

Calcium Bump as Indicator of the Mechano-Calcium Feedback in Cardiomyocytes and its Species-specificity in Mathematical Models

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Mechano-calcium feedback mechanisms manifest themselves as a number of experimental effects including a visible bending of the phase of the calcium transient decay ("calcium bump"). It has been experimentally established that the bump intensity depends on the mechanical conditions of the myocardium contractions, e.g. on the preload, i.e. on the cardiomyocyte initial lengthening (Jiang et al, *Am. J. Physiol.*, 1998). Moreover, McDonald et al (*Biochem. Res. Int.*, 2012) showed that the extent of the bump could be species-specific. In particular, in the absolute majority of cases, Ca^{2+} transients in the porcine cardiomyocytes revealed significant bumps. The authors emphasized that the pig was chosen due to the morphological and functional similarity of its heart to the human. In contrast to porcine Ca^{2+} transients, the bumps did not arise in their experiments in the mice cardiomyocytes.

Here, we compare simulations obtained in our mathematical models of the excitation-contraction coupling in human cardiomyocytes (Balakina-Vikulova et al, *J. Physiol. Sci.*, 2020) and in mouse cardiomyocytes (Khokhlova et al, *Front. Physiol.* 2020).

According to the predictions of the models, the bump is characteristic of human cardiomyocytes at any initial lengths, but in mouse the bump manifests itself clearly only at the initial lengths of $0.95 L_{\max}$ or bigger and completely disappears at $0.85 L_{\max}$ and smaller. These simulations correlate well with the data of McDonald et al.

Mice are one of the most common laboratory models for analyzing and predicting physiological mechanisms characteristic of warm-blooded animals, including humans. Obviously, such predictions should be made with great limitations. Our particular results indicate this once more.

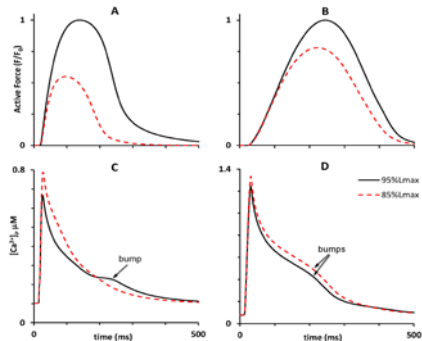


Fig. Active isometric force (A,B) and Ca^{2+} transients (C, D) in cardiomyocyte models: mouse (A,C) and human (B, D), at $95\% L_{\max}$ (solid lines) and $85\% L_{\max}$ (dashed lines).