Machine Learning models for analysis of behavior of Engineered Heart Tissues (EHTs)

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ABSTRACT

Nowadays, one of the most important issues is connected with preparation of new medications. Especially, it is hard when it comes to organs like human heart. It is not easy to appropriately test the medication without applying it to the organ. Such a procedure is extremely risky and can lead even to patient's death. To reduce that risk, scientists proposed to test the medication within synthetically grown tissues and even single cells. However, here we can observe another problem. To find some changes in the cell/tissue behavior (e.g., its stoppage), lab worker needs to observe the cell constantly through the microscope. It is hard, because such changes can be observed even after a couple of hours. It is why, the Author of that work would like to propose a procedure by which, the behavior of the cell can be automatically assigned in each second of its lifetime (also after application of new medication) – in real time. This procedure combines diversified techniques – both from the area of signal/image processing and Machine Learning - to recognize the stage of systole or diastole. It needs to be pointed out that all experiments were performed with the database of 3D videos (single cell is observable in the center of the scene). More than 50 videos were used to develop the proposed techniques. Obtained results were discussed with experienced biologists and bioengineers from Institute of Human Genetics, Polish Academy of Science (Poznań, Poland). On the basis of these discussions it was proven that the algorithm is precise and effective enough to be used in real biological experiments.

DATASET

During the experiments we consumed database consisting of 61 spatial videos. Duration of each of them was not shorter than 1 minute. In most of the cases, EHT was placed in the center of the frame – however, there were also videos where the cell was moved. The goal of this study was to observe the occurrence of systole and diastole cycles in the cell. It is why each, these cycles were observable in each video. Example of the single frame from the database is presented in Fig. 1.

Fig. 1. Example of the single frame from the spatial 3D video.

PROPOSED APPROACHES

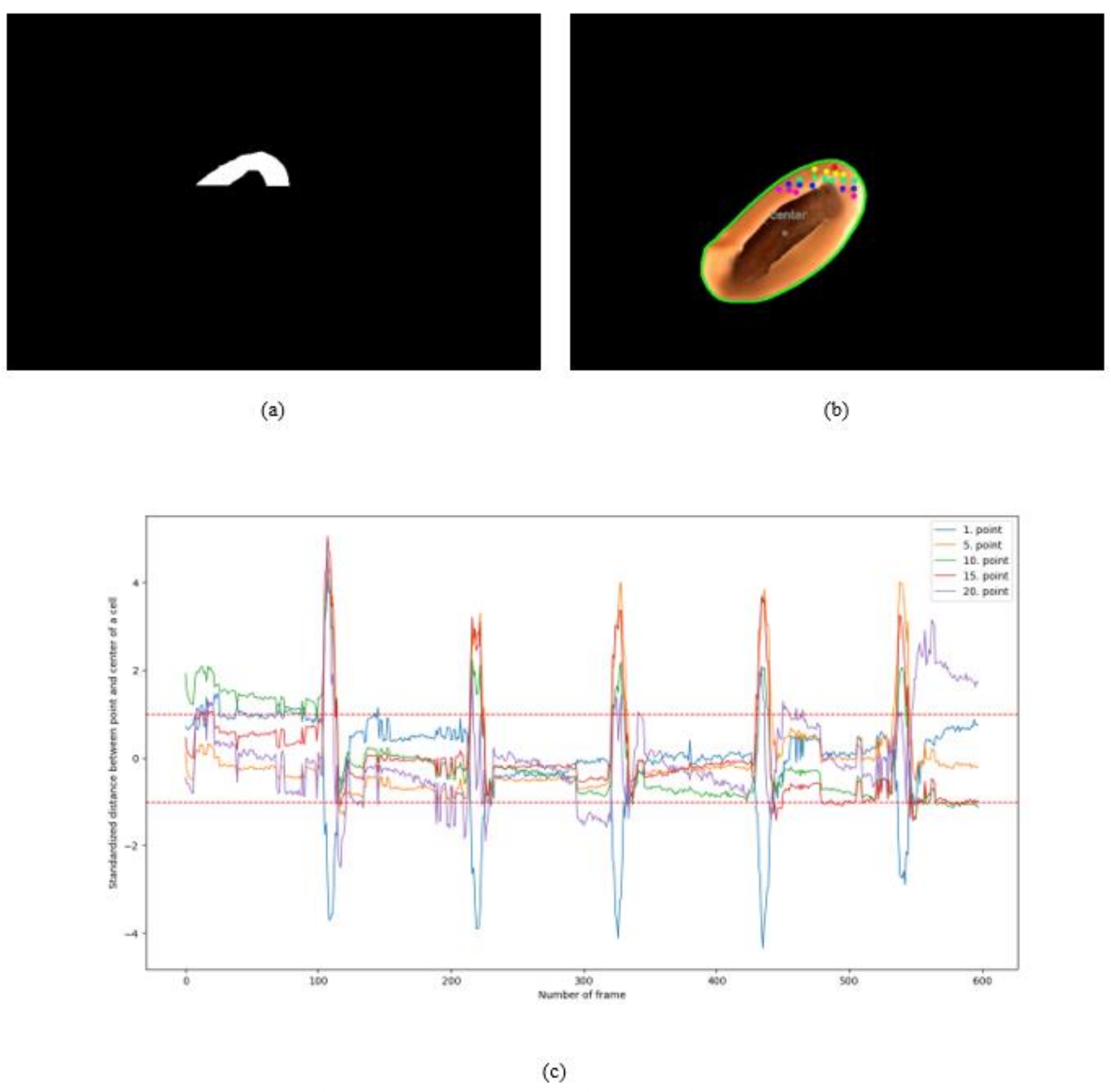

Fig. 2. CoTracker-based approach. (a) selected region of the cell for analysis of the movements, (b) points marked in the original cell (generated with CoTracker), (c) the chart with mean distance of the points cloud from the center (marked in the b) image).

