In an article by Silva and Rudy (Circ Res. 2003;92:261–263), “Mechanism of Pacemaking in Ik1-Downregulated Myocytes,” simulations of β-adrenergic effects on genetically engineered biological pacemaker cells did not take into account changes in $[\text{Ca}^{2+}]_i$ due to $I_{\text{Ca,L}}$ increase under β-adrenergic stimulation (βAS). Such changes were fully accounted for during pacemaking in the absence of βAS (intrinsic pacemaker rate of 101 bpm). When βAS-induced changes in $[\text{Ca}^{2+}]_i$ were accounted for, a steady state could not be achieved with a 300% $I_{\text{Ca,L}}$ increase. We repeated the simulations with a βAS-induced 100% increase of $I_{\text{Ca,L}}$, taking into account the dynamic $[\text{Ca}^{2+}]_i$ changes. The pacemaking rate increased transiently (110 bpm after 27.2 seconds) and then reached a steady state at a rate slightly below control (73 bpm). The long-term decrease in rate was a result of $[\text{Na}^+]_i$, accumulation that acted to increase outward $I_{\text{NaK}}$ and reduce inward $I_{\text{NaCa}}$ and $I_{\text{Na}}$, thus reducing net depolarizing current. As in the original publication, upregulation of $I_{\text{NaCa}}$ by 100% increased sensitivity to βAS, resulting in a maximum transient increase of pacemaking rate to 139 bpm after 17.9 seconds. The new simulations that account for $[\text{Ca}^{2+}]_i$ changes confirm the original finding that responsiveness to βAS depends on the level of $I_{\text{NaCa}}$ expression and that even for high expression levels the responsiveness is very limited, much smaller than that of native sinus-node cells.

For reference, all simulations used the current version of the Luo-Rudy cell model, which can be found online at http://www.cwru.edu/med/CBRTC/LRdOnline/. $[\text{Na}^+]_o$ was set to 132 mmol/L and $[\text{K}^-]_o$, to 5.4 mmol/L.
Correction ARTICLE

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