Mechano-Electric Feedbacks in a New Model of the Excitation-Contraction Coupling in Human Cardiomyocytes

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Aims. The study is aimed to develop a human cardiomyocyte model describing its electrical and mechanical activity and including both direct and feedback functional linkages between excitation and contraction.
Methods. We use the TNNP06 electrophysiological model of human cardiomyocyte and our model of the myocardium mechanical activity and its calcium regulation (Katsnelson ea; JTB, 2004) as components of the new electromechanical model.
Results. The combined electromechanical model TNNP+M (TNNP06 + mechanics) links both components through the equations describing intercellular calcium kinetics, which are intrinsic but differently detailed parts of the coupled models. For this linkage, we had to introduce thorough description of the calcium-troponin C kinetics, because it is a key mechanism of the myocardium contraction activation, whereas in TNNP06 this kinetics was implied as a part of a simplified single intracellular calcium buffer. Cooperativity of regulatory and contractile proteins underlies mechano-calcium feedbacks and mechano-electric feedbacks in the combined model. Importantly, the TNNP+M model maintains qualitative and even quantitative features of the calcium transients (i.e. changes in the cytosol calcium concentration) during the twitch. The latter is essential as the calcium transient significantly contributes via the sodium-calcium exchange to the repolarization phase of the action potential (AP). Therefore, the shape and duration of the calcium transient in the TNNP+M model (in common with the TNNP06 model) promote the AP shape and duration specific just for the human cardiomyocytes. Some additional tuning of original TNNP06 parameters turned out necessary to simulate correctly the effects of the sarcomere length changes during myocardium twitches on the AP duration.
Conclusions. The developed TNNP+M model may be thereafter incorporated in the models of multicellular myocardium up to that of the whole ventricles and used for systematical computational assessment of the mechano-electric feedback contribution to the regulation of mechanical and electrical functions in the human hearts.