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Cardiac mechanics, calcium overload and arrhythmogenesis

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*Motivation and Aim*:It is well-known that Ca2+ overload may cause cardiac arrhythmia. However, possible contribution of the mechanical factors to the arrhythmia development in Ca2+-overloaded cardiomyocytes has been insufficiently addressed. Earlier we have developed a mathematical model of cardiomyocyte electro-mechanical function [1] that predicted a significant role of the intra- and extracellular mechanical factors in arrhythmogenesys. Model prediction was verified in experiments on papillary muscles from the right ventricle of guinea pigs overloaded with calcium [2].

*Methods and Algorithms*: We utilized the cellular model to study effects of the electromechanical coupling between cardiomyocytes in a 1D heterogeneous muscle strand formed of 90% of normal (N) cardiomyocytes and 10% of sub-critical (SC) cardiomyocytes with decreased Na+-K+ pump activity. Single SC‑cardiomyocytes did not demonstrate spontaneous activity during isometric contractions at a reference length. Regular fiber twitches at the reference initial cell length were induced by 1 bps electrical stimulation applied at an edge of the strand. Excitation spread along the tissue via electro-diffusional cell coupling followed by cell contractions and force development in the fiber.

*Results*:Mechanical interactions between N- and SC-cells in the tissue resulted in the spontaneous activity emerged in the SC‑zone between the regular stimuli. If the excitation wave spread from SC- to N-region, the SC-cells developed delayed after-dеpolarizations (DAD) that caused a slowly developing beat-to-beat decrease in the force of fiber contraction. If the excitation spread in opposite direction, DAD in the SC-cells induced reflected downward excitation waves capturing the normal region and followed by extrasystoles in the whole fiber.

*Conclusion*: The results obtained in the model suggest that ectopic activity may emerge in a sub-critical myocardial region, e.g. comprising cardiomyocytes with moderately depressed N+-K+ pump, due to its mechanical interactions in the myocardial tissue. Moreover, such ectopic zone may expand by capturing normal regions in myocardium via the electro-mechanical coupling between cardiomyocytes.

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