Computational study of electrical restitution in cardiomyocytes

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The relationship between cardiac electrical instability and the slope of restitution curve has been established by many scientists by means of experimental methods and mathematical models.

This study is devoted to investigate the electrical restitution dynamics in cardiomyocytes electrically stimulated with use of different pacing protocols. The new approach to stimulate cardiomyocytes for modeling action potential (AP) alternans due to the heart rate variability is proposed.

Computational simulation of AP and currents for K^+, Na^+, Ca^{2+} ions in cardiomyocytes has been performed by using an improved parallel conductance model in *Matlab* environment. Areas with the maximum slope in electrical restitution curves for ventricular and atrial cardiomyocytes have been determined. The occurrence of action potential duration (APD) alternans in areas of the electrical restitution curve with a maximum slope has been received.

Obtained results suggest that the new approach to investigate cardiomyocytes' electrical activity unmasks mechanisms for appearance of alternans, which cannot be seen with current experimental stimulation protocols. The calculated restitution curves allow for identifying the maximum slopes, which determine the arrhythmogenic properties of heart cells.

Computational results are useful to interpret experimental results with human-induced pluripotent stem cells differentiated into cardiomyocytes (hiPSC-CMs) on the lab-on-chip platform and to propose the new design of the experiments for studies of heart disease, drug screening and tissue regeneration in cell-replacement therapies.