# Supplemental Text:

# Computational modeling for cardiac safety pharmacology analysis: Contribution of fibroblasts

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Nebivolol can inhibit $I_{Kr}$, $I_{Ks}$, $I_{Na}$, and $I_{to}$ channels within the range of concentration (0 to 100 µM) used in the simulations (Figure S1). Simulation results show that the AP of cardiomyocyte is significantly prolonged by increasing the concentration of nebivolol. The resting potential increases to about -20 mV and EAD occurs if the concentration increases to 100 µM (Figure S2A). Coupling the cardiomyocyte with fibroblasts can markedly shorten the prolonged action potential (Figures S2B and S2C).

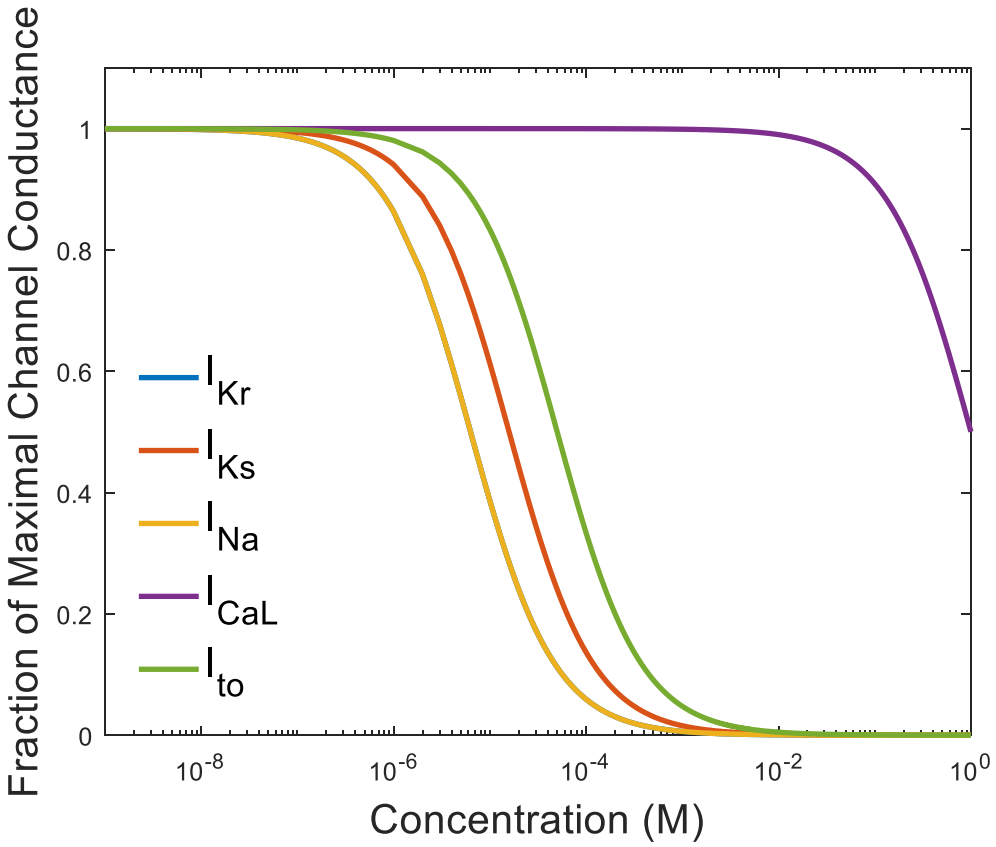


**Figure S1.** Effects of varying concentration of nebivolol on maximal conductance of five ion channels of the cardiomyocyte. For the range of nebivolol concentration used in the simulations (0 to 100 µM), nebivolol can block $I_{Kr}$, $I_{Ks}$, $I_{Na}$, and $I_{to}$ channels. Note that the $I_{Kr}$ curve is same as $I_{Na}$ curve.

