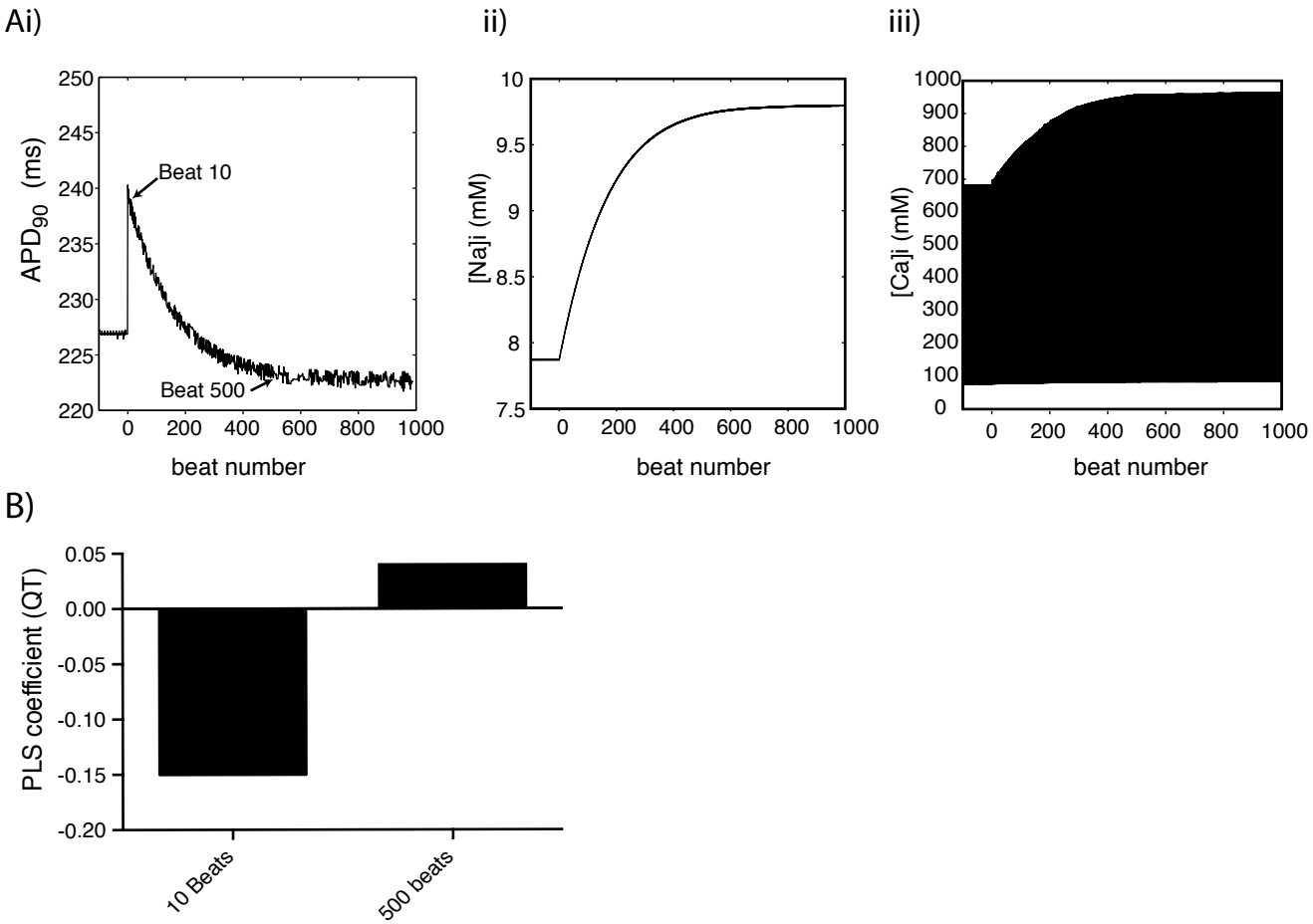

Supplementary Figure 1: Sensitivity coefficients are dependent on equilibration of the simultion system. Ai) A 50 % reduction in G_{NaK} at beat 0 causes an increase in APD_{90} as would be expected from block of a net outward current. After equilibration for 500 beats however, APD shortening is observed as block of NaK leads to a long term increase in the intracellular concentration of sodium ions (Aii). This in turn increases the intracellular calcium concentration because the activity of the sodium/calcium exchanger depends on intracellular sodium (Aiii). Together, this increased intracellular sodium and calcium decrease the driving force for entry of these ions through voltage gated channels and lead to a reduction in the action potential duration. B) PLS regression coefficients illustrating reversed sensitivity of APD_{90} with G_{NaK} after 10 beats versus 500 beats.