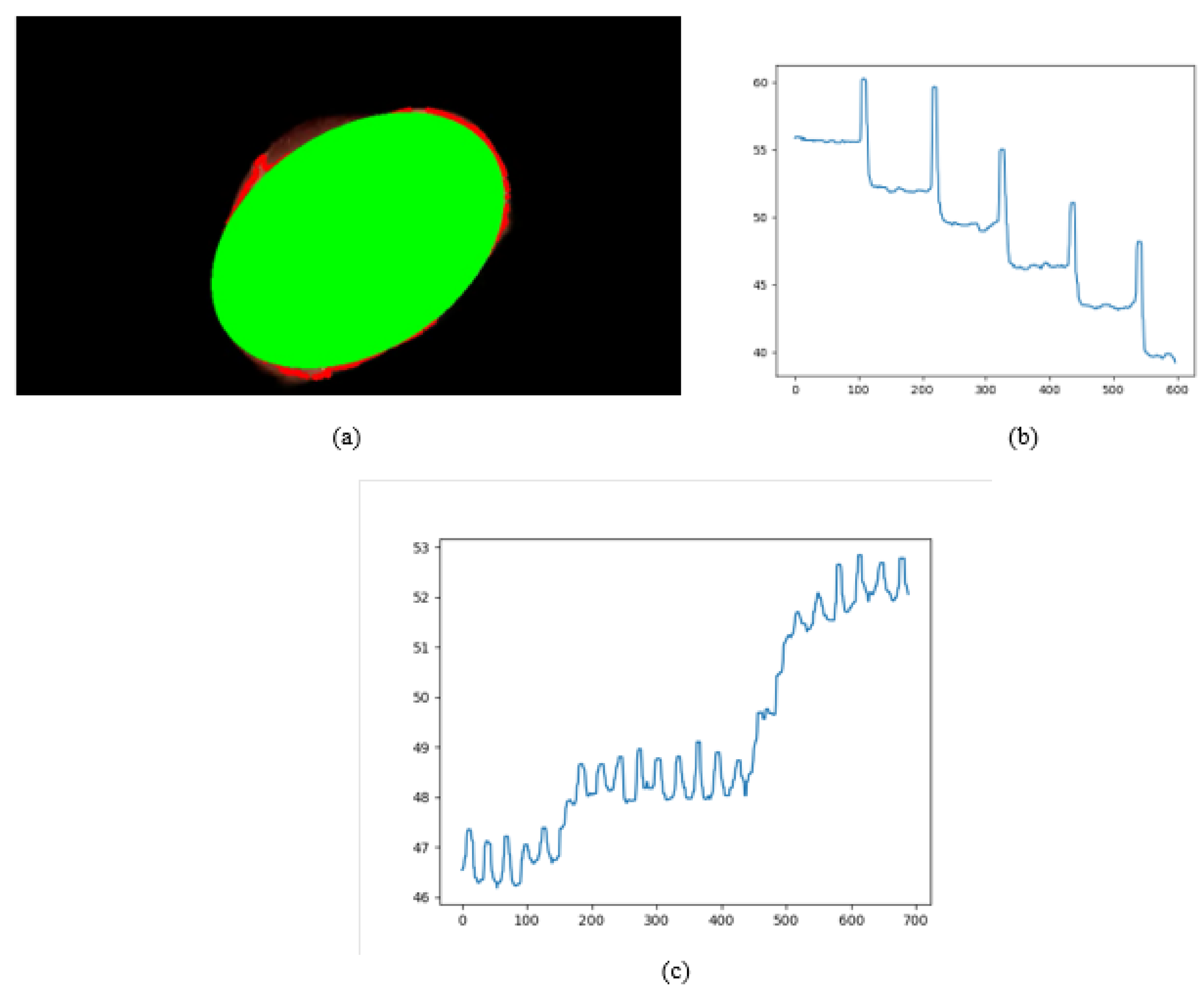

Fig. 3. Example of the frame with the ellipse fitted to the heart cell (a); plotted variability of ellipse angle – vertical axis: observed value of the ellipse angle; horizontal axis – number of video frame (b); plotted variability of ellipse angle in the case of second analysed movie – vertical axis: observed value of the ellipse angle; horizontal axis – number of videos frame

Table 1. Information about heartbeats per minute calculated with each method

Name and number of videos	Real BPM	Algorithm #1 – simple image processing	Algorithm #2 – CoTracker based	Algorithm #3 – ellipse-based
ETH_7 - #1	15.789 BPM	23.45 BPM	21.21 BPM	19.11 BPM
ETH_8 - #2	54.545 BPM	11.33 BPM	59.98 BPM	50.08 BPM

CONCLUSIONS

The main goal of this research was to observe whether it is possible to detect contractions in Engineered Heart Tissue (EHT) within recorded, spatial videos. All the worked-out algorithms are based on image processing and analysis techniques as well as simple Machine Learning methods. It is important as these approaches require computational power available for standard biological laboratory conditions and are still able to precisely show the moments of the contractions within the heart tissue. All of them provided information in the form of plots (contractions were observed as the changes within the organ – and measured with diversified techniques). It needs to be claimed that each method has sufficient precision and can observe the contractions. However, it needs to be also pointed out that some of them are better in the case of stable movies (when the EHT is not free-floating through the cell culture dish) whilst others can return more sufficient results for non-stable films (floating of the EHT or movement of the cell culture dish itself).

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