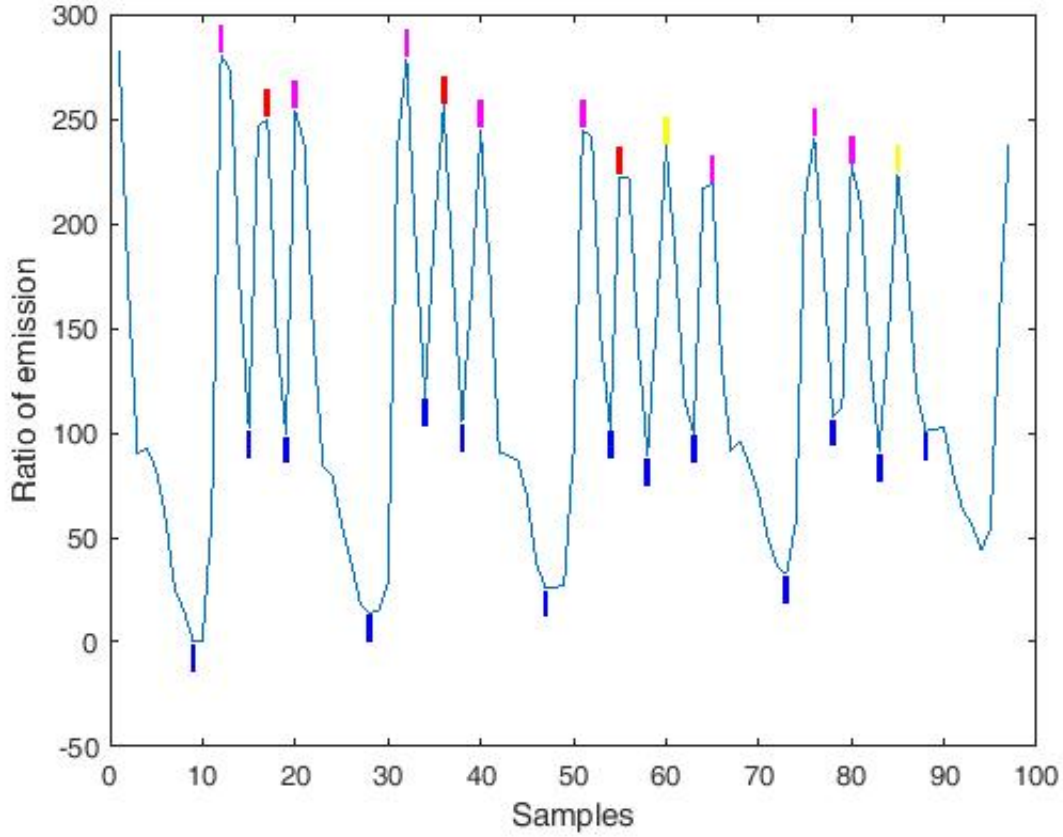

Fig. 2. A 9-second signal of all peaks detected to be abnormal (marked with other colors than green) represents abnormal cyclings. In the abnormal signal there are somewhat irregular peak forms occurring variably.

Figure 1 presents an example when all signal peaks were detected by the computer program to be normal. In Figure 2 all peaks are detected to be abnormal. If even one peak only were detected abnormal, the whole signal would be determined abnormal. This program can be used to study whether a drug has adverse cardiac side effects in terms of producing abnormalities in cardiac cyclings or whether the abnormal peaks can be normalized with another drug.

It is crucial to develop automatic computer software for the data analysis to aid biomedical researchers to cope with the enormous amount of data produced from single cells and, eventually, to enable industrial utilization of novel discoveries in cell biology and medicine.

Publication

Signal analysis and classification methods for the calcium transient data of stem cell-derived cardiomyocytes.
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