Mechanical Translation of Electrical Abnormalities with a New Electromechanical Model of Human Ventricular Cell

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Due to the complexity of all the processes within the heart (e.g. electric and contractile), it remains experimentally challenging to investigate the contributions of calcium-handling abnormalities to arrhythmogenesis. For this reason, computational modeling has become increasingly used to study the mechanisms of calcium-mediated arrhythmogenesis. In this scenario, we propose a new electromechanical model able to capture delayed afterdepolarizations (DADs), early afterdepolarizations (EADs), and contraction abnormalities in terms of aftercontractions triggered by either drug action or special pacing modes.

The new model arises from the coupling between the new human action potential ventricular model, published by Bartolucci et al. (BPS), and the most recent human contractile element from Land et al. This latter was chosen since it has been validated against human data, as the BPS. First of all, this electromechanical model (BPSLand) was calibrated both on the experimental active tension (TA) and on the action potential (AP) biomarkers. In addition, the $[Ca^{2+}]_o$-APD_{90} relationship has been preserved. Finally, to validate BPSLand model, different experimental data sets, again both AP and TA, have been used.

In order to investigate arrhythmogenesis phenomena, we have focused the attention on the subset of models which was able to reproduce EADs and DADs in the previously generated BPS population of models. Our results highlight that dofetilide simulation triggers EADs, but only in a case this was reflected in an aftercontraction. In particular, a second spontaneous Ca^{2+} release from the sarcoplasmic reticulum (SR) pours into the cytosol enough Ca^{2+} to trigger the aftercontraction. By stimulating with a specific protocol, BPSLand produces several DADs caused by a spontaneous release from the SR and it also was sufficient to induce aftercontractions.

Therefore, BPSLand extends its applicability for understanding the complex interaction between cardiac electrophysiology and mechanics to improve arrhythmia risk prediction.