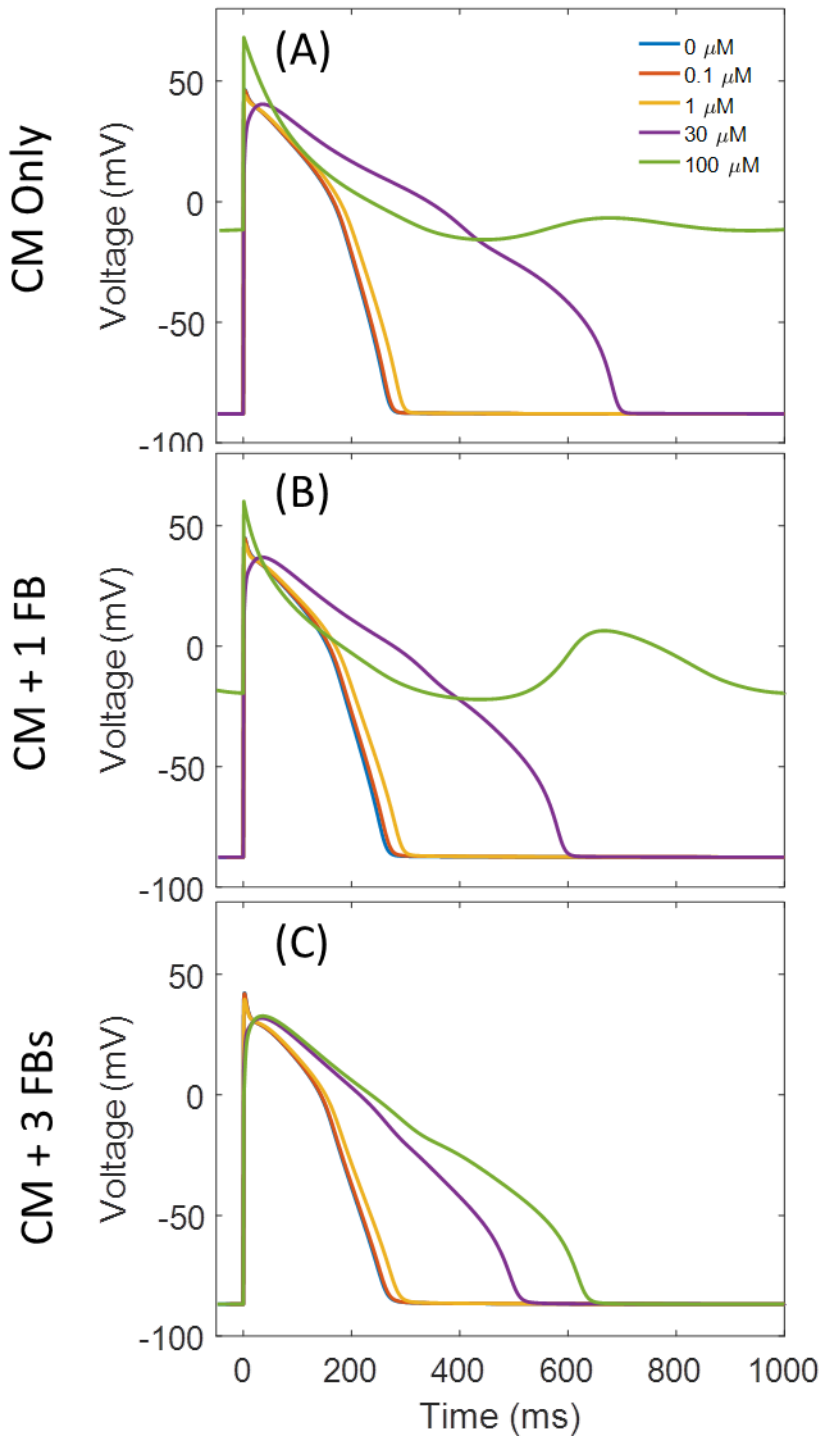


**Figure S2.** Simulation of AP with increasing nebivolol concentration for cardiomyocyte alone (a), cardiomyocyte coupled with one fibroblast (b) and cardiomyocyte coupled with three fibroblasts (c).