ELECTRON-CONFORMATIONAL MODEL EXPLAINS THE TEMPERATURE EFFECTS FOR CARDIAC CALCIUM RELEASE CHANNELS

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Temperature influences many aspects of cardiac excitation-contraction (EC) coupling, in particular, hypothermia increases the open probability of cardiac sarcoplasmic reticulum (SR) Ca^{2+}-release channels (ryanodine-sensitive RyR channels) rising the SR Ca^{2+} load in mammalian myocytes (see, e.g., Ref.[1]). However, to the best of our knowledge, no theoretical models are available for that effect. Traditional Markov chain models do not imply description of the temperature effects. Earlier we have proposed a simple physically reasonable electron-conformational model (ECM) [2] to describe gating both of the isolated RyRs and the RyR clusters in a cardiac cell. The model starts with the RyR energy depending on its electronic and conformational state. The RyR dynamics includes fast electronic transitions triggered by Ca^{2+}, tunneling effects and slow conformational Langevin dynamics which implies both effective friction and thermal fluctuation forces. Here we argue that namely the latter term (Gaussian–Markovian noise) via the temperature stimulation/suppression of the open-close RyR tunnelling can be considered as a main contributor to temperature effects on the RyR gating. Results of the computer modeling allowed us to successfully reproduce all the temperature effects observed for an isolated RyR under reducing the temperature [1]: increase in P_{open} and mean open time without any significant effect on mean closed time. At once the ECM is shown to describe on equal footing the temperature effects for oscillatory regime of the heart's cell release unit both in sinoatrial node (pacemaker) cells under normal physiological conditions and in ventricular myocytes under Ca^{2+} SR overload.

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References

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